Biopersistence of Man-Made Vitreous Silicate Fibers in the Human Lung

P. Sébastien

Institut de Recherche en Santé et en Sécurité du Travail du Québec, Montreal, Canada

There is now a substantial body of experimental data on the pulmonary biopersistence of man-made vitreous silicate fibers (MMVSF), but human data are seriously lacking. Our knowledge in this field is essentially limited to a few reports of measurements of fibers retained in lung tissue samples taken at autopsy from workers manufacturing these products. Three types of exposure were studied: fibrous glass, mineral wool, and refractory ceramic fibers. Overall, the available data do not provide evidence for substantial long-term retention of fibers in the human lung after occupational exposure to MMVSF dusts. A word of caution, however; the amount of data supporting the previous statement is much greater for fibrous glass than for either mineral wool or refractory ceramic fibers. There is no human data on the key question of the kinetics of pulmonary clearance of inhaled MMVSF. — Environ Health Perspect 102(Suppl 5):225-228 (1994)

Key words: man-made vitreous silicate fibers, lung retention, occupational lung diseases

Introduction

The term "man-made vitreous silicate fibers" (MMVSF) is generic for several types of fibrous insulating products, such as fibrous glass, mineral wool, refractory ceramic fibers, and certain specialized glass fibers. The MMVSF constitute only one component of the larger family of man-made fibers. The several types of MMVSF are distinguished from each other by their physical properties and their chemical composition. All are noncrystalline. The raw materials and the manufacturing process can be adjusted to obtain the properties suitable to the intended uses of the products. More information on the nomenclature, chemistry, physical properties, and manufacture is available elsewhere (1,2).

The MMVSF products, manufactured and used world-wide, have a definite economic importance. A few years ago they became a subject of occupational health concern (3). Occurring in powder form, they could be sources of dust exposures. But very little was known about the toxicity of the MMVSF dusts.

Because of some incomplete fiberization during manufacturing, MMVSF products contain—at the microscopic level—a very substantial amount of nonfibrous particles. For example, examination of some bulk samples of glass and mineral wool by scanning electron microscopy revealed that in the size range 5 to 20 μm, the number of fibrous and nonfibrous particles were similar; below 5 μm, the nonfibrous particles outnumbered the fibrous ones (4), but from a toxicological perspective, the emphasis has been exclusively on the fibrous particles. This was mainly because of a prevalent "fiber carcinogenesis theory" (5,6), according to which only the property of fibrous shape would confer on inhaled particles some specific toxicity towards the lung or the pleura.

The fiber carcinogenesis theory implies that physical contact between the fibrous particles and some target cells would be in itself a component of the toxicological process. In that context, pulmonary retention phenomena, mechanisms by which fibers get in touch with the cells, and all aspects related to the dose become of the utmost importance.

Overall, MMVSF are larger than the natural inorganic fibers such as asbestos, and it was pointed out that their large size would prevent MMVSF dust particles from penetrating deeply into the lung. Soon, however, more detailed information on the fiber size distributions became available for several occupational circumstances (7), and models were developed that allowed estimation of the probabilities of deposition in the human lung for each fiber size category (8). These models indicated that some MMVSF dust particles could in fact be inhaled and deposited in the several compartments of the human lung, including the respiratory compartment.

The concept of "durability" was introduced to define ability of the fibers to preserve their integrity in the pulmonary milieu, and inhaled MMVSF were considered to be of a poor durability. Some animal experiments demonstrated various physical and chemical alterations of MMVSF after their stay in the lung (9), but the phenomenon was complex and many parameters related to both the fiber and the test system were involved. Nevertheless, fiber chemistry and fiber size were identified as some determinants of durability.

The whole question of pulmonary retention, or "biopersistence," as a determinant of toxicity is important enough to justify reviewing the limited human data on the subject. Conceptually it would imply knowing, at any point after the first exposure, the amount and location of the fibers in the lung, together with their physical and chemical state. Viewed from this standpoint, the human data available so far are, indeed, quite limited, for they have been obtained by measuring at a single time fibers in pulmonary samples from workers with specific exposure.

