The biology of talc

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Hildick-Smith, G. Y. (1976). *British Journal of Industrial Medicine*, 33, 217-229. **The biology of talc.** Data are presented on the effects on health of talc dusts from exposure in industry and use of talc-containing health products. The mineralogy of talc and the composition of cosmetic and industrial grade talc dusts are described. Studies in animals are reviewed, and epidemiological data are considered in relation to exposures that occur during industrial and consumer uses of talc dusts. Hamsters exposed to 8 mg/m³ of respirable cosmetic grade talc dust for up to 150 minutes a day for 300 consecutive days showed no difference in incidence or nature of pathological lesions from those observed in a group of untreated animals. A retrospective study of the causes of death of 227 talc mine millers exposed to cosmetic grade talc at the threshold limit value for talc (20 million parts per cubic foot) for an average of 15.8 years showed that the causes of death were no different from those in a control cohort not exposed to talc dust. The available data indicate that talc dust exposure in the modern mining of cosmetic grade talc does not appear to be injurious to health. The significantly lower dust exposure in the normal use of cosmetic grade talc dusts in talc-containing health and cosmetic products confirms that their use is not a hazard to health.

Increasing interest in the impact of environmental influences on health has in recent years focused attention on the significance of pollutants and prompted a reappraisal of environmental mineral dusts that have had extensive long-term use, but on which there is a paucity of correlated scientific data by which to evaluate them (Davies, 1964a; Gross, DeTreville, and Cralley, 1970; Lee, 1972; Schaefer, Mohnen, and Veirs, 1972; Editorials, *British Medical Journal*, 1973; *Food and Cosmetics Toxicology*, 1973; *Lancet*, 1973; *New England Journal of Medicine*, 1973; Selikoff, 1973).

The effects of talc dusts on the health of miners and industrial workers have been studied extensively and dust level standards that are considered safe have been established by official agencies (Hogue and Mallette, 1949; Schepers and Durkan, 1955a; Kleinfeld *et al.*, 1964a, and b, 1967; Riley, 1965; Morgan, Ozolins, and Tabor, 1970; Murphy *et al.*, 1971; Smith, 1971; Hatch, 1973; Kleinfeld, Messite, and Langer, 1973; Leroux, Davey, and Paillard, 1973;

American Conference of Government Industrial Hygienists, 1973; Wegman *et al.*, 1974). The potential health hazard of dusts encountered by consumers who have no industrial exposure has become a subject of increasing interest (Henderson *et al.*, 1971; Merliss, 1971; Nam and Gracey, 1972; Blejer and Arlon, 1973).

Asbestos dust has been shown to be a health hazard (Wright, 1969; Gross *et al.*, 1970; Murphy *et al.*, 1971; Smith, 1971; Stanton and Wrench, 1972; Smith, 1973; Stanton, 1974; Haley, 1975) and can cause cancer (Wagner, Sleggs, and Marchand, 1960; Selikoff, 1970, 1973) after exposure above a calculated threshold level of 125 million parts per cubic foot years (Enterline, DeCoufle, and Henderson, 1973). As some talc dusts contain asbestos, attention has been focused on the possibility that talc dust contaminated by asbestos may be harmful or talc dust itself may be hazardous (Blejer and Arlon, 1973; Pelfrène and Shubik, 1975).

Talc was first mined by the ancient Greeks and

currently has wide use in a variety of products and industrial processes. Although talc dust has been used for many years, there is only limited modern scientific information available regarding its biological activity by which to assess accurately its safety when used in industry or by the consumer. The older information that is available is difficult to interpret, since the term talc is used to describe both the cosmetic grade of talc and also mineral powders of mixed composition that are used in industry and known as industrial grade talc (Smith, 1971). Accordingly, it seemed pertinent to review the available data on the biology of various talc dusts to determine whether the current guidelines for industrial exposure (American Conference of Government Industrial Hygienists, 1973) are adequate, and to assess whether exposure to the grade of talc in cosmetic products is a hazard to health under normal conditions of use.

Mineralogy

Talc as a pure chemical compound is defined as hydrous magnesium silicate, $\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$ and consists of a brucite sheet containing magnesium ions sandwiched between two silica sheets which are held together by relatively weak forces. A variety of elements such as nickel and iron may be included in the talc particle lattice but are so bound within the particle that they are not free to exert any biological action (Gross and Harley, 1973). Talc can be tabular, granular, fibrous, or platy but it is usually crystalline, flexible, and soft. It is commonly whitish to light green but it can be yellowish to reddish, the reddish colour being associated with small amounts of iron bound within the talc particle (Deer, Howie, and Zussman, 1962; Chudzickowski, 1975). Talc is a member of the family of silicate minerals which have a similar atomic structure and occur widely in a large number of different varieties. These silicate minerals are derived from metamorphic alteration of mineral rocks which sometimes include the amphibole and serpentine groups of asbestos after their exposure to specific temperatures, pressures, and circulating liquid solutions. Talc may also be formed by the thermal metamorphism of silicon dolomites.

The purity and physical form of any sample of talc dust as well as the other minerals that are associated with it are therefore directly related to the source of the talc and to the minerals found in the ore body from which it is mined. Talc commonly contains chlorites and carbonates, the former being sheet silicate minerals containing magnesium, aluminium, and iron. The carbonate mineral components of talc are mainly magnesite, dolomite, and calcite. Quartz (free silica), iron oxides, sulphides, and various silicates can also be associated with talc.

