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Fiber Toxicology and Occupational Health: The Integration of Research And Health Programs

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The potential toxic consequences involved in the manufacture and use of manmade fibers (especially fiber glass and other man-made vitreous fibers) invoke the sense that we have been here before. But the manmade fibers are physicochemically unique; they differ from the mineral fibers and from each other. Unlike the problems associated with asbestos, in which the untoward properties became apparent only after the long and widespread use of the mineral, there is continuing and worldwide investigation of the epidemiology and toxicology of many of the manmade fibers. The questions recently raised about the advisability of removing remainant asbestos from the environment has focused the attention of physicians and scientists on the potential for a new epidemic of occupational and environmental lung diseases caused by the newer fibers.

Background

There is growing contention about the risk of exposure to asbestos and the rationale for asbestos removal. This was recently pointed out by an article in *Science* (1990;247:294) by Brooke T. Mossman and her colleagues. They raised the question of whether there is a potential for a third wave of asbestos-related disease among persons neither engaged in manufacturing asbestos nor among its end users. The article was hotly debated in the letters to the editor of that publication.

The paper concerned the relative risks of removing chrysotile (the predominant form), crocidolite, and other forms of asbestos from buildings. The

Editor's Comment

It is premature to write an epilogue for the chronicle of asbestosis. There are chapters yet to be written and precepts begging formulation. But the lessons already at hand need to be indelibly taken to heart by every physician and by every member of society. It is clearly established that exposure to amphibole asbestos fibers imparts an important risk for fibrosing lung disease, and an important and specific risk for mesothelioma. Furthermore, there is little room for debate regarding the synergy for bronchogenic carcinoma when such an exposure coincides with cigarette smoking.

To establish these tenets as "facts" required more than a genius for clinical investigation: it required zeal and perseverance on behalf of the worker at risk[1] to convince the skeptic and overcome the inertia inherent in any attempt to shift moneys from profits to welfare. We have come that far. Asbestos exposure in the industrial setting is regulated; no more than two fibers in 10 mL of air is permissible. Furthermore, we have held perpetrators of exposure accountable after the "fact" for events that occurred before the "fact"—levels of accountability measured in tens of billions of dollars

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that drove such corporations as Johns Manville and Raybestos into bankruptcy to deal with the process.[1] Such is our collective guilt.

But here the issue doesn't rest. The same zeal drives extrapolations from these "facts":

1. What stochastic imperative defines the "permissable risk? How does one balance cost with conscience?

2. Most asbestos mined is not amphibole but serpentine fibers; more particularly, 90% or more of the world's asbestos mining yields chrysotile, a serpentine fiber. These fibers have far less toxicity than amphibole fibers. In fact, it has been argued that the risk is negligible[3] and that our national mandate to remove asbestos from public buildings is a waste of money and, possibly, a hazard[4] regardless of the fiber.

These issues engender debates that are fueled by emotion[5] wherein conviction supplants data. But conviction supplants data of necessity. Epidemiology can cope with rare events but only if they cluster or if they are qualitatively unique. Otherwise, so much goes on in any complex system, such as a population of people, that all manner of influences perturb the likelihood of a rare event.[6,7] The lingering debates about asbestos will rage *until all spleens are vented, and data is not likely to come to the rescue.*

Knowing the asbestos saga, how can we be prescient regarding other and new fibers that are taking their places in our environment? Addressing that question was my charge to Dr. Bunn and his co-authors. Dr. Bunn, my co-editor, and Dr. Bender are responsible for health and environment at two of the largest fiber manufacturers in the US. If any of us needs to learn lessons from the asbestos story, they do. We want to share their insights.

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authors questioned current risk-assessments on the grounds they were too conservative: the public faces a greater hazard in removal, they said, than in maintenance. Furthermore, the cost of removal programs, estimated at over $100 billion, might be better spent on primary asbestosis-prevention programs. Finally, there was some concern raised regarding the potential toxicity of asbestos substitutes.

The debate extended beyond *Science* and rapidly reached the public. It is unlikely the issue will soon be resolved scientifically; but, we may assume, even without such resolution, asbestos will be removed and the ban on asbestos-related products will continue, with or without modification.

Medical (and legal) practitioners will have to adopt positions in this debate: asbestosis and other pneumoconioses are difficult to diagnose in the early stages and often occur in the setting of other insults, such as smoking. Epidemiologic methods are less powerful in such a circumstance. Society and medicine both are wont to draw causal inferences from prominent individual cases. The result is that anecdote and emotion drive political, regulatory, and judicial activity at least as effectively as does science.

