Pulmonary Deposition and Clearance of Glass Fiber in Rat Lungs after Long-term Inhalation

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In this study Wistar male rats were exposed to glass fiber obtained by the disintegration of a binderless glass fiber filter, for 6 hr/day, 5 days/week for 12 months. The mass median aerodynamic diameter (MMAD) of the fiber, determined with an Andersen sampler, was 2.6 μm. The count median diameter and length of the fibers measured by scanning electron microscopy (SEM) were 0.51 and 5.5 μm, respectively. The daily average exposure fiber concentration was 2.2 ± 0.6 mg/m³. Some rats were sacrificed 24 hr after removal from the exposure chamber following the 12 months' exposure. Others were sacrificed 12 months after the end of exposure. The wet organ weights were recorded at the time of death and the silicon content of the lungs was determined by absorption spectrophotometry. After 12 months' exposure, the amount of glass fiber retained in the rat lungs was 1.49 mg, and after 12 months' clearance it was 0.61 mg. The biological half-life in a single exponential model was to be 8.7 months, much longer than the predicted value of 1.5 months obtained in a previous experiment in which rats were exposed for 4 weeks to the same glass fiber.

Key words: pulmonary deposition, clearance, glass fiber, inhalation, biological half-life, durability

Introduction

It has been shown that occupational exposure to various types of asbestos may lead to asbestosis, bronchial cancer, and pleural and peritoneal mesotheliomas. In avoiding these asbestos-related diseases, the use of man-made mineral fibers (MMMF) as asbestos substitutes has increased, but the effects of MMMF on health also need to be investigated. Studies generally attempt to relate measured environmental concentrations of a toxic agent to an observed pathological effect. However, an important step in establishing dose-response relationships is to determine how much of the inhaled fibers is deposited in the various regions of the respiratory tract. The observed biological effect can be related more directly to the quantity and location of the deposited toxicant, rather than to the environmental concentration.

In this study, 27 Wistar male rats were exposed to glass fiber by inhalation of 6 hr/day, 5 days/week for 12 months. Lung burdens were measured after 12 months' exposure, and 12 months after exposure had terminated.

Materials and Methods

The exposure system and the experimental procedure have been described (1). The glass fibers used in this experiment were made from a binderless glass fiber filter (GB100R, Advantec Toyo Co., Japan). The filter was disintegrated three times by an ultracentrifugal mill (Retch Co., FRG) at a speed of 10,000 rpm. The composition of the glass fiber is as follows: SiO₂: 63%, Na₂O: 15%, CaO: 6%, B₂O₃: 6%, Al₂O₃: 5%, MgO: 3%, and traces.

The glass fiber concentration in the chamber was monitored continuously by a light scattering method (Dust Monitor AP-632, Shibata Sci. Tech. Co., Japan). The mass concentration of glass fiber was 2.2 ± 0.6 mg/m³, measured gravimetrically each day by isokinetic sampling of air through a glass fiber filter.

The mass median aerodynamic diameter (MMAD: 2.6 μm) and the geometric standard deviation (GSD: 1.9) of the glass fiber in the exposure chamber were measured by using an Andersen cascade impactor (AN-200, Shibata Sci. Tech. Co., Japan). The count median diameter (CMD: 0.51 μm) and count median length (CML: 5.5 μm) of the glass fiber in the chamber were determined by a scanning electron microscope (S-700, Hitachi, Japan).

Twenty-seven Wistar male rats were used in this study. They were randomly allocated to control and test groups. The test rats were exposed to glass fiber for 12 months. Controls were exposed to clean air in identical, adjacent chambers under similar conditions of flow, temperature, and humidity.

To study deposition, some rats were sacrificed 24 hr after removal from the chambers, following exposure for 12 months. To study clearance, the remaining rats were killed 12 months after the end of exposure. The body weights and the wet organ (lung, kidneys, liver, and spleen) weights were measured, and the lungs were ashed at low temperature (approximately 150°C) in a plasma asher (LAT-2SN, Yanaco, Japan). These samples of ash were fused with sodium carbonate in a platinum crucible and the silicon content measured by absorption spectrophotometry (2).

Results

There were no significant differences in the body weight and wet organ weights between the exposed rats and controls at the time of sacrifice.

The amount of the retained glass fiber in the lung was estimated from the difference in lung silicon content between the exposed rats and the controls, taking into account that the SiO₂ content of the glass was 63%. The maximum glass fiber content in the rat lung was 1.49 mg, determined in the exposed rats at 1 day after the 12-month exposure; thereafter the retained glass fiber content of the lung decreased with the post-exposure time (Figure 1). The upper solid line in Figure 1 was calcu-
Comparison of these results show that there is a major difference between the biological half-life determined in a short-term exposure and that in a long-term exposure. Vincent et al. (7) proposed that the amount of lung burden can be predicted by simple models, and that during prolonged chronic exposure, the linearity of the increase in lung burden can be explained by a "sequestration" kinetic model.

The relationship between the lung burden per unit respirable dust exposure concentration and the exposure time in this present long-term exposure study was in fairly good agreement with the prediction using the "sequestration" kinetic model that suggests that the longer a particle remains in the lung without being cleared, the more likely it is to be sequestered.

Deposition and clearance are important factors in the inhalation hazard of fibrous particles and should be monitored continuously.

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