As serpentine is one of the minerals from which talc has evolved, it can be associated with talc and is sometimes a contaminant of talc dust. Tremolite, a member of the amphibole group of asbestos, and chrysotile or antigorite of the serpentine group, are the commonest asbestos contaminants of industrial talc dust, although chrysotile has never been reported to be present in the high-grade talc used in health and cosmetic products (Pooley, F. D., personal communication, 1975).

As talc dusts are obtained from different sources, the amount and specific form of talc, as well as the amount and nature of mineral contaminants, will be different for each dust.

The wide range of mineral components and talc forms in talc dusts has made it possible to identify grades of talc dusts with specific physical properties which make them suitable for use in various industrial processes as well as in health care and cosmetic products. It is important therefore to realize that the effect on health of talc dusts will relate to the specific mineral composition of a talc dust, although it may be possible to relate health effects to identified grades of talc. For instance, talc used in health and cosmetic products is of high grade and is identified as cosmetic grade talc which contains more than 90% mineral talc, is free of detectable asbestos, and contaminated by only limited amounts of other minerals. The talc particles in cosmetic grade talc are the flat, plate-like variety which are selected for their lubricity. Cralley *et al.* (1968) reported an average of 19% incidence of fibres in 22 cosmetic talc samples studied, but detailed analysis of such talcs shows their fibre content to be of a lower order, as the reported high incidence of fibre in platy talcs relates to the fibrous appearance of a broken plate or a talc platelet seen on edge when examined under a microscope.

Industrial talc dusts which are used in a wide range of industrial processes or products are selected for their desired physical properties and therefore have a varied mineral composition. Industrial talcs may not actually contain talc or they may have a low talc mineral content. They may contain asbestos or significant concentrations of free silica as well as a wide variety of other mineral dusts.

The particle size of a sample of talc powder will vary in relation to the process used to make the powder with common cosmetic talcs having particles ranging between 0.3 μm to 50 μm in size with only a minor fraction (by weight) consisting of particles usually considered to be of respirable size.

The precise mineralogical identification of fibres or other mineral contaminants is essential for determining the exact composition of a talc dust and among the analytical methods used to establish the identity of particles are differential thermal analysis, x-ray diffraction, and microscopical examination (Rolle, Schelz, and Hamer, 1976).

Commercial uses

Approximately 800 000 tonnes of talc are used commercially in the United States of America each year. Because of the lubricious property and chemical inactivity of talc, it is used in the leather, rubber, paper, textile, and machine construction industries. It is also used as an additive for paints, in the roofing and ceramic tile industry, and as a carrier for insecticides and herbicides. Altogether 30 000 tonnes of cosmetic grade talc are used in cosmetic and pharmaceutical products and as fillers, and in some foodstuffs (Wright, 1969).

Cellular and tissue response to talc

The development of pathological lesions in the lungs after inhalation of some mineral dusts has led to an interest in determining the amount required to produce pulmonary disease, the effect of dusts on cells and cell function, and the precise biological process by which disease is produced. One means of assessing the biological activity of dusts has been to study their effect on the viability and function of cells (Hayashi, 1971). In these studies, red cells, peritoneal and pulmonary macrophages, bacteria, and fibroblasts have been used (Stalder and Stoeber, 1965; Allison, Harington, and Birbeck, 1966; Parazzi, Secchi, and Pernis, 1968; Kleinfeld, 1970; Schnitzer and Pundsack, 1970; Beck, Holt, and Nasrallah, 1971; Bey and Harington, 1971; Schnitzer, Bunesco, and Baden, 1971; Rajan, Wagner, and Evans, 1972; Bowden, 1973; Harington, Ritchie, and King, 1973; Maroudas, O'Neill, and Stanton, 1973; Ackerman and Beebe, 1974).

Although the cellular effect of silica and asbestos dusts has been extensively studied (Allison *et al.*, 1966; Parazzi *et al.*, 1968; Beck *et al.*, 1971; Harington *et al.*, 1973; Rajan *et al.*, 1972) little research has been conducted on the effect of talc on cells. Schnitzer and Pundsack (1970), using a red cell haemolysis test (Stalder and Stoeber, 1965), reported that marked haemolysis occurred with chrysotile, but that none of the amphibole asbestiform minerals (crocidolite, amosite, and anthophyllite) was substantially active. Minerals described as non-asbestiform fibrous materials, including fibrous talc (the fibrous component being predominantly tremolite) were rated as actively producing haemolysis, but miscellaneous materials studied, which included platy talc, were found to be inactive.

Di Luzio, N. (personal communication, 1975) reported that commercially available cosmetic grade talc dust did not alter the viability of pulmonary macrophages in rats or interfere with their uptake of colloid particles.

Kleinfeld (1970) studied the effect of quartz, cristobalite, and a commercial talc containing magnesium aluminium silicate, manganese dioxide, and 3.2% free silica on the cellular growth of

primary embryonic lung explants grown *in vitro* and reported they produced an outgrowth of fibroblast cells, with relatively few epithelial cells. Chrysotile and anthophyllite asbestos fibres produced an outgrowth of epithelial cells that were invaded by sheets of cells resembling fibroblasts. Kleinfeld speculated that free silica and asbestos dusts accelerate the transformation of the macrophages to fibroblast cells with the production of collagen initiating the fibrotic process. In contrast, a pure crystalline talc produced a response similar to that of the control cultures, in which only epithelial outgrowth occurred.

Available information on the cellular effect of mineral dusts indicates that platy talc is inactive, unlike the fibrous dusts silica and crocidolite which have significant biological activity. The data suggest that platy talc itself produces minimal cell toxicity, but that when contaminated with significant amounts of either silica or cytotoxic minerals such as chrysotile, the tissue response within the body is related to the cellular response to the cytotoxic minerals rather than to the particles of talc.