The recent quandary faced by physicians over asbestos-related disease introduces the need for the medical community to understand pulmonary toxicity and fiber (or particulate) toxicology. These issues are not only controversial today, but, it must be re-emphasized, developing technology will have future impact.

The pneumoconioses in historical perspective

Asbestosis, the scarring of the lung, was known early in the 20th Century and perhaps as early as the 1890s. Because of the need to insulate ships rapidly during World Wars I and II, its incidence increased greatly. Although the association of asbestos exposure and lung cancer (lung tumors and mesothelioma) was once a matter of debate, the recognition of the association occurred during the 1950s and '60s. The most-recent research concerns the reduction of nonoccupational exposures stemming from removal of asbestos-containing products from buildings.

Perhaps the greatest lesson to be learned is that it is imperative that we anticipate the health effects of exposure to fiber. We still do not fully understand fiber toxicity, but the past hundred years of scientific scrutiny and public response must serve to guide consideration of other naturally occurring or man-made fibers and particulates. The recognition of the relationship to cancer in the '50s and '60s spurred a reaction that included regulations by the Occupational Safety and Health Administration (OSHA) and, in the '70s, litigation that has been going on since. In the '80s, concern for a low level of risk led to the removal of asbestos from public schools and other buildings and to a ban on asbestos-containing products. These latter measures have led to the current scientific debate.

Fibers are not the only fibrogenic pulmonary toxins. For example, that crystalline silica causes lung scarring has been known since the time of Hippocrates. Silicosis gained general attention after the Gauley Bridge incident in 1937, resulting in acute silicotic

reaction in a group of miners.* That attention led to social reform in occupational health regulations and compensation (primarily Worker's Compensation) for silicotic disease processes.

Coal workers' pneumoconioses have been well recognized since the early 1800s, but it took a century to awaken the public conscience—and then only after the Farmington mine disaster of 1968. The high-water mark of mine safety in the US was reached with the enactment of the Black Lung Act of 1969. Other pulmonary diseases, such as byssinosis and beryllliosis, have been the subject of regulation, litigation, and debate for many years.

THE EPIDEMILOGY AND TOXICOLOGY OF FIBERS

Natural fibers

Asbestos is a naturally occurring mineral fiber the toxicologic and epidemiologic effects of which have been well documented. Standards for workplace exposure and work practices exist in most developed countries. However, there is a need to evaluate the risk posed by other naturally occurring fibers (eg, erionite). A body of information is emerging on these fibers, but specific regulations exist in only a few countries.

Erionite

Zeolite is a naturally occurring, crystalline, hydrated aluminosilicate; erionite is a crystalline, fibrous form. It is found naturally in the western United States, Turkey, South Africa, and elsewhere. Erionite has very limited commercial application, but exposure occurs because it is a contaminant in the mining and manufacture of other zeolites (which do have commercial value, as molecular sieves and in ion-exchange processes).

Erionite can produce tumors, particularly mesothelioma, in mice and rats that inhale it. Villages near Turkish erionite deposits have been found to have high incidences of mesotheliomas, but the issue is somewhat clouded by the fact that other fibers—including asbestos—are present in these areas. In animals, erionite appears to be a more-potent mesotheliomogenic agent than is asbestos. No consensus has been reached on acceptable levels of occupational exposure to the fiber, so no recommendations have been made, nor have definitive regulatory reviews been conducted for erionite, wollastonite, or attapulgite.

Wollastonite

In such products as ceramics, insulation, and wallboard, wollastonite—a monocalcium silicate fiber—is used as an asbestos replacement. It is a durable fiber, but it has less tensile strength than asbestos. Toxicologic studies of wollastonite are limited: the only inhalation study in animals failed to produce a significant tumor-response. Injection and in vitro studies suggest that wollastonite is less toxic than asbestos. Epidemiologic studies of the neoplastic potential of wollastonite have not been conducted, and studies of its fibrotic potential are limited.

Overall, the health studies of wollastonite are sparse. Exposure levels vary widely with the application and the industry: fiber levels of up to 40 to 50 fibers/cc (f/cc) have sometimes been reported.

Attapulgite

A fibrous aluminum silicate and magnesium silicate, attapulgite is used as a thickening agent and an absorbent, as in pet litter. It is mined primarily in the United States. The fibers are short and relatively thin, although the size varies with the geographic region of the deposit. The effect of attapulgite in animals has varied significantly from study to study. These differences appear to be related to the origin of the fiber. Inhalation studies in animals suggest that the longer the fiber the greater the toxicity. This result is consistent with injection and in vitro studies, although there is considerable variability.

