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THE ASBESTOS INSTITUTE

sensible management of a natural resource

Towards an Understanding of the Carcinogenicity of Fibrous Materials

The last decade has seen great advances in scientific understanding of the carcinogenic potential of some fibres. Recent studies of fibre dimensions, durability and dose-response relationships are helping to explain why some fibres, such as chrysotile asbestos are considered safe at low levels of exposure.

Twenty years ago, scientists had no clear understanding of the mechanisms of the carcinogenicity of fibrous materials. The principal parameter studied was fibre dimension, and the nature of the correlation between the length and width of a fibre and its carcinogenicity. It became clear from research programs of this nature that, although dimensions could explain some of the variations in the carcinogenic potential of different fibres, other factors were also involved.

With increased sophistication in analytical methods, scientists discovered that in addition to vast differences in fibre dimensions, there were also large variations in the durability of different fibres. The structure of some fibres were such that they could be cleared by the body's natural defense mechanisms more quickly than others.

Over the last 10 to 15 years, the concept of durability or biopersistence has played an increasingly important role in our understanding of the carcinogenicity of fibrous materials. Today, scientists are evaluating carcinogenicity of fibrous materials as an interaction between dose, dimension and durability or bio-persistence.

The dose makes the poison

In the 16th century, the Swiss physician Paracelsius wrote that all substances can be toxic. The difference between the remedy

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Inside

Asbestos Fibres in the General Environment

Studies find extremely low concentrations of mostly short asbestos fibres in the general environment.

A number of studies have been conducted in recent years to respond to concerns over what health risks, if any, arise from asbestos emissions in the general environment. Air sampling was conducted in various rural and urban environments as well as in the vicinity of asbestos-containing materials. Three major conclusions have emerged from this avenue of study.

Asbestos occurs naturally in the environment

The vast majority of asbestos fibres in the environment (air, soil, water, etc.) are the result of natural phenomena such as erosion. In fact, asbestos was present in the environment in similar quantities long before it was mined and used commercially.

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Environment...

Asbestos-containing materials contribute little to environmental fibre levels

Several studies have examined the effects of weathering on asbestos-cement products. Meyer (1986) concluded that the increase in asbestos fibre concentrations in the near vicinity of asbestos-cement cladding and roofing material caused by weathering is so small that it moves into the range below the limit of detection of SEM. In a similar study of emission measurements, Borneman and Hildebrandt (1986) found that airborne asbestos levels were significantly lower than 0.001 f/cc. In 1991, the Western Australia Department of Occupational Health, Safety and Welfare conducted an extensive review of environmental asbestos. The final report was comprised of school surveys, measurement studies and a literature review of the topic. The report found, based on air monitoring data gathered around schools with asbestos-cement roofs, that concentrations are unlikely to exceed 0.002 f/cc and are more likely to be less than 0.0002 f/cc.

Most particles released into the environment are innocuous short fibres

In addition to the fact that environmental concentrations have been found to be exceedingly low, other data shows those fibres detected are likely to be short. Chatfield (1983) reported to a Government of Sweden Symposium, that between 95 to 98% of fibres observed were shorter than 5µm. The 1984 *Report of the Royal Commission on Matters of Health and Safety Arising From the Use of Asbestos in Ontario* published similar findings. In its review of environmental asbestos, it noted the prevalence of very short fibres and low counts (a maximum of 0.0084 f/cc of all lengths). ■

References available from The Asbestos Institute.

The Health Effects of Low Levels of Chrysotile Exposure

The October 1992/January 1993 edition of The Asbestos Institute Newsletter published as its lead story, a summary and analysis of the preliminary results of a landmark study of the health effects of exposure to chrysotile. The study was of 5,351 Quebec asbestos workers born 1891-1920 who had survived into 1976. It was conducted by Drs. F.D.K. Liddell, A.D. McDonald and J.C. McDonald who found that "In each of six classes of exposure up to 300 mpcf x years, the lung cancer SMR [Standard Mortality Ratio = observed mortality/expected mortality] was close to 1.3 (a total of 254 cases of lung cancer among 4,384 men, against 190.6 expected): there was no evidence of a trend." (Abstract presented at the 9th International Symposium of Epidemiology in Occupational Health, Cincinnati, 1992).