Pharmacogenetic studies

As talc dust can come into contact with a variety of cell types when inhaled, its mutagenic potential was assessed using the host-mediated assay (Gabridge, Denunzio, and Legator, 1969), cytogenetic studies (Legator, 1969), and the dominant lethal assay (Epstein and Shafner, 1968; US Food and Drug Administration, 1974), using both *in vitro* and *in vivo* tests.

In the *in vivo* studies which were conducted in rats, the talc was given orally in doses of 30, 300, and 3000 mg/kg and the results compared with an oral dose of 0.3 mg/kg of triethylene melamine.

In the *in vitro* studies talc dose levels of 2, 20, and 200 µg/ml were used and compared with 0.1 µg/ml of the positive control triethylene melamine. In the *in vitro* host-mediated assay the results were negative while in the *in vivo* studies there was no significant increase in the mutant or recombinant frequencies in the *Salmonella* and *Saccharomyces* species used.

The *in vitro* cytogenetic studies showed that talc produced no significant aberration in the anaphase chromosomes of human tissue culture cells. In the *in vivo* cytogenetic study no detectable significant aberration of the bone marrow metaphase chromosomes was seen in rats given talc.

In the dominant lethal study, male rats were fed the talc doses used in *in vivo* studies and mated with virgin female rats. The number and nature of fetuses from matings with rats treated with talc as well as the active and passive control were recorded. Talc did not alter the number and type of fetuses and could be considered non-mutagenic.

The data obtained from these sophisticated studies show that talc is not a mutagen and therefore is

unlikely to produce cancer or induce congenital deformity in fetuses.

Studies in animals

Animal studies have been used extensively to simulate industrial conditions and to assess the histological response to test dusts (Schulz and Williams, 1942; Saxen and Tuovinen, 1947; Schepers and Durkan, 1955b; Luchtrath and Schmidt, 1959; Bluemel, Pizá, and Zischka-Konorsa, 1962; Cygielman and Robson, 1963; Grigor'ev, 1963; Rakowski, 1964; Bethge-Iwanska, 1971; Pott and Friedrichs, 1972; Stanton and Wrench, 1972; Wagner, Berry, and Timbrell, 1973; Stanton, 1974).

In most studies conducted with talc dust the precise mineral composition, particle size, and dose administered have not been defined and only recently have data on these variables been reported. Useful information can be obtained from experiments in animals in which talc was studied specifically or was used as a control in the study of other materials.

Grigor'ev (1963) compared the tissue reaction of the shaved skin of rabbits when spodumena (triphane LiAl/SiO_2) talc and silica were separately applied to the skin under patches daily for 90 days. The skin treated with spodumena showed marked histological changes while no abnormal changes were reported with talc or quartz. These data indicate that talc dust is not a primary irritant to the skin nor will it induce sensitization in animals, a finding which has been well confirmed in man.

Talc can produce local fibrosis when introduced into tissues (Saxen and Tuovinen, 1947); Cygielman and Robson (1963) showed that while 10 mg of talc administered intramuscularly in rats every day for four days produced no local fibrosis, 50 mg of talc similarly administered produced a local granuloma.

Bluemel *et al.* (1962) studied the histological response of talc powder and a starch surgical glove product when the two powders were administered intraperitoneally in rats. Approximately 400 mg of the starch product and talc were introduced by laparotomy into the peritoneal cavity of two groups each comprising 30 rats; 10 rats were used as a control and were untreated except for a sham operation. Histological examination of the talc-treated animals showed production of granuloma, and in the starch-treated animals loosely structured granulation tissue.

Pulmonary studies in animals

As inhaled talc dusts may produce pulmonary disease, animal inhalation studies have been conducted to assess the pulmonary response to various talc dusts (Schepers and Durkan, 1955b; Luchtrath and Schmidt, 1959; Bethge-Iwanska, 1971).

Schepers and Durkan (1955b) conducted studies in rabbits, rats, and guinea-pigs to assess the individual

and collective histological effects of tremolite anthophyllite, quartz, serpentine, and dolomite present in a commercial talc mined in upper New York State which had produced pneumoconiosis in some mine workers. In the study the dusts varying in particle size were administered intravenously or intratracheally to animals and the histological response of the lung tissue was assessed at various times after administration. The authors concluded from their extensive studies that talc was dominantly cytogenic while tremolite and anthophyllite have cytogenic and fibrogenic properties, and that silica modifies the effects of these materials.

In 1959, Luchtrath and Schmidt conducted a study in rats designed to determine whether pulmonary fibrosis reported in some talc workers was due to the talc itself or its contamination by silica. Four separate samples of talc were used in which 50 mg of four talc samples containing 0, 2, 3, and 10% silica were suspended in water and administered intratracheally to rats which were subsequently followed-up for up to 660 days. It was shown that talc containing up to 3% silica produced minimal fibrosis of pulmonary tissue compared with marked fibrosis produced by talc containing 10% silica, and that pulmonary fibrosis reported in talc miners was related to exposure to talc containing significant amounts of silica and other fibrogenic minerals.

Bethge-Iwanska (1971) conducted a study in rats to assess their pulmonary tissue response after exposure to an aerosol of undefined cosmetic talc and a talc dust used industrially in rubber manufacturing and to check the effectiveness of the Polish regulations which allow an industrial talc dust level of 10 mg/m³. Cosmetic and industrial talc dusts were introduced separately six times a day into special chambers containing rats for six days a week up to nine months with animals killed for histological examination at 7 and 14 days, and at three, six, and nine months. Dust samples that were taken on introduction of the dust and one hour later showed an initial dust concentration of 383 mg/m³ and 23 mg/m³ after one hour for cosmetic talc. The data show that when the groups of rats were killed after nine months' talc exposure they had undergone a time-weighted exposure to 16 848 mg per hour/m³, which is 2790 times the total dust exposure to which a baby is exposed in a two-year period.