The epidemiologic data on attapulgite is very limited and does not yield data useful for assessing its hazards. Overall, the data suggests that two risk-profiles exist, one for origin the other for fiber length. The data on exposure is variable, but dust levels for certain operations approach the standards for nuisance dust (15 mg/m³ total, 5 mg/m³ respirable).

MAN-MADE VITREOUS FIBERS

For more than 50 years, the man-made vitreous fibers (MMVFs) have been produced and used in a wide variety of applications. They are synthetic, inorganic, and amorphous; the family is sometimes referred to as "man-made mineral fibers" (MMMFs), but, technically, MMVF is more correct. These fibers are all created from molten masses of raw material under highly controlled conditions. Fiber glass is one MMVF, which also includes rock/slag (mineral) wool and refractory ceramic fiber (RCF).

"Man-made fibers have similar irritant effects the extent of which depends on the diameter and flexibility of the fiber."

Much more is known of the epidemiology of vitreous fibers than is known of other man-made fibers or non-asbestos natural fibers. In addition, chronic inhalation and other toxicologic testing has been performed. Specific standards do not exist in the United States (except as nuisance dust), but broader standards are currently under consideration and multiple international bodies have already reviewed the scientific literature on man-made vitreous fibers.

Fiber glass

Two basic forms of fiber glass are in general use: wool-type fibers and textile fibers. Fiber glass was originally developed in the early 1930s for use in home panel filters and home insulation; textile fibers appeared commercially in the late 1930s, followed by fine-diameter glass fibers in the early 1940s.

Wool fiber-glass is generally used in thermal and acoustical insulation. These products include air-duct insulation, pipe insulation, ventilation-system air-filters, roof insulation, and insulation for

*At Gauley Bridge, West Virginia, workers were exposed to high levels of crystalline silica when tunnelling through a mountain with a high quartz content. The minimum exposure necessary to produce silicosis was then thought to be two years, but a number of workers with less than two years' exposure developed an acute pulmonary process and many died. The event led to the recognition of acute silicosis and triggered a deeper scrutiny of the chronic effects of crystalline silica.

homes, automobiles, aircraft, cooling appliances, and refrigerators.

Glass fibers are also manufactured with diameters of less than one μ. This fine-diameter material is produced in the United States in limited quantities that constitute less than 1% of the total fiber glass production. Special-purpose, fine fiber is limited to use in specialty filter papers, battery components, and sophisticated aerospace insulations.

Textile fiber-glass finds wide application as a component of curtains, industrial fabrics, electrical yarns, roofing shingles, and reinforcement for plastics, papers, rubber, and other materials. It is generally not of respirable size.

Health effects of fiber glass

Skin irritation. Fiber glass may irritate the skin of some workers in glass-fiber–manufacturing facilities and of some workers who fabricate or install fiber-glass–containing materials. The skin irritation and possible inflammation is a mechanical reaction to sharp broken ends of fiber that rub or become embedded in the outer layer of the skin. Skin reactions vary directly with the size and the stiffness of the fiber: those with diameters greater than 4 to 5 μ are more likely to cause irritation than are finer-diameter fibers. When the diameter is less than 1.0 μ, the fibers usually do not cause skin irritation. Normally, the irritation does not persist for long, and it can usually be relieved by using mild soap and warm water to gently wash the exposed areas. Most workers find that any irritation experienced when first working with fiber glass lessens over time. Allergic contact dermatitis has not been associated with exposure to fiber glass, but there have been reports of allergic reactions to the uncured-resin finishes that are used in some fiber-glass products.

Some persons may be more affected by irritation from fiber glass than are others, and a few may be forced to seek other types of employment. The vast majority of workers, however, can control skin irritation by using appropriate work practices. Man-made fibers have similar irritant effects the extent of which depends on the diameter and flexibility of the fiber.

Upper respiratory irritation. Some workers may experience a temporary upper respiratory irritation manifested as a scratchiness or burning of the nose or throat. This is especially likely if, during the manufacture or handling of glass-containing products, more than 3 to 5 f/cc are released and if they are of large diameter (more than 5 to 6 μ). Like skin irritation, upper respiratory irritation is a mechanical reaction to sharp, broken fibers.

Accidental exposures to high concentrations of airborne glass fiber may, like exposure to dust, produce a nonspecific, transitory, lung condition usually manifested by coughing or wheezing. The effects subside soon after the worker is removed from exposure, and there should be no further effect on the worker's health and well-being. Exposure to fiber glass does not sensitize the lung nor produce allergic reaction.

