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Towards an Understanding of the Carcinogenicity of Fibrous Materi

The last decade has seen great advances in scientific understanding of genic potential of some fibres. Recent studies of fibre dimensions, dura dose-response relationships are helping to explain why some fibres, suc 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 carc materials. Today, sc carcinogenicity of fi interaction between durability or bio-pers

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Inside

Asbestos Fibres in the General Environment

Studies find extremely low concentrations short asbestos fibres in the general envir

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 environment

The vast majority of ronment (air, soil, w natural phenomena asbestos was presen similar quantities i and used commercia

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

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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 lim-

its. It is only logical that research grams devised to better understand nature of the health effects of fibr materials provide data in a manner th meaningful and useful to those conce 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

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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.

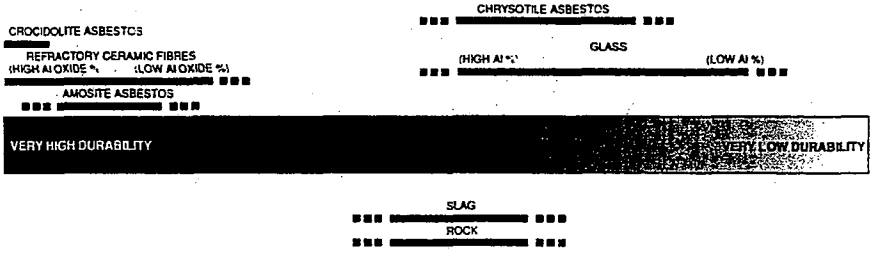
Both *in vivo* (animal studies) and *in vitro* (biological fluid simulation) research have been conducted to evaluate the biopersistence of different inhalable fibres. It has been demonstrated that for asbestos fibres, chrysotile has low durability and short persistence, while amphiboles are highly durable 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 vitro* 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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