The authors have expressed concern to us that the article's subtitle "Important study finds that at exposure levels below a threshold of 50 f/cc, chrysotile asbestos is not linked to any increased incidence of lung cancer" could lead to misunderstanding. The notion of a threshold was entirely our interpretation and not a direct quote of any of the authors or the study's abstract, which made no mention of such a concept. We wish to add that our use of the threshold concept was not meant to refer to a level below which the exposure risk is zero, since this cannot be proven with absolute certainty. However, it did refer to a level of exposure below which excess risk is not statistically significant.

At the conclusion of the presentation of the study's preliminary report, Dr. J.C. McDonald noted that 300 mpcf x years could be regarded as approximately equivalent to 1,000 fibre years, which could have been accumulated over 20 years at about 50 f/cc. He concluded that "The significance of this study is that any deaths from asbestosis or lung cancer arising from current occupational exposure levels are most unlikely."

In publicizing Dr. McDonald's comments and the findings of the preliminary report, The Asbestos Institute is in no way endorsing relaxed chrysotile occupational exposure limits. The group of experts convened by the WHO in 1989 recommended that chrysotile exposures should not exceed 1 f/cc. This has been and continues to be the level which we urge producers and users to meet. To believe otherwise would clearly be a distortion of the Institute's position. In fact, since its inception, The Asbestos Institute has been dedicated to actively promoting, through close to one hundred training seminars and information sessions in more than 60 countries, the application of internationally accepted safe exposure limits and work place practices. The Asbestos Institute has never suggested that this, or any other study is an invitation to relax standards, but rather that it supports our view that current exposure limits are realistic and acceptable. ■

Changes Required to Fibre Research Methodology

The practice of using fibre mass rather than number does not allow for accurate comparisons of the health effects of different fibres

It is widely known that different fibre types have different masses. A similar mass of two different fibrous materials can vary significantly in fibre number (see table).

David L. Coffin, of the U.S. Center for Environmental Medicine and Lung Biology and his former EPA colleagues P.M. Cook and J.P. Creason have warned for many years against inappropriate comparison of pathological potential of different fibre preparations when only gravimetric (measurements of weight) units were used to report biological effects.

The need for a meaningful common measurement unit is underscored by a recent study by Hesterberg et al. (in press) of the health effects of man-made vitreous fibres (MMVF). For the purposes of comparison, the authors included the results of concurrent studies on the effects of refractory ceramic fibres (RCF) and chrysotile asbestos. Close scrutiny of the experimental design reveals that the results reported are from animals exposed 6 hrs/day x 5 days/wk for 24 months to ~250 f/ml for MMVFs, ~180 f/ml for RCF and 10,000 f/ml for chrysotile asbestos!

A workshop on fibre toxicology conducted by the National Institute of Environmental Health Sciences (NIEHS) came to a similar conclusion. Its summary indicated that "A major failing of past experimental studies has been the use of mass as the main dose parameter. Data are needed on fibre comparisons by fibre number... Most studies using fibres *in vitro* have in the past expressed dosage on the basis of fibre mass as opposed to number of fibres per cell, which now appears to be a more valid means of comparison of fibre effects in relation to their potential to cause human disease."

In addition, the results of air monitoring are expressed in f/cc, as are exposure limits. It is only logical that research programs devised to better understand the nature of the health effects of fibrous materials provide data in a manner that is meaningful and useful to those concerned with protecting worker safety. ■

A) THE EXPERIMENTS AS CARRIED OUT			
	Dosage used		
	Mass	**Fibre number**	Observations following 24 months exposure 5 hrs/day; 5 days/week
MMVF10*	30 mg/M^3	**232 f/cc**	Wagner PGS+: 2.5 to 3
MMVF11*	30 mg/M^3	**246 f/cc**	Wagner PGS: 2.5 to 3
RCF*	30 mg/M^3	**187 f/cc**	Wagner PGS: 4 Lung tumours: 16 (13.0%) Mesothelioma: 2 (1.6%)
Aramid**	Not stated	**100 f/cc**	Fibrosis and cystic keratinizing squamous tumours
Chrysotile*	10 mg/M^3	**10 600 f/cc**	Wagner PGS: 4 Lung tumours: 13 (18%) Mesothelioma: 1 (1.4%)
B) THE EXPERIMENT WHICH WAS NEVER CARRIED OUT			
Chrysotile	0.18mg/M^3	**200 f/cc**	?