> *"Exposure to fiber glass does not sensitize the lung nor produce allergic reaction."*

Epidemiologic studies

Respiratory system diseases are the primary subjects of most epidemiologic studies involving fiber glass and other MMVFs. Tens of thousands of workers have been employed in manufacturing fiber glass since its initial development over 50 years ago, and two major studies have addressed the mortality of workers engaged in that production. Researchers at the University of Pittsburgh studied the mortality of almost 15,000 workers from 11 fiber-glass–manufacturing facilities. This study has been expanded to include over 30,000 workers from 14 such facilities. The first results from the enlarged study will be available in 1992. In Europe, researchers at the International Agency for Research on Cancer (IARC) have conducted a five-country study of mortality among almost 12,000 workers at six plants manufacturing fiber glass. An update of this study is under way.

In 1984, Saracci et al published their study of the mortality of 23,609 workers (including 11,852 workers producing fiber glass) in 13 European factories producing MMVFs. There were 2,836 deaths. That study was updated by Simonato et al in 1986. The authors reported that, compared to regional rates, glass workers suffered no excess mortality from lung cancer. However, they did report an "excess of lung cancer among rock wool/slag-wool workers employed during an early technological phase before the introduction of dust-s[illegible]essing agents." They concluded that "fiber exposure, either alone or in combination with other exposures, may have contributed to the elevated risk. More-recent studies have shown several potential confounders in the mineral wool industry." The authors also reported that "no excess of the same magnitude was evident for glass-wool production." Also, "there was no evidence of an increased risk for pleural tumors or nonmalignant respiratory diseases."

The University of Pittsburgh comprehensive mortality study of over 16,000 workers, many with long-term exposure (up to 40 years), was undertaken at 17 fiber-glass– and mineral-wool–manufacturing plants (14,800 fiber-glass workers in 11 plants). The original report, published in 1982, covered mortality from the 1940s to the end of 1977. The same group of workers was followed through 1982 (reported in October, 1986, with additional analyses in June, 1987). The 1987 report contained, for the first time, local area mortality statistics for each of the plants. The study was further updated through 1985, with publication in 1990. Through 1982, malignant respiratory disease had caused no statistically significant excess of deaths in any of the 11 fiber-glass plants, nor in any grouping that distinguished those plants on the basis of glass-wool or textile production (textile fibers are referred to as "glass filament" in the manuscript and by IARC).

The update through 1985, however, did show a statistically significant excess of deaths from respiratory cancer among workers employed in glass-wool and mineral-wool plants. To see if the data were consistent with a cause–effect relationship specific for exposure to glass fibers, the researchers investigated possible associations of excess cancer deaths with length of employment, dose response, time from initial employment, and the manufacture of still-finer glass-fibers (microfibers). There were no statistically significant findings in support of a relationship between respiratory disease and exposure to glass fibers.

A recent case–control study was undertaken in which those workers were studied who had manufactured fiber glass and who had participated in the University of Pittsburgh study. The interview portion of the later study showed that smoking is the most-important nonworkplace factor in lung cancer among the fiber-glass–manufacturing employees. Smoking at the Newark, Ohio, plant in 1955 was significantly greater than in the rest of the US, suggesting that cigarettes could account for

some of the excess lung cancer previously reported in the University Pittsburgh study.

Other than the statistically significant standardized mortality rate, no noteworthy mortality findings—such as from nonmalignant respiratory disease or mesotheliomas—were associated with exposure to fiber glass.

Morbidity among fiber-glass workers has also been studied. None of the major studies reported a consistent pattern of respiratory disease; nor was any impairment found of the respiratory function of manufacturing workers, even among those with extensive exposure. In the most-comprehensive study, Weill reported on the respiratory health of 1,089 workers at five fiber-glass and two mineral-wool plants in the United States during 1979 and 1980.

The researchers noted that the subjects were generally healthy. However, small opacities did show on the chest x-rays of some workers. In summarizing their findings, the authors noted that, in general, "the minimal evidence of respiratory effects detected in the investigation, which cannot, at present, be considered clinically significant, is encouraging concerning the question of potential health effects of exposure to man-made vitreous fiber." A follow-up study with controls, reported by Weill in 1985 and 1990, found no adverse pulmonary effects associated with work in the MMVF industry.

