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Man-made Mineral Fibres

J. W. HILL

Group Medical Adviser, Pilkington Brothers Ltd., St Helens

Summary

Insulation wools from glass fibres have been in production for over 40 years and similar products made from slag wool have been made since the 1880s. These products contain a significant proportion of fibres of respirable diameter. Continuous filaments for textile fibres have been made since the 1940s and contain only extremely small quantities of respirable fibres. The relatively high falling speed of large diameter fibres means that high gravimetric estimations may be associated with very small quantities of airborne respirable fibres in production plants. Fibres above 5 μm in diameter act as a primary irritant on the skin but continued exposure leads to hardening and a cessation of symptoms, sensitization does not occur. Prevalence studies of groups of workers exposed for lengthy periods to glass fibres in several countries produced evidence of the absence of pulmonary fibrosis, respiratory impairment and symptoms of bronchitis. Epidemiological studies have failed to show an excess risk of lung or other cancers. Reports of a small number of individual cases with respiratory disease and an exposure to glass fibres have not demonstrated a causal effect. Post-mortem studies of workers with long-term exposure to glass fibres have shown no evidence of lung damage.

Animal inhalation studies, in general, show that man-made mineral fibres elicit a macrophage response and the reaction is typical of a nuisance dust, significant fibrogenic reaction is not produced and carcinogenesis has not been demonstrated by inhalation. Injection of fibres into the pleura produces an incidence of tumours related to the number, diameter and length of fibres. The order of diameter of biological significance is believed to be between 0·5 and 1 μm in diameter. Such effects have not been observed in man and are obtained with all durable fibres, asbestos being the only substance for which a similar effect is known to occur in humans. Cell culture work suggests the mechanism of tumorigenesis differs from that of most carcinogens and may resemble the Oppenheimer effect.

Introduction

Man-made mineral fibres (MMMF) defined here as those made from glass, natural rock or any readily fusible slag, differ from naturally-occurring fibres such as asbestos in several important respects. Firstly, they are amorphous silicates whose surface properties differ chemically from those of asbestos and are further modified by a very thin coat or resin which is normally applied to the glass types. The resin is normally fully polymerized in the final product and is therefore chemically inert.

Secondly, the fibres are manufactured to a controlled nominal diameter which, together with the method of production, regulates the number of fibres of respirable diameter in the product.

Continuous filament fibres for textiles and resin or cement reinforcement are thick fibres of 12–20 μm in diameter, made by mechanical drawing at very high speed. This method produces a very narrow spread of diameter around the nominal size with an exceedingly small number of fibres in the respirable range, arising from attenuation of strands at the end of runs (*Fig.* 1).

Insulation wools are usually about 6 μm in nominal diameter, although in Europe some products go down to 2 μm. These are made by creating fine streams of glass through apertures in a rotating spinner and further attenuating them by air or stream blowing. This method results in a much wider distribution around the nominal diameter (*Fig.* 2).

Finally a combination of drawing and flame attenuation is used in the USA to make fibres of 1 μm or less diameter. These are made for a very limited specialist market and represent about 1 per cent of world production.

The third major difference between asbestos and MMMF is that because of their glass-like nature the fibres can only break transversely, and cannot be split longitudinally even by milling (Assuncao and Corn, 1975). They therefore retain their diameter at forming in contrast to asbestos which can split into finer fibres both *in vitro* and *in vivo* (Suzuki and Churg, 1969).