Evaluation of the particle sizes of the dusts showed that 30% of the industrially-used talc was less than 10 μm and 12% less than 5 μm . For the cosmetic talc 55% was less than 10 μm and 19% less than 5 μm . Histological changes from the specific talc dusts were increased mucus secretion after 14 days with both dusts; fibrocellular nodules and emphysematous foci at six months, with thickened small artery walls were noted after six and nine months' exposure. At 14 days, alveolar macrophages were

seen to contain talc dust, and at three and six months the macrophages filled the alveoli.

Bethge-Iwanska (1971) concluded that the two talcs studied produced similar non-specific inflammatory changes associated with fibrocellular reaction and some focal fibrosis without evidence of pneumoconiotic changes. It was noted that the degree of fibrosis seen with talc was significantly less than the confluent fibrosis seen in asbestosis or the fibrosis seen in silicosis.

Wehner *et al.* (1975) studied the effect of inhalation of a commercially available cosmetic talc powder in Syrian golden hamsters. The talc dust consisted of 97% mineral talc in platy form free of detectable asbestos and silica. Separate groups each containing 50 male and female hamsters were exposed to aerosols of the product for 3, 30, and 150 minutes a day for 30 and 300 consecutive days. The total aerosol dust concentration was adjusted to maintain an average of 8 mg/m³ of respirable talc dust in the animal chambers.

The cumulative exposure of the groups of hamsters to the respirable talc dust ranged from 12 mg hours/m³ to 6000 mg hours/m³, the latter corresponding to 1700 times the dose to which an infant is exposed during an equivalent period of time when dusted with a commercial talc-based baby powder (Sivertson, J. N., personal communication, 1976). There was no difference in viability or body weight between the treated hamsters and the untreated control animals. In addition, histological examination and the incidence of tumours of lungs, heart, stomach, liver, kidney, testes, and ovaries showed no difference between treated and control animals.

Wagner *et al.* (1975) evaluated the effect of a commercially available cosmetic grade talc dust administered orally, intrapleurally, and by inhalation in rats and compared the histological findings at natural death or when killed with data obtained by similar administration of a superfine chrysotile asbestos in another group of rats, and in an untreated group of rats. Altogether 20 mg of talc or chrysotile suspended in physiological saline were injected into the right pleural space of two groups each containing 48 rats. Eighteen of the rats injected with chrysotile developed mesotheliomas while none was observed in the talc-treated or untreated animals. In two groups each containing 32 rats 100 mg of talc or chrysotile were fed daily for 101 days and the gastrointestinal tract of each animal was examined at natural death. One stomach leiomyosarcoma was found in the talc-fed rats and a similar tumour noted in the chrysotile-fed rats.

In an inhalation study (Wagner *et al.*, 1975), groups of 48, 24, and 24 rats were exposed to a respirable concentration of 10.8 mg/m³ of talc or chrysotile for 7½ hours a day for five days a week for 3, 6, and 12 months respectively providing cumulative

doses of 4140, 8094, and 16 363 mg hours/m³. The highest doses of respirable talc dust to which the rats were exposed represent an exposure of 5400 times the maximum exposure to which a baby is exposed during an equal period of time when using talc as a dusting powder. The total dust exposure to the animals receiving the maximum duration of exposure is 2700 times the maximum cumulative exposure for an infant during a two-year period. At natural death of the animals the histology of the respiratory tract was compared with that of rats similarly exposed to chrysotile dust as well as that of an untreated group of rats. The lungs of animals exposed to the higher talc and chrysotile doses had fibrosis rated as minimal to slight compared to the control rats' lungs which had a minimal amount of fibrosis. No lung tumours were observed in the control animals while one adenoma of the lung was noted in the talc-treated animals and three adenomas, two adenomatoses, and one adenocarcinoma occurred in the chrysotile-treated animals.

These studies indicate that talc administered orally or intrapleurally does not cause cancer in rats, and malignant disease did not occur after its inhalation.

Cancer studies in animals

Appraisal of the carcinogenicity of talc is important as it has been suggested that prolonged exposure to talc, with or without asbestos contamination, may be associated with malignant changes (Henderson *et al.*, 1971; Merliss, 1971; Blejer and Arlon, 1973; Pelfrène and Shubik, 1975), and that fibrous particles with specific dimensions may be carcinogenic (Stanton and Wrench, 1972; Maroudas *et al.*, 1973). Pott and Friedrichs (1972) evaluated the role that fibrous particles of different chemical compositions and non-fibrous particles of similar chemical compositions played in the production of neoplastic tissue change. In their study, 25 mg of test dusts dispersed in 2 ml of sodium chloride solution were injected intraperitoneally in groups of 40 female rats on four occasions at weekly intervals with the rats being followed-up for 530 days. Fibrous dusts (chrysotile, nemalite, and glass fibre), which are similar in form but different in chemical composition, produced abdominal tumours while actinolite, biotite, pectolite, and talc which chemically resemble chrysotile but occur in grain or plate form did not produce abdominal tumours. In this study the authors reported that necropsies of animals treated with talc revealed detectable talc in the peritoneal cavity while chrysotile was not visible microscopically because of the severe fibrotic tissue response in chrysotile-treated animals.