Reviewing the Evidence

Most of the human data most relevant to biopersistence have been obtained from analysis of fragments of lung parenchyma taken at autopsy on exposed workers in manufacturing industry, or samples of bronchoalveolar lavage fluids. Because the physicochemical characteristics of the fibers will determine pulmonary deposition or durability, it seems appropriate to present the data for each type. Data are available

---

This paper was presented at the Workshop on Biopersistence of Respirable Synthetic Fibers and Minerals held 7-9 September 1992 in Lyon, France.

Thanks to Bruce Case for reviewing the manuscript.

Address all correspondence to Dr. P. Sébastien, IRSST, 505 Boulevard de Maisonneuve Ouest, Montréal, Québec Canada H3A 3C2.

Environmental Health Perspectives 225
concerning three types of MMVSF exposures: fibrous glass, mineral wool, and refractory ceramic fibers.

**Fibrous Glass**
The first work in this field, published by Gross, Tuma, and de Treville in 1971 (10), was a postmortem study of the lungs of 20 men formerly employed in the fibrous glass production industry. Their duration of employment ranged from 16 to 32 years, but the time since last employment was not indicated. The men had all been exposed to the dust of fibrous glass, but no actual measurements of air concentrations in the workplaces were reported. The severity of exposure was estimated. Men and women resident in the same city, who presumably had not been exposed occupationally to the dust of fibrous glass, constituted a comparison group. The age distributions were similar in both groups (38 to 81 years, average 57.5).

Fragments of formalin-fixed lung parenchyma were chemically “digested” with sodium hypochlorite. The extracted particles were examined by light microscopy. Fibers longer than 5 μm were counted, and length and diameter measured. No details are given of the microscopic technique, nor are there data on the chemical types of the fibers. Ferruginous bodies also were counted. The numerical concentrations of fibers and bodies were reported per unit weight of dry lung.

Fibers were encountered both in the workers’ lungs and in those of the nonexposed residents. The concentrations and sizes of the fibers were similar in both groups. The average concentration in workers was 95 fibers/mg of dry lung, and the mean diameter was 2.0 μm and the mean length, 25 μm. The average percentage of fibers with diameter <3 μm was about 90% in both groups. Attempts to correlate the individual fiber pulmonary concentrations with duration or severity of exposure of the workers were fruitless. Ferruginous bodies were, on average, more plentiful in the lungs of the nonexposed residents: 0.9 fibers/mg, compared with 0.2 fibers/mg for the glass workers.

To interpret their findings, the authors made the hypothesis that “the fibrous glass workers were exposed to fibrous glass particles very similar, with respect to concentration in the inhaled air and also with respect to dimensions of the fibers, to those of the nonexposed residents.” There was no reference to the biopersistence of the fibers in the human lung.

The second study was published almost 20 years later by McDonald et al. (11). Their exposed group was the epidemiological cohort of American MMVSF workers studied by Enterline et al. (12). In the cohort were workers from 17 production plants, 11 of them producing fibrous glass and 6, mineral wool. In the fibrous glass group, autopsies were recorded in 585 of 4210 deaths. Lung tissue samples were sought from all the pathologists and 120 samples were obtained, together with similar samples from very carefully matched referents. For each worker in the study, a referent was selected in the same hospital, from the next available male autopsy in the same or adjacent year of death, having the same or adjacent year of birth, from causes other than malignant disease. On average, workers were born in 1912, hired in 1948, worked for 11 years, left employment in 1960, and died in 1972. For fibrous glass production workers in the whole cohort, the average intensity of exposure was estimated at 0.04 fibers/mc.

All lung samples were paraffin-embedded, formalin-fixed blocks. Samples from matched pairs were analyzed in tandem. Inorganic particles were extracted by low temperature ashing followed by filtration through membrane filters; no chemical digestion was used. Filters were examined by phase contrast optical microscopy (PCOM) and by analytical transmission electron microscopy (ATEM). The microscopic analyses were selectively restricted to particles >5 μm in length and with aspect ratio greater than 3:1. Such particles were called fibrous particles even if they had irregular contours and a nonuniform diameter. No attempt was made to identify the fibrous particles visible by PCOM. In electron microscopy, the fibrous particles were characterized individually using essentially elemental microanalysis by energy dispersive spectrometry (EDS), and accessibly selected area electron diffraction. The number of microscopical fields scanned was adjusted to achieve the same detection limit for every case analyzed. Numerical concentrations of fibers per unit weight of dry lung were calculated.