Respirability

The falling speed of a fibre in air is determined predominantly by its diameter (Timbrell, 1965,

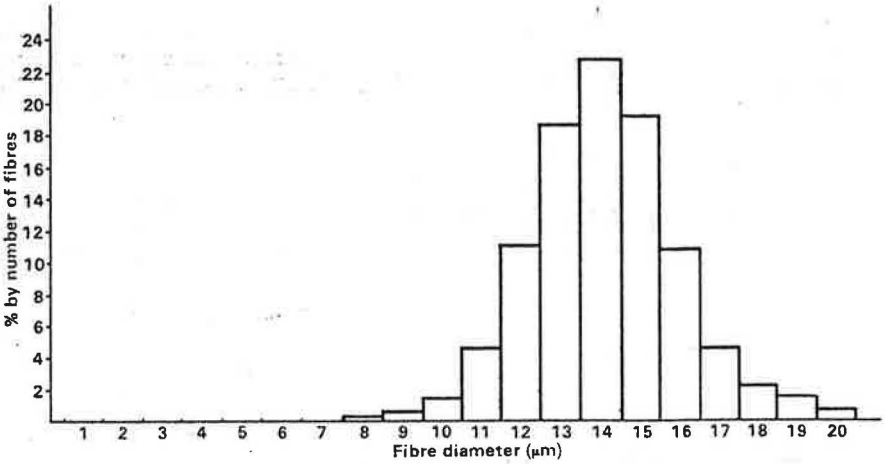

Fig. 1. Continuous filament for reinforcement: typical fibre diameter distribution, glass fibre staple tissue. Median diameter = 14·1 μm. Mean diameter = 14·1 μm. Standard deviation = 1·9 μm.

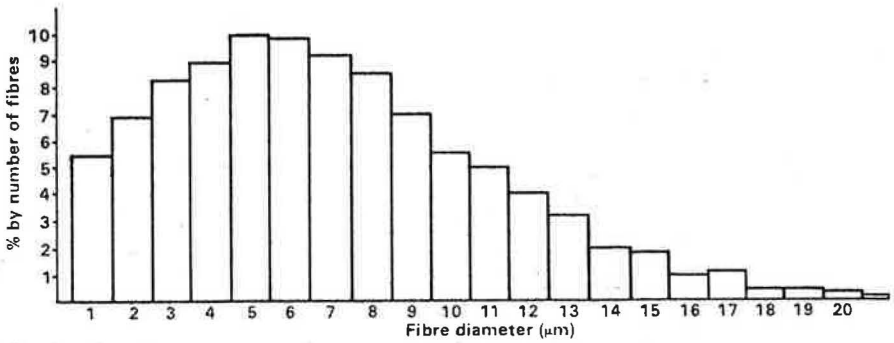

Fig. 2. Insulation wool: typical fibre diameter distribution, glass fibre wool. Median diameter = 6·9 μm. Mean diameter = 7·0 μm. Standard deviation = 4·0 μm.

1976), and examination of human and animal lungs (Gross, Cralley, Davis et al., 1971; Gross, Tuma and deTreville, 1971; Timbrell and Skidmore, 1971) are in agreement with mathematical studies (Timbrell, 1965, 1976) in showing that only fibres less than approximately 3–3·5 μm are retained in the lung (*Fig.* 3). Examination of human lungs, mainly in relation to asbestos, shows that the range of diameters found in association with pathology is largely 0·5 μm in diameter or less and 5·0 μm in length or less (Sebastien et al., 1975).

Occupational Exposure

Bearing these factors in mind, we may next consider the levels of airborne respirable fibres encountered in occupational exposure. There is general agreement as to the techniques of sampling (Dement, 1975), and both optical and electron microscopy (EM) have been used for counting. With large nominal diameter products there is very little difference between the two methods, but in the special plants in the USA where the nominal diameter is less than 1 μm, the EM finds about three times the number observed in optical counts.

There is in addition a correlation between the nominal diameters of the product and the average airborne fibre concentration, showing decreasing numbers of fibres with increasing nominal diameter (Esmen et al., 1977).