In a study in hamsters (Smith *et al.*, 1965; Smith, 1973) 25 mg of test dusts dispersed in 0.5 ml saline were administered intrapleurally to groups of 50

animals which were allowed to live their normal life spans. Dusts of chrysotile and amosite were studied, as were a sample of talc composed of platy particles and a sample of talc used for industrial purposes which consisted of both fibrous and platy talc together with 57% tremolite and a small amount of antigorite. Eight and 10 of the animals in the groups of 50 given chrysotile and amosite developed pleural mesotheliomas while there were no tumours in the animals treated with the two separate talc dusts. Pleural granulomatous lesions which were small and focal were observed in the talc-treated animals as opposed to the large and more fibrous lesions that were observed in the pleura of the animals treated with chrysotile or amosite.

Gross *et al.* (1970) conducted a study in which chrysotile alone and chrysotile combined with nickel chloride were given intratracheally to rats and the results compared to a similarly given talc with a natural high nickel content and a talc with a naturally low nickel content. The animals were allowed to live out their lives. Necropsy failed to reveal any evidence of cancer in the animals treated with the two talc samples but cancerous lesions were produced in animals to which chrysotile was given.

In the animal studies so far conducted, talc has not been found to produce tumours when injected into the peritoneum or the pleural space, or when it was administered orally, intratracheally, or by inhalation and the animals were allowed to live out their life spans before necropsy. These animal data indicate that talc is not carcinogenic.

Human exposure to talc

The greatest human exposure to talc dust is when it is used industrially or while it is mined or milled. Exposure to cosmetic grade talc as used in cosmetic and health care products is infrequent and of short duration.

Published cases of talc pneumoconiosis, therefore, primarily concern subjects engaged in the mining or processing of talc and usually refer to data obtained before modern mining and environmental standards were implemented (Dreessen, 1933; Dreessen and Dalla Valle, 1935; Porro, Patton, and Hobbs, 1942; Greenburg, 1947; Millman, 1947; Hogue and Mallette, 1949; McLaughlin, 1950; Jaques and Benirschke, 1952; Alivisatos, Pontikakis, and Terzis, 1955; Kleinfeld, Messite, and Tabershawe, 1955; Schepers and Durkan, 1955a; Hunt, 1956; Nagelschmidt, 1960; DeVilliers, 1961; Coscia *et al.*, 1963; Gaido, Capellaro, and Delmastro, 1963; Scansetti, Rasetti, and Ghemi, 1963; Dettori, Scansetti, and Gribaudo, 1964; Kleinfeld *et al.*, 1964a, b, 1965, 1967, 1973; Graham and Gaensler, 1965; Weiss and Boettner, 1967; Fristedt, Mattsson, and Schutz, 1968; El-Ghawabi, El-Samra, and Mehaseb, 1970; Kleinfeld,

1970; Selikoff, 1973; Wegman *et al.*, 1974). In people not employed in the talc industry, only isolated cases of pulmonary changes have been reported where there was either accidental exposure or excessive usage of talc (Jacobziner and Raybin, 1963; Jenkins, 1963; Gouvea *et al.*, 1966; Zientara and Moore, 1970; Atlee, 1972; Nam and Gracey, 1972).

The development of pulmonary disease associated with exposure to talc dust is directly related to the amount of dust in the environment, the duration of exposure, the nature of the talc and its contaminants, and the amount of respirable dust that enters the bronchi (Davies, 1964a and b; Muir, 1972; Léophonte *et al.*, 1975).

The lung can clear the bronchi of dust by phagocytosis (Bowden, 1973), by ciliary action or via the lymphatics, thereby preventing pulmonary tissue damage when the dust load is not overwhelming or the dust is not inherently toxic. (*Lancet*, 1973). The clearing mechanism however can be affected by noxious agents such as cytotoxic drugs, cigarette smoke, or a dust load that is so excessive that the normal cellular functions are impaired (Haynes, 1931; Davies, 1964a; Morgan *et al.*, 1970; Lee, 1972; Schaefer *et al.*, 1972; *Lancet*, 1973; *New England Journal of Medicine*, 1973; First, 1973; Ackerman and Beebe, 1974; Golde, Byers, and Finley, 1974).

Early reports of pneumoconiosis in talc miners were on men working in uncontrolled environments, often associated with excessive exposure to high concentrations of dust. The recognition that limitations were required for mining environments produced standards for various dusts. In the United States of America the legal limit for exposure to talc in industry is 20 million particles (non-fibrous) per cubic foot and 2 fibres per millilitre. The limit is modified for total dust including a percentage of quartz in accordance with the following formula,

$$\frac{10 \text{ mg/m}^3}{\% \text{ quartz} + 3},$$

and for respirable dust containing a percentage of quartz as follows:

$$\frac{10 \text{ mg/m}^3}{\% \text{ quartz} + 2}$$

(Morrow and Cohen, 1959; *Federal Register*, 1969; Leroux *et al.*, 1973; American Conference of Government Industrial Hygienists, 1973).

Although Thorel (1896) first reported pulmonary changes in talc miners, it is only recently that controlled epidemiological studies have been conducted to define precisely the factors that contribute to pulmonary changes in talc miners, and to determine the amount of talc dust to which they can be exposed without hazard to health.

Pulmonary morbidity studies in mine employees

Kleinfeld *et al.* (1973) compared the health of 39 talc

miners with a matched control group of 41 individuals who had not been exposed to talc. The study is of interest as the mined talc contained fibrous particles of tremolite and anthophyllite. Dust particle counts averaged 18 million particles per cubic foot (range 6 to 62), with the fibre averaging 43 fibres greater than 5 μm long per 1 ml (range 8 to 260/ml). The miners had a mean exposure of 16.2 years (range 11 to 22 years). Although one of the miners had *x*-ray evidence of pneumoconiosis, clinical findings and chest radiographs in the mining group were similar to those of the non-mining group except that nine miners (25%) had dyspnoea as opposed to three (7%) of the non-mining group.