Experimental studies

Researchers have studied the effects of surgically implanting fibrous material in the pleural and abdominal cavities of animals and of injecting fibers directly into the trachea. In 1977, it was found in such work that tissue changes, including cancer and scarring, were produced by specialty glass-fibers with diameters of less than 1.0 μ. Other fiber-glass compositions, including those used in building insulation, did not produce such results.

These experiments are valuable in the study of the mechanisms of tissue reactions, but, because they are based on the introduction of large amounts of fiber by routes that bypass normal body-defense-mechanisms, they do not justify the conclusion that inhalation of glass fiber is hazardous to workers. As a consequence, several inhalation studies in animals were initiated at independent research centers. Commercially available fiber-glass products and, more recently, specially prepared fibers with carefully specified lengths and diameters were used. None of these studies demonstrated tumor induction or fibrosis by fibrous glass.

Risk evaluation

International and US agencies have conducted a number of reviews of the health aspects of glass fibers. These agencies included the National Institute for Occupational Safety and Health (1977), the World Health Organization (1984), and the National Academy of Sciences (1984). Recently, there have been two additional major reports prepared on the health effects of glass fibers.

In 1986, the International Agency for Research on Cancer (IARC) reviewed man-made mineral-fibers. After reviewing the epidemiologic data on over 400 deaths from lung cancer among the 27,000 fiber-glass workers in the European study (by Simonato et al) and the US study (by Enterline and Marsh), the 1987 IARC working group of the World Health Organization stated that the evidence was inadequate to conclude that either glass wool or glass filaments were carcinogenic to humans. No evidence of fibrosis or other morbidity was found by the IARC panel.

Despite seven negative inhalation studies in animals, implantation of microfibers of two special-purpose glasses induced cancer. This is the basis for the determination by the IARC that glass wool is "2B"—a possible human carcinogen. Continuous-filament fiber-glass was designated "Group 3"—it is "not classifiable as to human carcinogenicity."

In 1987, a second major, international evaluation of the safety of glass fibers by the World Health Organization (WHO), led to the report of the International Programme on Chemical Safety (IPCS): "The overall picture indicates that the possible risk of cancers among the general public is very low, if there is any at all, and should not be a cause for concern if the current low level of exposure continues." The IPCS does allow the weighting of evidence, and the inhalation studies in animals were given greater weight in their analysis. In 1988, the US Environmental Protection Agency announced its agreement with the IPCS conclusion when it stated that the evidence for the carcinogenicity of fiber glass "is considered inadequate."

Mineral wool

The fibers known as "mineral wool" are produced by spinning or blowing molten basalt or the slag obtained from refining ores. These latter consist of metal silicates—silicates of aluminum, boron, calcium, iron, sodium—and various metal oxides. Depending on the source, the average fiber diameter ranges from 3 to 15 μ.

Major application

In the early 1900s, mineral wool was developed as insulation. The fiber is generally supplied in three basic forms: loose wool, wool bonded into a batt or blanket, and acoustical tile and panels. Today, mineral wool is widely used to control temperature and sound. Its major applications are in commercial insulation, acoustical control products, pipe insulation, and insulation for automobiles, ships, mobile homes, refrigerators, domestic cooling appliances, and a wide variety of other appliances and equipment.

Health effects

The skin, eye, and upper respiratory irritations of mineral wool are similar to those of fiber glass.

Animal studies

Several inhalation studies with animals have been done at independent research centers. Commercially available mineral-wool was used. In two of these studies, the animals were exposed to high concentrations of fiber for one year or more and then allowed to live out the rest of their lives. Compared to the controls, none of the test animals demonstrated fibrogenesis, carcinogenesis, or permanent changes of the respiratory system; nor did the exposure reduce life expectancy to a significant degree.

Other studies of implanted, injected, or instilled mineral wool have shown that virtually all fibrous materials can, at very high dosages and regardless of physical or chemical makeup, have adverse effects. However, evidence from other experiments indicates that mineral wool is attacked by the fluids normally present in the lung. This may cause fragmentation into shorter fibers that may be biologically less active or may even lead to the total disappearance of very fine fibers.

Epidemiologic studies

Thousands of workers have been employed in plants that manufactured mineral wool during the 50 years since its development. A number of epidemiologic studies of workers have been done, but the two major mortality studies were those discussed above in the fiber-glass section. The excess lung cancer found in slag- and rock-wool workers was the most-disturbing finding, but that excess might be related to early production phases and to compounding

exposures to such carcinogens as lead, asbestos, or arsenic. In addition, the studies were difficult to control for other factors—smoking, for example—that could have contributed to the excess.