A typical plant producing insulation wool of 6 μm nominal diameter is associated with a range of respirable airborne fibres on interference optical

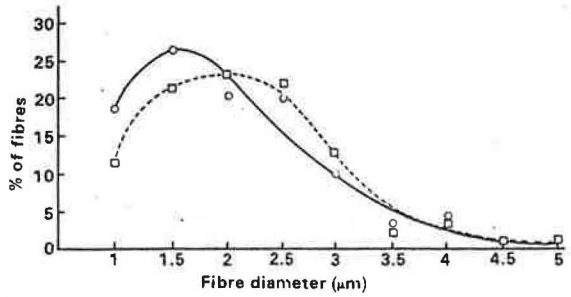

Fig. 3. Graph of distribution of fibres isolated from lungs and classified according to diameter. □ — — — □ = Fibre glass workers (2395 fibres). O ——— O = Pittsburghers (3092 fibres).

microscopy of 0·003–0·051 fibres/cm³ with a mean of 0·022 fibres/cm³. Such a count may be accompanied by quite high gravimetric estimations ranging from 0·36 to 8·12 mgms/m³. The rapid falling speed of large diameter fibres, causing them to settle out quickly, accounts for these extremely low respirable fibre counts in plants which to the naked eye, Tyndal Beam or by gravimetric measurement alone would appear to be quite dusty.

In illustration of the property of MMMF, that they cannot be broken down longitudinally into finer fibres, it is of interest to compare the sawing of glass fibre reinforced board with chrysotile asbestos reinforced board. The fibres generated from the glass fibre reinforced board were 2000 times less numerous than those from the asbestos and retained the original diameter of parent product—in this case, 12 μm. The glass fibres were fractured transversely, progressively reducing them to shorter lengths until the point was reached when length approximated diameter and they became effectively spherical dusts (Hounham, 1973).

During the development of the industry in the last 40 years, nominal diameters have been reduced from 14 to 6 μm on average in the insulation wools, but it is useful to know in relation to the epidemiology that old products contain substantially more rather than fewer fibres in the respirable range than contemporary products (Klingholz, 1977).

The effects of MMMF on the skin are well documented (Siebert, 1942; Sulzberger and Baer, 1942; Heisel and Mitchell, 1957; Heisel and Hunt, 1968) and consist of a fine, punctate, itching erythema affecting the exposed surfaces and disappearing with continued exposure—a phenomenon described as 'hardening'. The reaction is due to histamine release induced by the mechanical effects of superficially embedded fibres (Possick et al., 1970) and sensitization does not occur, as the resin coating is fully polymerized and therefore inert in the finished product. The skin reaction is associated with the heavier fraction of fibres, mainly those above 5 μm in diameter, and there appears to be an upper diameter limit which is ill-defined but where the fibres are too large or too flexible to penetrate without the application of considerable mechanical force.

Human Cases

Review of the literature for other adverse human effects reveals remarkably few human cases in spite of the fact that slag wool has been produced since the late 1800s and glass fibres since the 1930s.

One fatal case of pneumonia in 1947 in an upholsterer has been reported, where the illness commenced one month after exposure had ceased, but where glass fibres were found in the lung (Kahlau, 1947).

In 1957 a chest illness with consolidation of the lower lobe was reported in a man repairing an incubator, again about three weeks after exposure had ceased. The condition responded to antibiotics (Bezjack, 1957).

A third case was reported in 1961 in which glass fibres were found following lobectomy with an X-ray diagnosis of bronchiectasis and pathological findings compatible with this diagnosis (Murphy, 1961).

These three cases seem to have been associated primarily with infection and the findings of glass particles in the lung may have been incidental rather than causal.

A small number of cases of asthmatic symptoms attributed to glass fibres have been reported (Tara, 1945; Dadash'ian, 1969) but fail to withstand critical evaluation as reporting has been either insufficiently detailed or other non-occupational conditions have not been excluded, particularly in view of the probability of any dust exacerbating pre-existing chest disease.

Although large populations have been extensively exposed to MMMF with the continued growth of the industry over 40 years, the development of diseases of the lung has not been confirmed by other investigators and no repeatable or identifiable pattern has emerged.

Upper respiratory tract irritation has been reported without significant lung involvement (Champeix, 1945; Roche, 1947; Cirla, 1948; Mungo, 1960; Milby and Wolf, 1969) and usually takes the form of nasal or pharyngeal irritation. It is normally seen only in unusually dusty conditions such as when excessive dust is generated in confined spaces, and these situations may be an indication for a simple cloth mask of the Martindale type.