Data from a group of 35 miners previously studied in another talc mine, the nature of which was not indicated, were also compared with data from the 39 miners more recently surveyed. The 35 miners had been exposed to an average dust count of 23 million particles per cubic foot (range 2 to 70) with an average count of 159 fibres (62 to 371/ml) over 5 $\mu\text{m}/\text{ml}$ for a mean exposure of 17.1 years. Twelve (31%) of the 35 miners had *x*-ray findings compatible with pneumoconiosis as opposed to one (2%) ($P = < 0.01$) for the 39 miners exposed to less dust. In addition, 22 (70%) of the 35 subjects had dyspnoea in the high dust exposure group as opposed to 10 (25%) of the 39 low dust exposure ($P = < 0.01$), while eight (22%) had lung crepitations in the former group as opposed to two (5%) in the latter group ($P = < 0.05$).

The data obtained from the 39 miners with low exposure indicate that talc miners with industrial exposure five days a week, eight hours a day for a mean of 16.2 years were not significantly affected by an environment in which there was an average of 18 million particles per cubic foot of talc containing an average of 43 fibres greater than 5 μm .

Fine *et al.* (1975) studied the effect of talc dust on the respiratory system of men working in the rubber industry. Eighty employees exposed to talc dust were studied and compared with a control group of 189 employees who worked in three separate adjacent plants and were not exposed to curing fumes, carbon black, or talc dust. Data on past health, occupation, smoking habits, and respiratory symptoms were collected by using a modified British Medical Research Council (MRC) questionnaire (Medical Research Council, 1960). Pulmonary function data were obtained using a Stead-Wells spirometer in which FEV₁ and flow values at 50, 25, and 12.5% of the forced vital capacity (FVC) were measured. The flow rates were size standardized by determining the flow rates of the largest FVC reading. Postero-anterior and lateral chest radiographs were taken, reviewed, and classified in accordance with the UICC—Cincinnati classification (UICC, 1970) for pneumoconiosis by a physician confirmed as a reader

by the National Institute of Occupational Safety and Health.

The industrial grade talc to which the workers were exposed contained 42% mineral talc but it was considered to be uniform for the period during which the workers were exposed and contained less than 1% silica and 2 fibres per ml. The dust count ranged from 0.51 mg/m³ to 3.55 mg/m³ with most of the workers being exposed to less than 1 mg/m³. It was considered that the maximum lifetime exposure of any worker was 2 million particles per cubic foot $\times$ 30 years, or 60 million particles per cubic foot years, or approximately 1 mg/m³ $\times$ 30 years, or 30 mg/m³ years.

The pulmonary function of the 69 workers exposed to talc for up to nine years, and that of the 141 control workers showed no significant change as indicated by FEV₁, FVC, and ratio of FEV₁/FVC.

A review of pulmonary symptoms showed that there was no difference in the incidence of cough, phlegm, or wheezing in 22 non-smoking talc workers when compared with 51 non-smoking control subjects. However, there was a statistically significant increase in the incidence of these symptoms among the 58 talc workers who smoked as opposed to the 138 control subjects who smoked.

A study of lung radiographs of the talc workers revealed no changes definitely consistent with pneumoconiosis, although one of the exposed group had opacities rated greater than 1/1 profusion in the UICC classification.

It was concluded from the data obtained on individuals exposed to the specific industrial talc used in processing rubber that in the light of the pulmonary morbidity noted the current threshold limit value for non-fibrous industrial talc should be lowered to avoid possible pulmonary disease from prolonged exposure to industrial talc dust.

Green and Sylwester (Hildick-Smith, 1975) initiated a pulmonary morbidity study in 70 employees working in a talc mine that produces cosmetic grade talc. Symptoms, pulmonary function data, and chest radiographs were compared in the employees and in a matched control group working in non-dusty industries. A Stead-Wells spirometer was used to obtain pulmonary function data and health data were gathered with the use of an MRC questionnaire. The employees had worked for an average of 4.6 years exposed to an average dust count of 7.6 million particles per cubic foot (34-96 years). Initial findings in the study showed that there was no difference in radiographic findings between the two groups studied or in the pulmonary function measurements of FVC₁, FEV₁, or FEV₁/FVC ratio when assessed as a percentage of predicted values using predictions derived from workers in non-mineral industries. The incidence of pulmonary symptoms was similar in the non-smokers in the two

groups studied but in 62 miners who smoked the incidence of sputum production was statistically significantly higher than in the 247 matched non-smoking control subjects.

The initial data obtained by Green and Sylwester (Green, G. M., 1974, personal communication) indicate that the environmental conditions so far encountered by the talc miners have not produced evidence of pulmonary disease but that smoking in talc miners produces pulmonary symptoms. The data obtained in the studies conducted by Fine *et al.* (1975) and Green and Sylwester indicate that under the environmental conditions described pulmonary function was not impaired in non-smoking workers, but pulmonary symptoms were associated with workers who smoked, the exact significance of which will be determined in future prospective studies (Bossé *et al.*, 1975).

Causes of death of talc mine employees

Rubino *et al.* (1976) conducted a retrospective study of talc mine employees to determine whether the causes of death were different compared with a control population of agricultural workers not involved in dusty industries. Record was made of the cause of death of employees who had worked for more than one year between 1921 and 1950 in a talc mine producing cosmetic grade talc. Data were obtained on the cause of death of 704 miners and 227 millers who had worked for an average of 14.9 to 15.8 years respectively.