* Hesterberg, T.W. et al. (1993), Fund. Appl. Toxicol. (in the press)
** Lee, K.P. et al. (1988), Fund. Appl. Toxicol. 11:1-20

\+ PGS: Wagner Pathology Grading Scale

Cellular changes
1. Normal
2. Minimal: Macrophage response
3. Mild: Inflammation, bronchiolization

Fibrosis
4. Minimal: Minimal fibrosis
5. Mild: Linking fibrosis
6. Moderate: Consolidation
7. Severe: Marked fibrosis and consolidation
8. Severe: Complete obstruction of most airways

Dose-response research using mass rather than fibre counts has resulted in overestimations of the health effects of chrysotile asbestos.

References:

Coffin, D.L., Cook, P.M. & Creason, J.P. *Relative Mesothelioma Induction in Rats by Mineral Fibres: Comparison with Residual Pulmonary Mineral Fiber Number and Epidemiology*. Inhal Toxicol. 1992:4:273-300.

Dement, J.M. *Overview: Workshop on Fiber Toxicology-Research Needs*. Environ Health Perspect 1990:88:261-268.

Dunnigan, J. *Comparing Biological Effects of Mineral Fibres*. Brit. J. Ind. Med., 1989. 46 : 681-682.

Hesterburg et al. *Chronic inhalation toxicity of size-separated glass fibers in Fischer 344 rats*. Fund Appl Toxicol. (in press)

and the poison lies in the amount: thus the often-cited expression "the dose makes the poison". A few centuries later, the issue of low-dose risk remains a hotly debated topic in the scientific community. Although the techniques, models and jargon have changed, the controversy essentially revolves around the same basic question: "Is something that is toxic at high doses necessarily toxic at much lower doses?" Elegant theoretical models of toxicity and carcinogenicity are presented in response to this question, and yet in some respects we are no closer to a conclusive answer. The principal point of contention centers around the possibility that even though no health effects may be observed, it is possible that these effects exist, but are undetectable using current data and methodology.

Some scientists maintain that for the purposes of regulatory policy, the weight of animal and human epidemiological evidence is more important than theoretical postulations. In the case of chrysotile asbestos, there is a large body of evidence that demonstrates that at low levels of exposure, the carcinogenicity is zero or undetectably low. The research of Churg, 1986; Newhouse & Sullivan, 1989; Ohlson & Hogstedt, 1985; Thomas et al. 1982; Liddell et al. 1992 and others detected no significant excess mortality amongst workers exposed to low levels of chrysotile. Moreover, the low levels of exposure, as defined in some of these studies, are still much higher than current occupational exposure limits.

Fibre Dimensions Mediate "Respirability" and Carcinogenicity

Progress in the study of asbestos and other fibres made during the last 15 years has confirmed that fibre length and diameter are important parameters to consider in evaluating carcinogenic potential. Fibre dimensions are important in that they determine whether a fibre is respirable. Some particles or fibres are too large to infiltrate into the lungs. They are blocked by the body's natural filtration system. Although some larger fibres are able to find their way into the lungs, many are still too large to penetrate deep into the alveoli and as such are not a carcinogenic risk. Those fibres, which are capable of bypassing these physical barriers, generally fibres of up to 3µm in diameter, have been termed "respirable". Thus in order for fibres to have carcinogenic potential, they must first be of respirable size. Scientists are clear to point out however that respirability, though necessary, is not sufficient in explaining carcinogenic potential. Fibres which are respirable are not necessarily carcinogenic.

A significant body of research has examined why some fibres of respirable size are either less carcinogenic or not carcinogenic at all. Several factors seem to come into play. Generally speaking, there is ample evidence from experimental studies which demonstrates that while long, thin fibres are associated with pathological manifestations in animals, no such association is found with fibres shorter than 5µm long.

In 1989, world-renowned epidemiologist Sir Richard Doll, indicated that "there is increasing evidence that short fibres — properly described as elongated particles — are much less carcinogenic, if they are carcinogenic at all. We should base our estimate of potential risk on both the chemical constitution of the fibres and their size, counting only those fibres that are respirable and more than 5µm long" (IARC Scientific Publication No. 90, Lyon).