Epidemiology

The absence of clinically identifiable lung disease has prompted extensive epidemiological investigations as offering the only other form of potential direct evidence of adverse human effects, and these have been focused upon the possibility of effects analogous to those associated with asbestos.

Prevalence studies examining chest X-rays and lung function in a group of 1389 workers with 10 or more years of exposure to glass fibres in the insulation wool industry in the USA were negative (Wright, 1968; Utidjian and DeTreville, 1970). These studies were followed by a further chest X-ray survey which confirmed Wright's negative findings in 1832 production workers in the same factory. Nineteen per cent of the observed group had over 25 years' exposure to glass fibres (Nasr et al., 1971).

A similar study in the UK, examining 70 production workers with an average of 20 years' exposure and comparing them with accurately matched controls, used chest X-rays with a randomized method of reading by independent radiologists, pulmonary function and also a questionnaire on symptoms of bronchitis. This was also negative (Hill et al., 1973).

A further study in Germany of the chest X-rays of 36 glass fibre workers with more than 10, and 196 with more than 15, years of exposure, showed no pathology attributable to occupation. The average period of exposure is given as 19·7 plus or minus 5·5 years, but whilst the findings are in agreement with other work it is difficult from the data given to assign numbers to the category of 20 years' exposure or more, which would be desired by many as a necessary basis of interpretation.

A cohort study in the USA followed all of a group of 1448 employees who had worked in a glass wool plant for a minimum of 5 years betwen 1940 and 1949, and ascertained their vital status over 25 years later in 1975 (Bayliss et al., 1976). There was no overall excess mortality in comparison with a control group, no case of mesothelioma was observed and there was no excess in deaths due to cancer, respiratory or otherwise. The only positive finding was a statistically significant excess of deaths in the category 'non-malignant respiratory deaths excluding pneumonia and influenza'. This finding has been criticized (Hill, 1977), on the grounds that smoking habits were not considered, but more importantly, that the control group consisted of the total white male population of the USA which contains a substantial rural population, whereas the subject group lived predominantly in industrial towns and was likely to suffer an excess rate of bronchitis for reasons other than exposure to glass fibres.

Efforts were made in a further development of this study to explore an exposure of a very small part of the subject population to fibres of 1 μm nominal diameter. This part of the study has been criticized not only because of the small numbers, but also in terms of the statistical methods, and incorrect attribution of exposure of some members.

A further study of 416 retired glass fibre workers revealed no evidence of a health hazard, excepting a small excess of bronchitis (3 observed versus 0·5 expected), but the author was disinclined to attach clinical significance to this, because of both the possible vagueness of the disease entity and the probability of social factors influencing the attribution of diagnosis in relation to retirement (Enterline, 1975).

One post-mortem study is available where the lungs of 20 glass fibre workers with exposure varying from 16 to 23 years were compared with those of a control group. No specific disease or tissue alteration was found which could be attributed to fibrous dust.

Although anecdotal, it may be of interest to note that for over more than 20 years the author has not come across a case of mesothelioma in a glass fibre worker despite diligent enquiry of the three hospitals which serve the catchment area of the glass fibre factories. These factories have been manufacturing insulation wool since the mid-1930s.

Animal Studies

Animal studies in 1955 by Schepers using inhalation and intratracheal injection of glass fibres of 6, 3 and less than 3 μm in diameter have confirmed the

clinical observation that glass fibres are non-fibrogenic, the reaction produced being predominantly a macrophage response (Schepers, 1955; Schepers et al., 1958). Guinea-pigs simultaneously infected with tuberculosis showed regression and healing of the lesions despite continued exposure to glass fibre dust. Some limited pulmonary reactions were observed, however, which were typical of inert dusts or endemic rat bronchitis. Others were seen in the intratracheal series (bronchial epithelial hyperplasia) which are now considered to be due to the method of administration, as they were repeated by another investigator and found to disappear with time, and furthermore are not observed in inhalation experiments (Gross et al., 1960, 1970).