Pulmonary concentrations of PCOM-analyzed fibers were similar to those reported earlier (10) with a geometric mean of 100 fibers/mg for workers and 80 fibers/mg for referents. The ATEM-analyzed lung contents were similar in workers and referents, with a total of 875 fibers for workers and 748 for referents. Four chemical types were distinguished: asbestos, talc/anthophyllite, unidentified fibers, and “siliceous MMVSF.” Siliceous MMVSF yielded an EDS spectrum with only a silicon peak present. These fibrous particles exhibited interesting morphological features. Some were in their native cylindrical shape and had regular contours. Others were probably partly dissolved and showed either a needle-like morphology or irregular contours. Such siliceous fibrous particles were supposed to be degradation products from possibly several types of vitreous fibers. The geometric mean of siliceous MMVSF concentrations detected by ATEM was 70 fibers/mg for workers and 60 fibers/mg for referents. Overall fiber dimensions were similar in both groups (mean length 7.3 μm, mean diameter 1.1 μm), although fibers from workers’ lungs exhibited higher aspect ratios. Correlations between exposure variables and fiber concentrations in the lung samples as measured by ATEM were examined, but none approached significance.

The most notable finding reported was the absence of MMVSF from most workers’ lungs, from which it was concluded that the fibrous dust particles to which production workers had been exposed were either essentially nonrespirable or, more probably, did not survive the pulmonary environment.

Very recently, Kilburn, Powers, and Warshaw (13) reported on the lung content of one worker, who had been insulating refrigerators for 25 years. Ferruginous bodies, all with glass cores, were present at a concentration of 0.8 fibers/mg. Glass fibers were also encountered by transmission electron microscopy.

**Mineral Wool**
In their study of the American cohort of MMVSF production workers, McDonald et al. (11) obtained lung tissue samples from 11 men employed in mineral wool plants. The methods for selecting referents and analyzing the fiber content of the paraffin blocks were similar to those for the fibrous glass group.

As in the fibrous glass group, lung concentrations of fibers detected by PCOM and siliceous MMVSF detected by ATEM were low and similar for workers and referents. No other type of MMVSF was detected by ATEM. The fiber concentrations were, perhaps, slightly lower for the mineral wool group than for the fibrous glass group, but the difference was not statistically significant.

**Refractory Ceramic Fibers**
Sébastien et al. (14) analyzed by ATEM the fibers recovered in bronchoalveolar
lavage (BAL) fluids obtained from seven current workers in a ceramic fiber plant in France. These men (aged 33 to 56 years, four current smokers, two nonsmokers, one ex-smoker) had been employed exclusively at primary production for periods ranging from 10 to 21 years. All were healthy and volunteered for BAL. No precise information was reported on the chemical types of fibers produced. Recent dust measurement in this plant indicated that airborne fiber concentrations were in the range 0.2 to 1.4 f/cc. Fibers were extracted from the biological fluids using a combination of filtration, low temperature ashing, and light chemical treatment with sodium hypochlorite.

Both native and highly transformed ceramic fibers were detected. The native fibers exhibited an aluminosilicate type of chemistry typical of ceramic. Their mean fiber length was 9.9 μm and mean diameter, 0.6 μm. The concentrations of fibers detected by ATEM >5 μm in length in BAL fluids ranged from 63 to 764 fibers/ml. There was a positive relationship between the native fiber content and the cellularity of the BAL fluids.

The transformed fibers exhibited a spectrum of morphological features and elemental compositions. Some retained a typical ceramic chemistry but were heavily coated with iron-containing material. Others had a hollow tube morphology, made up of fine iron-containing granules without any of the normal major ceramic elements, and were sometimes found lying under a bed of siliceous leachate.

The size distributions of the native and transformed fibers were similar. The numerical concentrations were in the range 69 to 1069 f/cc. The ratios of transformed to native fibers were higher in the two nonsmokers. There was no relationship between the concentrations of fibers of either type and the duration of exposure. The transformation process was considered first, to involve a coating of the ceramic fibers with iron-containing granules, followed by a progressive dissolution of the structural elements, indicating that ceramic fibers may not be durable in the human lung.