In attempting to explain this phenomenon, researchers have discovered that short fibres can be cleared by the body's natural defenses without provoking inflammation or mesothelial injury. However, long fibres appear to induce the secretion of inflammatory substances by macrophage cells. A recent report by scientists at the Institute of Occupational Medicine in Edinburgh, has identified such a substance called TNF or Tumor Necrosis Factor, which is released by activated alveolar macrophages.

As scientists have continued to unravel the reasons for the pathogenicity of longer, respirable fibres, they have discovered that fibre length alone cannot explain the wide variance in the carcinogenic potential of different substances. Different fibres of similar dimensions may vary significantly in their health effects. With the evolution of new techniques of chemical and mineral analysis, referred to as tissue burden, an additional parameter of fibrous materials is now recognized as of paramount importance to our understanding of the pathogenic potential of respirable fibres.

Chrysotile Low on the Continuum of *In Vivo* Durability

Durability varies widely among different respirable fibres. It appears to be related to a substance's chemical composition and crystalline configuration. In terms of health effects, researchers have focussed on the extent to which the durability of a substance determines its "biopersistence", or the length of time which inhaled fibres persist in the lung before they are eventually dissolved and/or cleared. In general, the longer an inhaled particle persists in the lung, the more likely it is to adversely affect surrounding tissues.

Biopersistence studies have been carried out on a number of different respirable fibres.

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Carcinogenicity...

and it has now become clear that there are vast differences among various respirable fibres presently used in industry. At the 1992 WHO/IARC (Lyon) Symposium on Biopersistence of Respirable Synthetic Fibres and Minerals, there was a strong consensus that there appears to be a continuum of values for biopersistence ranging from very short persistence (low durability) to practically indefinite persistence (very high durability) among the various respirable materials tested.

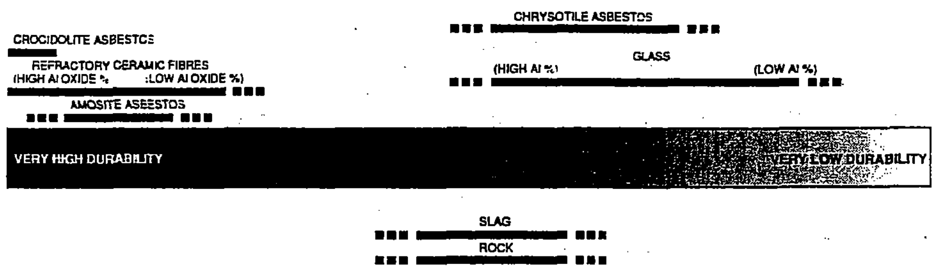
Both *in vivo* (animal studies) and *in vitro* (biological fluid simulation) research have been conducted to evaluate the biopersistence of different inhalable fibres. It has been demonstrated that for asbestos fibres, chrysotile has low durability and short persistence, while amphiboles are highly durable and persistent. While chrysotile is cleared within weeks or a few months, it is recognized that amphiboles, in particular crocidolite and amosite have clearance half-times in the range of decades.

For man-made mineral fibres (MMMF), data has shown wide variability in the biopersistence and solubility of different fibres, depending on their respective manufacturing process and chemical composition. For example, glass fibres with high aluminum (Al) content were shown to be more durable than those with low Al content.

A major German study undertaken by scientists at the Fraunhofer Institute in Hanover compared a whole series of MMMFs (from glass to RCFs) and natural fibres for *in vivo* durability. Half times for fibre elimination from the lung ranged from 10 to 500 days. Another study on durability from the U.S. reported that inhaled RCFs showed no chemical alterations two years following end of exposure, whereas glass fibres showed that some components had leached (broken down). Animal studies from the Institute of Occupational Medicine in Edinburgh showed that chrysotile asbestos and the glass fibres tested were cleared at approximately the same rate, whereas there was very little clearance of crocidolite asbestos.

with the various forms of asbestos, different man-made mineral fibres vary greatly in each of the three D parameters discussed. A sound regulatory policy must recognize the existence of a continuum of pathological potential for all respirable fibres, natural and man-made and establish exposure standards predicated on this continuum. ■

Current research points to a continuum in the durability of both natural and man made mineral fibres



All fibres are not created equal

Today, scientists view the three D's (dose, dimension and durability) as interactive and interdependent. Moreover, as with durability, the parameters of dose and dimension exist on a continuum of pathogenic potential. At low doses, many fibres produce no detectable health effects. All other things being equal, as the dose increases so too will the potential health risks. Similarly, fibres which are less than 5µm in length can be easily eliminated by the body's natural defense mechanisms. Fibres of 10, 20 or 30µm and longer are increasingly likely to escape macrophage elimination and remain in the lungs.