The millers were exposed to cosmetic grade talc containing no detectable asbestos but 0.5% silica at an average concentration of 20 million particles per cubic foot of talc dust, and the miners were exposed to 600 million particles of talc dust containing 5% silica, from 1920 to 1950. Respiratory deaths in the talc miners were significantly higher than in the controls, although the incidence of pulmonary cancer, all cancers and cardiovascular disease was statistically significantly lower for the miners than the control group. Millers exposed to commercially available cosmetic grade talc had a similar incidence of deaths from respiratory disease, lung cancer and all cancers, but a statistically lower incidence of cardiovascular deaths.

Rubino's data indicate that prolonged exposure to cosmetic grade talc at the current threshold limit value for talc (20 million particles per cubic foot) did not increase deaths from pulmonary cancer or pulmonary disease compared with a control group.

Cancer

Exposure to some mineral dusts in appropriate amounts can cause pneumoconiosis and in some instances can be associated with the development of cancer (Henderson *et al.*, 1971; Murphy *et al.*, 1971;

British Medical Journal, 1973; Wagner *et al.*, 1973). There is a possibility that talc alone or talc contaminated with asbestos may be associated with cancer formation (Merliss, 1971; Blejer and Arlon, 1973), although cancer has not so far been reported from its use therapeutically in the pleural cavity (Honma *et al.*, 1963) or accidental introduction into the abdominal cavity from ruptured surgeons' gloves.

Merliss (1971) suggested that the high incidence of stomach cancer in the Japanese was related to the presence of chrysotile in the talc with which rice in California is dusted before being shipped to Japan. Smith (1973), however, failed to induce cancer in animals by feeding them 1% chrysotile in their diets during their lifetimes. Henderson *et al.* (1971) reported finding particles they believed were talc in cancerous and normal ovarian, cervical, and endometrial tissue. In the study, Henderson used a replica technique in which particles were identified by microscopical examination but their mineral composition was not confirmed by analytical procedures.

Kleinfeld *et al.* (1973) analysed 91 death certificates in a talc mining population of 220 in order to determine not only the cause of death, but whether any specific illness occurred in the miners as opposed to the general population. The talc miners were drawn from a mining population in New York State and mined talc admixed with serpentine and tremolite as well as 5% silica (Weiss and Boettner, 1967). The average age at death of the miners was 60.4 years (range 38-84 years) as opposed to the 54.4 years' life expectancy of comparable white men in the USA.

The mean duration of exposure was 24.7 years (15-27 years), with dust counts ranging from 2 to 2800 million particles before 1945 and 0 to 360 million particles per cubic foot since 1946, depending on the location within the mine. The elapsed time from exposure to death from pneumoconiosis or its complications averaged 25.9 years. The deaths from carcinoma of the lung and pleura showed an overall mortality that was four times the expected rate for the population with the increase occurring in the 60 to 70-year age group rather than in the 40 to 50-year age group.

In 1973, Kleinfeld reviewed recent data on the cause of death of talc miners on whom he had previously published papers (Kleinfeld, 1970; Kleinfeld *et al.*, 1967, 1973). He reported that during the years 1945-49 the mortality from cancer was four times the expected incidence, but that this incidence dropped and approached the expected mortality in the years 1960-64 and 1965-69. By May 1973, there was no difference in the expected and observed mortality from malignancy of lungs, pleura, peritoneum, or gastrointestinal tract.

The difference between the observed and expected mortality for cancer was statistically significant during 1950-54 but not significant in 1960-64 or

1965-69. Kleinfeld concluded that the reduction in cancer mortality in the mines was directly related to improved environmental control which, when implemented in 1945 resulted in appreciable reduction in dust counts, although the fibre counts still exceeded the permitted threshold (2 fibres per ml).

Rubino *et al.* (1976) showed that the overall incidence of pulmonary and all cancers reported in talc miners was statistically significantly lower than that observed in the control population, while the incidence of cancers for talc millers and their control groups was similar (Kerr and de Mesquita, 1975). The available data from animal and epidemiological studies show that talc dust is not carcinogenic.

Cosmetic use of talc dust

Cosmetic talc is used as a face powder and body powder by both adults and children to lubricate the skin and prevent chafing and discomfort caused by moisture and heat. It has been used as a cosmetic throughout the world for many centuries and there is no evidence that its normal use poses a hazard to health. However, in view of increasing interest in identifying hazardous dust pollutants in the environment, it was considered important to review reports on experience with cosmetic talc.

Although talc is used as a body powder by people of all ages, it is widely used for babies after bathing or nappy changing. The normal use of cosmetic talc in infants has not been reported to be harmful (*Food and Cosmetics Toxicology*, 1973) although the accidental aspiration of excessive amounts in infants has been reported to cause serious but reversible acute respiratory disease in some instances and death in isolated cases (Cless and Anger, 1954; Molnar, Nathenson, and Edberg, 1962; Jacobziner and Raybin, 1963; Jenkins, 1963; Hughes and Kalmer, 1966; Tortorolo and Romano, 1966; Lund and Feldt-Rasmussen, 1969; Paoli and Brandigi, 1970; Neimann *et al.*, 1971).

A review of the literature since 1954 reveals 27 reported cases of accidental aspiration of excessive amounts of talc by infants and children aged between six months and three years of whom six died (Cless and Anger, 1954; Molnar *et al.*, 1962; Jacobziner and Raybin, 1963; Jenkins, 1963; Gouvea *et al.*, 1966; Hughes and Kalmer, 1966; Tortorolo and Romano, 1966; Lund and Feldt-Rasmussen, 1969; Paoli and Brandigi, 1970; Neimann *et al.*, 1971). It is noteworthy that when corticosteroid administration was added to the usual supportive treatment, possibility of recovery was increased (Hughes and Kalmer, 1966; Lund and Feldt-Rasmussen, 1969).