**Discussion**

For more than 20 years, several laboratories around the world have been involved in measuring fibers in human lung tissue, and the large body of data so produced has been reviewed (15). There are many references to asbestos and other types of mineral fibers, but only incidental reports on man-made fibers. There is not a single report of a substantial pulmonary concentration of MMVSF, which may be an indication that the biopersistence of MMVSF in the human lung is rather low, at least lower than that of asbestos. Even for chrysotile asbestos, the biopersistence of which is lower than that of amphibole asbestos, but for which high pulmonary concentrations have been reported.

Although the studies reviewed here focused on cases with specific occupational exposure to MMVSF, the available data did not provide evidence of substantial long-term retention of fibers in the human lung. These data, however, have serious limitations. A first limitation comes from the fact that not all fiber types were equally documented. Two major studies were devoted to fibrous glass, but data are very scanty for mineral wool and refractory ceramic fibers. Because the chemical composition of the fibers is probably an important determinant of biopersistence, the possibility cannot be excluded that some types of MMVSF, not sampled so far by the analytical laboratories involved in pulmonary fiber measurements, could biopersist in the human lung. For example, there is a strong indication that silicon carbide fibers, a special type of man-made crystalline inorganic fiber, are biopersistent in the human lung (16).

For fibrous glass, two well designed studies share several interesting features. Both involved occupationally exposed groups with long duration of employment and carefully selected comparison groups, and both were able to detect the presence of some glass fibers in fragments of human lung parenchyma. This constitutes the first direct demonstration that some fibers of this type are respirable. A deposition model (8) relates the probability of alveolar deposition in the human lung to the equivalent mass diameter (EMD) of the fibers. The EMD of a fiber is defined as the diameter of the unit density sphere having the same mass as the mass of the fiber. An EMD value of 3.4 μm can be calculated using the average dimensions of the fibers analyzed by transmission electron microscopy by McDonald et al. (11). In the range 0.5 to 10 μm EMD, the model indicates that the probability curve has a bell shape. Interestingly enough, the alveolar deposition is maximum for 3.0 μm EMD, a value very close to the 3.4 μm EMD measured for the lung fibers. Both studies reported low concentrations of fibers in lung parenchyma and failed to detect excessive lung retention at death for the occupational groups. These negative findings could be explained either by similar exposure experiences to respirable airborne glass fibers of workers and controls or by the fact that although the workers experienced specific occupational exposure, the inhaled fibers rapidly disappeared from the lung after the end of employment and were not detected in the tissue samples taken at death.

In support of the first explanation, the average intensity of exposure in fibrous glass production plants was rather low, estimated at 0.04 f/cc of fibers <3 μm in diameter and visible by light microscopy, for the American cohort (12). A very similar mean value of 0.03 f/cc was reported for European plants (17); but even if, by occupational standards, these exposures were low, it is not reasonable to think that the controls from the "general population" were not exposed to these same levels. The alternative explanation would be that of a certain nonbiopersistence of the fibers in the human lung. In the study of the American MMVSF workers (11), the period between last employment and lung tissue collection at death averaged 12 years. If fibers dissolve quickly in the lung, what has been measured in both the occupational and control groups could correspond to trivial concentrations of recently inhaled fibers, reflecting a general background of air pollution by glass fibers. Other lung studies using a sufficiently low detection limit also reported trivial concentrations of glass fibers (18).

These considerations, together with direct observation by electron microscopy of pulmonary fibers with clear morphological signs of dissolution (11), and many experimental data, make highly plausible the hypothesis of nonbiopersistence of glass fibers in the human lung. Although the supportive data are too preliminary, the same hypothesis also may apply to other types of MMVSF. In this context, the kinetics of pulmonary clearance constitutes a key question. Can the inhaled fibers survive long enough in the pulmonary environment to express their toxicological potential?

There is no human data on the pulmonary clearance of MMVSF. Samples of lung tissue taken at death were not very informative, probably because the time between exposure and retention measurement was too long. In this respect, the previously reported analyses in BAL samples of workers currently exposed to ceramic fibers appeared as a quite unique
opportunity to have made observations in the course of the dissolution process (14).