In a similar experiment in 1970 using good controls and fibres entirely in the respirable range (3 μm or less in diameter) Gross et al. (1970) found that there was no difference between uncoated, phenolformaldehyde resin or starch-coated fibres. Each group produced a predominantly macrophage reaction and in so far as the alveolar architecture remained intact, there was minimal stromal proliferation consisting mainly of reticulin, and the tissue reaction was potentially reversible, the criteria for considering glass fibre to be a 'nuisance dust' were regarded as satisfied.

Similar inhalation experiments with asbestos reproduced fibrosis, carcinoma of the lung and mesothelioma.

Inhalation has also been used to study the effects of long fibres in animal lungs and it has been shown that many of these fibres are encapsulated with ferro-protein, subsequently fragmented and later cleared from the lungs (Botham and Holt, 1971, 1973). Glass fibres are cleared by this mechanism faster than asbestos.

Intratracheal injection of paired samples of long and short fibres has shown length to be an important parameter of fibrosis. While long asbestos fibres produced gross effects, long glass fibres produced only a minimal response. As important defence mechanisms are bypassed by intratracheal injection, this result does not invalidate the conclusions reached from inhalation experiments.

Totally bypassing the normal lung defence mechanisms, Pott and Friedrichs (1972) in Germany and Stanton and Wrench (1972) in the USA investigated the effects of fibres injected or implanted into the pleura and peritoneum of rats. They found that tumours were produced independent of the chemical nature of the fibre by substances as different as asbestos, ceramic fibres, aluminium oxide and glass fibres. The carcinogenic potency was related to the fibre diameter and it was postulated (Timbrell, 1976) that the carcinogenic response was correlated with the number of 'significant' fibres present—i.e. a dose/response relationship was found. Further work has endeavoured to identify the dimensions of such fibres and Wagner et al. (1973, 1976) have shown that glass fibres of 0·5 μm diameter produce mesothelioma and this has also been confirmed by Davis (1976), whereas fibres greater than 3 μm in diameter have little biological effect. Since then further work by Pott and Stanton (personal communication) has demonstrated the maximum potential to be in the range 0·5–1 μm in diameter. Although it is generally considered that increased length is also important (probably above 10 μm), Pott has found tumours with fibres of the above diameter but less than 5 μm in length.

These experiments have been criticized on several grounds. The nature of the tumours has been debated, but Wagner has published his criteria, and also the histology of the tumours is similar whatever fibre has produced it. It is also true that mesothelium is a highly reactive tissue and some tumours were found in the controls. Nevertheless, the dependence of the tumorigenic effect upon diameter remains significant. That the doses used are quite unrealistic in terms of human exposure is of course true and underlines the difficulties of extrapolation, particularly as similar effects are obtained only with asbestos in inhalation experiments in animals. Human observations of occupationally induced mesotheliomas are confined to asbestos.

Cell Culture Studies

Cell culture studies with fibres of 0·25–1 μm in diameter show the leakage of cellular constituents associated with ingestion by macrophages of fibres larger than the cells themselves (Beck et al., 1971). *In-vitro* studies with lung fibroblasts showed a continuing collagen synthesis with chysotile, but only an initial reaction which soon subsided with glass fibres (Richards and Morris, 1973). Dusts of fibrous shape have been found to behave similarly and to form giant cells in intraperitoneal studies (Sethi et al., 1975).

In vitro, the growth of fibroblasts is dependent upon the presence of a solid substrate and in the case of fibres this has been found to require a minimum length of 20 μm—rate of growth increasing up to a length of 200 μm (Maroudas et al., 1973). Attention has been drawn to a correlation between the numbers of fibres of these dimensions in tissue cultures and the frequency of induction of mesothelioma in Stanton's experiments. It has been suggested that fibres above 20 μm in length are capable of stimulating mesenchymal hyperplasia, whereas shorter fibres are phagocytosed.