Refractory ceramic fiber

There are three broad categories of refractory ceramic fiber (RCF): kaolin-based fibers, in which the clay is obtained by mining; blends of alumina, silica, and a refractory metal oxide (eg, zirconia); and high-purity products that are a blend of alumina and silica processed to limit the levels of impurities that are found in other RCF products. The fibers are produced by spinning molten mixtures. The average diameter of the fibers produced in this manner is in the range of 1.2 to 3.5 μ. Fiber length can be varied from long fibers down to μ-sized.

Major application

Applications vary, but all are used in high-temperature, specialty environments. Blankets are used primarily as furnace and kiln-wall liners; loose fiber is used as a filler in packing voids and expansion joints; custom-molded shapes are widely used in metal molding and as furnace combustion-chamber liners.

Health effects

Skin irritation and upper respiratory irritation are largely the same as those found with fiber glass.

After-service effects

RCF that has been in service at elevated temperatures (greater than 1,800°F) will undergo partial conversion to cristobalite, a form of crystalline silica that can cause silicosis.

Epidemiologic studies

There are no published reports dealing with the health experience of people who work with RCFs. Two investigations, one in Europe and the other in the United States, are studying the health of workers engaged in the manufacture of RCFs. In October, 1989, a preliminary report from the European study of over 650 RCF-plant workers was made available. It noted that no evidence was found of pneumoconiosis and no effects were found in the lung-function tests of nonsmokers. Among current and former cigarette-smokers, the results of lung function tests were consistent with minimal obstruction associated with cigarette smoking and also, but to a lesser extent, with exposure to ceramic fiber. Some symptoms of dry cough and breathlessness were also found.

Small opacities were present on 13% of 594 chest x-rays. Primarily, these were related to age and to smoking habits and there was some evidence of an association with time spent in the industry (but not with cumulative exposure to RCF). It is not clear what the long-term biological significance may be of the small effects apparently related to ceramic fibers, and the study is likely to be continued.

Results from the US study will soon be available. Preliminary reports indicate a decrease in pulmonary function that is not clinically significant and a possible increase in pleural plaques among RCF-exposed workers. The latter findings may have been confounded by exposure to asbestos.

"Recent studies on animals may affect the risk evaluation for RCFs."

Inhalation studies

There have been four known investigations of the effects that high concentrations of airborne RCF have on animals. In one, 48 rats were exposed to RCF by inhalation for seven hours a day, five days a week, for 32 weeks. Fibers longer than 5 μ had airborne levels of 95 f/cc. Animals sacrificed at the end of the study had interstitial fibrosis in an average of 5% of the lung area; eight rats had pulmonary tumors, of which three were carcinomas; there was also one peritoneal mesothelioma.

In contrast, inhalation work at Los Alamos showed no cancer and little pulmonary fibrosis in rats; 50 hamsters showed one mesothelioma but no fibrosis. The exposures were conducted at 200 f/cc, six hours a day, five days a week, for 24 months. One of 157 control animals unexposed to fiber developed a spontaneous tumor.

In June, 1988, to help clarify some of the uncertainties, a two-year inhalation study in rats and hamsters was begun by TIMA (Thermal Insulation Manufacturing Association). Groups of rats were exposed for six hours per day, five days a week, to 30 mg/m³ of four different types of RCF: kaolin, zirconia, high purity, or "after service" (ie, a kaolin-based, ceramic fiber, containing 27% crystalline silica that had previously been exposed to high temperatures). Approximately 200 to 250 f/cc were greater than 5 μ in length. Hamsters were exposed only to kaolin RCFs. In both the rat and the hamster studies, positive controls inhaled 10 mg/m³ of chrysotile asbestos and negative controls received filtered air.

A total of 35% of the hamsters exposed to the kaolin RCF-fibers developed mesotheliomas. A nonmalignant mesothelial proliferation was found in the pleura of one of the asbestos-exposed hamsters; negative-control hamsters had no lung lesions. Cytologic examination of the lungs of the kaolin-exposed hamsters revealed pulmonary fibrosis in the terminal airways and pleura.

In the RCF-exposed rats, pathological studies revealed lung tumors (some benign), pulmonary tumors, and mesotheliomas. In asbestos-exposed rats, benign and malignant lung tumors were reported; the final results are not yet available. Cytologic examination of the rats sacrificed at one year showed that exposure to kaolin RCF, zirconia RCF, high purity RCF, "after service" RCF, and asbestos all resulted in pulmonary fibrosis. After the first year, the fibrosis progressed more slowly.