In addition to the scientific ramifications of this avenue of study, there can be practical and regulatory implications as well. Increasingly, regulations will have to focus on fibre characteristics and descriptions rather than on mineral or trade names. As

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MMMF Research Update

A Case-Control Study of Malignant and Non-Malignant Respiratory Disease Among Employees of a Fibreglass Manufacturing Facility
Chiazze, L. et al. British Journal of Industrial Medicine, 49, 1992.

A case-control study conducted on workers of a fibreglass plant has concluded to a statistically significant increase in respiratory cancer. The results of this study have been reevaluated to include non-workplace factors, such as cigarette smoking. Results of the interview portion of the case-control study clearly indicate that smoking is the most important non-workplace factor for risk of lung cancer in this group of workers.

Lung Function in Insulation Workers
Clausen, J., Netterström, B. & Wolff, C., British Journal of Industrial Medicine. 1993; 50: 252-256.

To evaluate the effects of working with modern insulation materials (rock and glass wool) the members of the Copenhagen Union of Insulation Workers were invited to participate in a study based on a health examination that included lung function tests such as forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). No differences in FVC were observed between the experimental and control groups, but insulation workers were found to have significantly lower FEV_1 values, independent of smoking.

In addition, a follow-up of workers who had participated in a similar study six years earlier found that the decline in FVC for insulation workers who smoked was significantly greater than for smokers from the control group. In the present study, the decline in FEV_1 was significantly higher for insulation workers, independent of smoking habits. Self-assessed former exposure to asbestos was not associated with lung function in insulation workers.

The study concludes that working with modern insulation materials is associated with increased risk of developing obstructive lung disease. ■

Environment Canada and Health and Welfare Canada Conduct a Study on the Potential Adverse Effects of Man-Made Mineral Fibres

Mineral fibres are on Canada's Environmental Protection Act's priority list. All substances that appear on this list must be assessed to determine whether they are toxic, as defined in Section 11 of the Act (i.e. whether exposure to these substances causes harm to human health or the environment).

The first part of this Federal Government study will evaluate exposure to these substances in Canada. In order to develop a profile of MMMF use, Environment Canada has commissioned an industry survey to obtain information on the amounts of these materials, which are produced in, imported to and exported from Canada. ■

Source:
Thermal Insulation Association of Canada, TIAC Times, March 1993

We have moved...

Our new offices are located at 1002 Sherbrooke St. West, Suite 1750, Montréal, Québec, Canada, H3A 3L6. Our phone and fax numbers have remained the same.

Reading List

Health Risks from Exposure to Mineral Fibres: An International Perspective
Edited by G.Gibbs, J. Dunnigan, M. Kido & T. Higashi, Captus University Press, 1993

A timely contribution from international experts in the field of health-related effects of mineral fibres: Papers presented at the International Symposium on the Health Effects of Low Exposure to Fibrous Materials (Kitakyushu, Japan: Nov.,1991) represent an updated overview of the current assessment of health effects of mineral fibres in both the occupational and general environment. The report of the workshop on biological indicators represents an in depth evaluation of modern practices in health monitoring. The satellite symposium introduces the reader to current studies on mineral fibres in Japan and other Asian countries.

The Effects of an Environmental Controversy on Industry: The Asbestos Experience
ECODECISION, March 1993

Each year, growing public awareness of the environment creates scientific controversies that can have major impacts on the business activities of many industries. The analysis presented shows that the effects on business depend much more on the fierceness of the controversy than on the regulations that are ultimately implemented. The experience of the asbestos industry is cited as an example of how an environmental controversy can open the door to scientific inexactitude and arouse strong public opinion from the outset. A frequent consequence is that too much attention is given to some problems to the detriment of others, leading to a wasteful use of resources. Finally, environmental controversy raises society's "implicit ecological standards". For industries, preventing such controversies by ensuring that their products meet these standards has become a necessity.

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