Minimal data are available on the frequency with which talc dusting powders are applied to the body, let alone the amount of dust to which the individual is exposed. In an attempt to define the amount of talc to which infants are exposed during normal use

of talc dust, a study was conducted (Eden, A., personal communication, 1972) in which the frequency of use in various sites as well as the duration of usage was determined. Information collected from 76 mothers normally using talc in the care of their babies, showed that the site and method of application of talcum powders varied widely. In 62% of applications only the nappy area was dusted, while the whole body, except the head, was dusted in 20% of the applications, with other body sites being dusted in the remaining 18%. Mothers applied the talc by either dusting the skin directly or placing talc in the hand before application. Babies were powdered from one to nine times a day with a median frequency of dusting the nappy area five times each day, with the duration of powdering the nappy area being 3 to 25 seconds with a median time of 10 seconds.

In order to determine the amount of talc to which an infant and mother are exposed, a simulated study was conducted (Pooley, F. D., personal communication, 1972). As dusting of infants is of short duration, in order to attain a satisfactory sample the contents of a container of a commercially available product were either continually or intermittently dusted into a shallow tray from a height of 7 to 13 cm (3 to 5 inches). Air inlets of a gravimetric dust sampler were placed in the appropriate site for the infant's nose and 40 cm (16 inches) above the tray at the estimated nose site of the mother. The dust concentration for a simulated mother and infant were similar in the study conducted. Analysis of the data (Sivertson, J. N., personal communication, 1976) indicates that during a 10-second dusting period the total median dust concentration is 0.243 million particles per cubic foot. The median concentration then decreases to an average of 0.124 million particles per cubic foot during the 65 further seconds required for the dust to settle.

Therefore, a median exposure per application can be estimated at 0.1752 million particles per cubic foot-minutes by summing the 10-second (0.17 minutes) application of 0.0413 million particles per cubic foot-minutes (0.243×0.17) with the 65 second (1.08 minutes) exposure of 0.1339 million particles per cubic foot-minutes (0.124×1.08). A median weekly exposure for five times a day, seven days a week would be 0.102 million particles per cubic foot-hours.

A further study to determine the respirable dust to which an infant is exposed during talc dusting showed that the average respirable dust concentration was 0.10 mg per min/m³ when dust samples were obtained in actual use of talc by mothers (Sivertson, J. N., personal communication, 1976).

The threshold limit value for talc dust in the USA is 20 million particles per cubic foot exposure for an eight-hour work day giving a 40-hour exposure a week, which gives an exposure level of 800 million

particles per cubic foot-hours per week to talc dust. An infant dusted on an average of five times a day for seven days a week is exposed to an estimated median weekly exposure of 0.102 million particles per cubic foot-hours, which is 7840 times less than that of a miner working for eight hours a day for five days a week in a dust environment of 20 million particles per cubic foot.

Pulmonary fibrosis was seen in an adult as a result of bizarre and excessive use of talc (Nam and Gracey, 1972). The patient died from causes not associated with the fibrosis which was discovered coincidentally at necropsy. The patient was reported to have used talc excessively for 20 years and for four years had applied it liberally three times a day and dusted his sheets with it nightly to an extent that his wife refused to sleep in the same bed. This excessive use apparently did not clinically impair the patient's health.

Moskowitz (1970) reported on a female patient who developed radiographic reticular densities and hazy nodules in both lungs after working for six years as an inspector of aerosol talc sprays. The patient worked one week out of every six by spraying each can briefly into the air at a rate of 25-50 sprays an hour, with no protection against dust inhalation. The patient improved symptomatically after treatment with corticosteroids and subsequent radiographs showed remarkable clearing of both lung fields. Her vital capacity also increased after treatment from 1150 to 1550 in three months. The response of this patient suggested to Moskowitz that if the diagnosis of talc pneumoconiosis is made early, the process can be arrested and reversed.

Data are available concerning the duration and frequency of use of talc dusts used normally for cosmetic purposes by adults. Some indication of the extent of exposure of a consumer to cosmetic talc dust can be obtained when a 1-minute a day exposure to cosmetic talc dust is compared with the 480-minute exposure to talc dust that is encountered by a miner in a single day. A consumer using a cosmetic talc dust for 10 seconds and allowing 65 seconds for settling would be exposed to 0.102 million particles per cubic foot-hours of talc dust a week as opposed to an eight-hour exposure a day of a miner working at the threshold limit value level of 20 million particles per cubic foot of talc dust which provides an exposure of 890 million parts per cubic foot hours a week.

On the basis of these calculations the million particles per cubic foot-hours of talc dust exposure of a miner each week is approximately 7800 times that of consumer exposure each week.

Conclusion

The increased interest in the effect of environmental

dusts on consumers and industrial workers has prompted a review of available data to assess the hazard to health that exists under current conditions of exposure to talc dusts.

Prolonged exposure to cosmetic grade talc at the threshold limit value for talc in industrial environments has not been associated with the development of pneumoconiosis or cancer.

Any health hazard that may exist is confined to the industrial use of industrial talcs rather than industrial exposure to cosmetic grade talcs.

The concern that has been expressed about the possible health hazard from consumer exposure to cosmetic talc is unwarranted as the consumer exposure is greatly below the time-weighted levels considered as a safe exposure to cosmetic grade talc in an industrial environment.

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