Risk evaluation

In 1987, IARC designated RCF as Group 2B, "possibly carcinogenic to humans," on the basis of animal studies. IPCS evaluated RCF with other MMVFs. Crystalline silica in the form of cristobalite has been classified by IARC as 2A, "probably carcinogenic to humans."

MMVF regulations

Although no US regulatory guidelines exist for any fibers, save asbestos, there are multiple recommendations. NIOSH (the National Institute for Occupational Safety and Health) recommended a 3 f/cc or 5 mg/m³ guideline in 1977. Fiber glass and mineral wool manufacturers recommend a standard of 1 f/cc, based on irritation. The Safety and Health Committee of the Building and Trades Department of the AFL-CIO also recommends a standard of 1 f/cc. An OSHA proposal is expected for fiber glass, mineral wool, and refractory ceramic fibers over the next year. Recent studies on animals may affect the risk evaluation for RCFs.

Control of levels of respirable particles or fibers is accomplished by a combination of engineering changes, work practices, and protective equipment. In addition, regular medical surveillance of exposed populations is recommended.

SYNTHETIC FIBERS

Aramid fibers

Aromatic polyamides constitute the aramid fibers, which are durable and have high tensile strength. These fibers generally fall outside the respirable range, but certain of them have fibrils that may break off and become respirable. It is not clear that fabrication generates either a fibrous or particulate respirable component.

Only a single experimental study of chronic exposure to aramid fibers has been conducted. Thin aramid fibers at a concentration of 100 f/cc produced fibrosis and rat-specific tumors. Short-term inhalation studies suggest that respirable organic fibers do generate a tissue response in animals; intraperitoneal injection studies have shown a slight increase in the incidence of tumors and of fibrosis. Exposures measured at manufacturing locations indicate fiber levels ranging from undetectable to less than 1.0 f/cc.

Carbon fibers

The term "carbon fibers" refers to both carbon and graphite fibers. They are synthetic fibers prepared by the high-temperature processing of polyacrylonitrile, pitch, or rayon. They are characterized by light weight, high tensile strength, and flexibility. The average diameter of the fiber is 5 to 8 μ, but up to 25% of the fibers are respirable by humans.

There have been two short-term inhalation studies, one subchronic and one chronic, of carbon-based fibers. Unfortunately the studies were conducted with materials that had large proportions of particulate matter or fibers that were not respirable by rats.

Injection studies have not shown a significant increase in tumors, but in vitro tests have shown both genotoxic and cytotoxic effects. Dermal studies have not shown statistically significant increases in tumors.

There have been only limited studies of exposed populations, and epidemiologic data is not available for risk assessment. What data there is on respirable carbon-fibers in the occupational setting indicates only minimal exposure.

Polyolefin fibers

The family of polyolefin fibers consists of polypropylene, polyethylene, and polycarbonate fibers. The major uses are in home furnishings such as rugs, upholstery, curtains, and bedding. These fibers are generally not respirable even though fine fibers are used for lightweight, insulating clothing and for air filtration.

There has been one subchronic inhalation study with sized polypropylene fibers; it showed biologic activity at 90 days, but no fibrosis. Variable, low levels of toxicity were found with injection and in vitro studies. No epidemiologic studies or data on workers exposed to polyolefin fibers have been published.

SUMMARY

This review of the scientific data shows that, in terms of physiologic effects, there are major differences from one man-made or natural fiber to the next. Most of the data is reassuring, but we do need to reduce levels of exposure and to detect disease at an early stage.

Personal risks and workplace protection-programs may become the subject of judicial or regulatory scrutiny. In that context, it is worth noting that, historically, the recognition of occupational pulmonary disease has come only *after* the fact, from the study of mortality patterns. This retrospective approach is no longer morally or sociopolitically acceptable. This paper, we hope, will supply the perspective and scientific overview that will allow physicians to make informed judgments about the risks currently associated with man-made and mineral fibers. ■

Special thanks to Thomas W Hesterberg, PhD, Senior Toxicologist, and Gerald R. Chase, PhD Chief Biostatistician/Epidemiologist, of the Manville Technical Center, Denver, Colorado They also contributed to this article

Suggested Reading

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MEDILEGAL BULLETIN

Regulation of the Manufacture and Use Of Potentially Hazardous Substances

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In the United States, the evaluation and regulation of the health effects of commercial products is both intensive and comprehensive; internationally, scrutiny is increasing. Before a new commercial product is introduced, it undergoes several levels of review.