Overall, for practical and ethical reasons, a direct assessment of the pulmonary
clearance of MMVSF in humans is not possible. This justifies the ongoing theoretical
and experimental efforts to understand the behavior of MMVSF in several biologi-
cal environments, with the ultimate goal of predicting their behavior in the human lung.

REFERENCES

1. TIMA nomenclature committee. Man-made Vitreous Fibers: Nomenclature, Chemistry and Physical Properties. Thermal
Insulation Manufacturers Association, Inc. Stamford, CT, 1991.
2. Cooke TF. Inorganic fibers—a literature review. J Am Ceram Soc
74:2959–2978 (1991).
3. WHO. Biological Effects of Man-made Mineral Fibers, Vol 2. Proceedings of a WHO/IARC Conference held 20–24 April 1982
in Copenhagen. Copenhagen: World Health Organization, 1984:1–17.
4. Wastiaux A, Blanchard O, Trolard F, Pianka N, Guillemette A, Oisel AM, Sébastien, P. Études sur la Durabilité des Fibres
Minérales de Synthèse en Milieux Biologiques. Verneuil en
Halatte, France: Institut National de l’Environnement Industriel et
des Risques, 1991.
5. Stanton ME, Layard M, Tegeris A, Miller E, May M, Smith A. Relation of particle dimension to carcinogenicity in amphibole
asbestos and other fibrous minerals. J Natl Cancer Inst 67:965–975 (1981).
6. Pott F, Ziem U, Reiffer FJ, Hurth F, Ernst H, Mohr U. Carcinogenicity studies on fibres, metal compounds and some
other dusts in rats. Exp Pathol 32:129–152 (1987).
7. Brown SK. Characterization of the fiber diameter distributions of synthetic mineral fiber products and their dusts. Am Ind Hyg
Assoc J 53:27–33 (1992).
8. Asgharian B, Yu CP. Deposition of inhaled fibrous particles in the human lung. J Aerosol Med 1:37–46 (1988).
9. Sébastien P. Pulmonary deposition and clearance of airborne mineral fibers. In: Mineral Fibers and Health (D. Lidell, K. Miller, eds). Boca Raton, FL:CRC Press, 1991;229–248.
10. Gross P, Tuma J, de Treville RTP. Lungs of workers exposed to
fiber glass—a study of their pathologic changes and their dust con-
tent. Arch Environ Health 23:67–76 (1971).
11. McDonald JC, Case BW, Enterline PE, Henderson V, McDonald
AD, Plourde M, Sébastien P. Lung dust analysis in the assessment
of past exposure of man-made mineral fibre workers. Ann Occup
Hyg 34:427–441 (1990).
12. Enterline PE, Marsh GM, Henderson V, Callaghan C. Mortality
update of a cohort of U.S. man-made mineral fibre workers.
Ann Occup Hyg 31:625–656 (1987).
13. Kilburn KH, Powers D, Warshaw RH. Pulmonary effects of expo-
sure to fine fibreglass: irregular opacities and small airways obstruc-
tion. Br J Ind Med 49:714–720 (1992).
14. Sébastien P, Vergnon JM, Blanchard O, Wastiaux A, Emonot A. Durability of ceramic fibres in the human lung. Presented at the
Seventh World Occupational Hygiene Society International Symposium on Inhaled Particles held 16–20 September 1991 in
Edinburgh. In press.
15. Churg A, Wright JL. Persistence of natural mineral fibers in human lungs—an overview. Environ Health Perspect (Suppl
5):229–233 (1994).
16. Duffresne A, Loosemewani B, Harrigan M, Sébastien P, Perrault
G, Bégirin R. Pulmonary dust retention in a silicon carbide worker.
Am Ind Hyg Assoc J 54:327–330 (1993).
17. Dodson J, Cherrie J, Groat S. Estimates of past exposure to respi-
rable man-made mineral fibres in the European insulation wool
industry. Ann Occup Hyg 31:567–582 (1987).
18. Roggl V. Nonasbestos mineral fibers in human lungs. In: Microbeam Analysis (PE Russell, ed). San Francisco:San Francisco
Press, 1989:136–138.