Chromosomal damage has been reported in cell cultures with asbestos fibres (Sincock and Seabright, 1975), but no similar reports have been made relating to MMMF.

Again, the very large number of variables which intervene between cell culture *in-vitro* studies and *in-vivo* effects in the intact organisms make extrapolation difficult and at present gives no clear indication.

Asbestos and glass fibres have been studied in mutation tests using auxotrophic strains of *Escherichia coli* and *Salmonella typhimurium*, using positive control mutagens in the form of ultraviolet light, potassium chromate, ethyl methanesulphonate and benzo(a)pyrene. Over a wide range of concentrations neither asbestos nor glass fibres were found to have mutagenic activity. This suggests that the carcinogenic activity of fibres in the pleura has a different mechanism to the radiomimetic effects of ultraviolet light, the alkylating effect of ethyl methanesulphone and the effects of weak inorganic compounds like potassium chromate or metabolic activation like benzo(a)pyrene. Since the bacteria did not engulf the fibres as do macrophages, further tests on suitable preparations of mammalian cells may be required, but the suggestion has been made that the mechanisms of action of fibres in the pleura may not be related to mutagenesis but may be similar to the Oppenheimer effect (solid state carcinogenesis observed in rats) (Chamberlain and Tarmy, 1976).

In summary, one may conclude that:

1. MMMF are not fibrogenic, but may exacerbate pre-existing lung disease in the same way as any other nonspecific dust. High concentrations may cause upper respiratory tract irritation.

2. Carcinoma of the lung is not a hazard, as the epidemiology has adequately catered for the time-lag or latent period effect, and animal experiments have produced no effects of this type. There are further possible reasons for not anticipating such an effect with MMMF because of the absence of fibrosis and because of the different surface and chemical properties which make the effects of smoking unlikely to be synergistic.

3. Mesothelioma may be associated with an extremely lengthy 'latent' period. No cases have been described in MMMF workers. The length of the history of the industry may be relevant. Slag wools have been made since the 1880s. Glass wools have been produced since the 1930s in the UK and earlier in Germany, and the USA. Continuous filament manufacture commenced in the UK in the mid-1940s. The more recent production in Germany and the USA of special purpose fibres, entirely below 1 μm diameter, associated with high airborne counts shall be distinguished clearly from standard production as it may represent a special case. The finding of more, rather than fewer, respirable fibres in old insulation wool products suggests that historically occupational exposures have probably been comparable to contemporary levels, which are in any case exceedingly small in terms of respirable airborne fibres. Tumour induction has not been found in animal inhalation experiments in spite of life-time exposures to dust clouds composed of fibres entirely below 3 μm in diameter with a mean of 1 μm, and therefore containing substantial numbers of fibres in the diameter range incriminated in the intrapleural experiments. The authors of the intrapleural experiments are careful to point out the tissue specificity of their work, the bypassing of the normal lung defence mechanisms and the dangers of facile extrapolation. Nevertheless, the industry is actively supporting independent research in epidemiology, further animal work and occupational hygiene studies.

Author's Note

In 1975 Baris reported an exceptionally high incidence of mesothelioma confined to a Turkish village and this was originally considered due to environmental asbestos exposure, but it has since been suspected that the causal agent might be one of the zeolite group of naturally occurring fibres. The suspected fibre is crystalline silicates. The fibres were predominantly in the 0·5 micron range of diameter and used as building materials, road surfacing etc., and are likely to have resulted in very high levels of exposure. Further suspicion has arisen in five cases reported in India where silica fibres in the same diameter range may have been generated in the burning of bamboo.

Work published by Morgan in 1977 has shown that chrysotile asbestos fibres from which 80 per cent of their magnesium content has been leached retain their fibrous morphology but lose their carcinogenic potential in the pleura. This work is important in so far as it demonstrates carcinogenesis at this site involves factors additional to pure morphology.

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Requests for reprints should be addressed to: Dr J. W. Hill, Medical Centre, Pilkington Brothers Ltd., Prescot Road, St Helens WA10 3TT.