For pharmaceuticals, pesticides, and consumer products, there are specific standards for full evaluation and regulatory review; appropriate testing is mandated before a new product can be approved. For chemicals, petroleum products, and other new commercial introductions, regulatory review is required by the Toxic Substances Control Act (TSCA). Regulatory authorities may also require special studies of po-

tential exposure. This evaluation of possible exposure and toxicity is intended to provide an assessment of risk and to lead to recommended practices that will minimize that risk to workers, downline manufacturers and distributors, and users. Specific labels may be required by the agencies involved.

The review extends to current products going into new uses or to new markets. For example, significant new use regulation (SNUR) requires review of significant new uses of a product; special review is required of materials manufactured in foreign countries when the products first enter commerce in the United States.

Because of the natural origin of the raw materials, most fibers have generally been thought to be excluded from TSCA-mandated review. However, a joint committee of industry and government has been formed to review test methods for the evaluation of the health effects of fibers and to consider guidelines for testing fibers entering commerce. This group is being coordinated through the Chemical Industry Institute of Toxicology.

Once a product enters the marketplace, multiple health and safety regulations, from multiple regulatory agencies, apply. Which regulatory agency is primary is usually determined by the circumstances of exposure, although there is substantial overlap and integration of regulatory functions: workers exposed to a potentially toxic substance are an Occupational Safety and Health Administration (OSHA) responsibility; the Environmental Protection Agency (EPA) regulates exposure of the general public.

The role of OSHA

OSHA directives include communication, general training, and specified methods of compliance. A permanent function of OSHA is to assure adequate communication of the potential hazards from the manufacturer of the product to the worker. The Hazard Communication Standard mandates a written program, including the labelling of products and work areas, the preparation of material safety data sheets, and training relative to specific hazards. Specific substances are regulated by imposing exposure limits for engineering controls and respiratory protection; work practice requirements; medical monitoring and surveillance standards; and other substance-specific conditions.

The role of EPA

The scope of EPA's functions is extensive and growing. In addition to initial review by the Office of Toxic Substances (OTS) under the authority conferred by the TSCA, a comprehensive program has evolved dedicated to reducing the risks associated with various particular media. For example, standards have been derived for clean water, clean air, the treatment and disposal of solid and liquid hazardous waste (under the authority of RCRA [the Resource Conservation and Recovery Act] and, subsequently, remediation under CERCLA [the Comprehensive Environmental Response, Compensation, and Liability Act]). Therefore, each emission from a manufacturer or user of a product is regulated. The liability is retrospective, joint, and several (ie, any and all parties are liable).

EPA is also required to communicate with communities that may be affected by storage and use of potentially hazardous substances through Title III of the Superfund Amendments and Reauthorization Act (SARA). The EPA also controls the quantities of chemicals that may be emitted, generates reports to encourage the reduction of waste, and develops Indoor Air Quality (IAQ) programs to protect the public from untoward exposures. The intention is to provide comprehensive, cradle-to-grave regulation of potentially hazardous substances.

Other venues

In addition to federal law, state and local laws regulate occupational and environmental exposures. States have laws requiring special labelling and imposing restrictions on release of substances. California, for examaple, has its Proposition 65 and "Toxic Hot Spots" regulations. Other states have implemented their own regulations, but most state and local regulations follow federal guidelines; even when they do, however, the implementation time or exposure limitations may be substantially different. The US government mandates diligent, ongoing review of federal, state, and local statutes.

International regulations pose unique problems for exporters and multinational corporations. The European Community has implemented regulations similar to the comprehensive regulatory structure in the US. Elsewhere in the world, health standards are rapidly expanding and evolving.

In addition to this regulatory framework, a second area of legal control is exercised through the tort system. Over the years, case law has evolved a series of precedents that impose significant liabilities on corporations (and individuals) that do not adequately test products, assess risk, communicate possible risks, and recommend work practices to assure the safety of persons exposed to the product. There is increasing recognition of a duty not only to inform but to perform a product-stewardship role.

Strict standards of liability for potentially hazardous products, and punitive damages for failure to institute effective programs, make this area of law—and medicine—particularly challenging. The multitude of regulatory standards, the development of common-law expectations, and the increase in worker and consumer awareness will make the 1990s a period of tremendous challenge for health professionals working with manufacturers, workers, and consumers. The combination of expanding sociopolitical concerns and new technologies and materials means the problems will increase, not lessen. Health professionals, then, must engage in risk evaluation and communication. This process begins with the recognition of the complexity and comprehensive nature of the regulations and includes a sensitivity (and an action-oriented approach) to both worker and consumer protection. ■

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