

Mineral Fibres and Cancer

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Summary

A synthesis is presented of the salient findings to date from laboratory and epidemiological research, on the health effects of asbestos and other natural and man-made mineral fibres. Experimental evidence suggests that all mineral fibres are capable of causing fibrosis and malignancy, with chrysotile at least as pathogenic as other fibres. However, penetration, retention and phagocytosis are affected by size and shape and reactivity and durability by physico-chemical properties. Thus it is not surprising that in man the results of exposure vary considerably with fibre type and industrial process. A considerable body of evidence suggests that chrysotile has seldom, if ever, caused peritoneal mesothelioma and that the great majority of pleural mesotheliomas are also attributable to crocidolite or amosite. Without more reliable information on intensity and duration of exposure by fibre type, the epidemiological evidence on this point cannot be wholly conclusive. There are stronger grounds from a limited number of cohort studies for believing that in relation to estimated exposure, the risk of lung cancer has been much higher in textile plants than in fibre production or in the manufacture of friction products, with asbestos-cement plants somewhere in between. The data on man-made fibre production remains equivocal. It is concluded that attempts to regulate asbestos without regard for fibre type, although perhaps adequate for lung cancer and fibrosis, may do little to reduce the risk of mesothelioma. The search for safe fibre substitutes for asbestos will remain difficult until the parameters of pathogenicity are better understood.

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Industrial process
Lung cancer
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Mineral fibres

Introduction

Concern for the health effects of exposure to mineral fibres rose out of the commercial exploitation of asbestos which began 100 years ago. The first problem recognized was pulmonary fibrosis, then lung cancer, then mesothelial tumours and finally the question of other malignant diseases. The concern spread to naturally occur-

ring mineral fibres such as the zeolites, fibrous clays, wollastonite, etc. and attention now focuses on man-made fibres, glass and rock wool in particular. At the same time the scope of the problem has moved beyond the workplace into the general environment and encompasses both airborne and waterborne exposures.

While the very varied chemical and physical characteristics of this wide range of materials demand that any differences in their biological effects be identified, the diseases which they share imply that they also have important features in common. Both aerodynamic studies and research in laboratory animals and tissues have demonstrated that shape and dimensions are critical. Another factor of great significance is the possibility of interaction with other exposures, as clearly demonstrated for tobacco smoking in man. The relative importance of all these various components is still not fully understood and is the object of considerable experimental and epidemiological research.

This paper will attempt to review the results of studies to-date, looking particularly at findings since the 1979 IARC Lyon Conference.¹ So far as asbestos is concerned, it will concentrate on similarities and differences between the main fibre types, possible only in studies which take note of exposure-response in quantitative terms. The way in which thinking has moved away from threshold towards linear models and the implications of this will be discussed. The question of industrial process will be considered and results of recent studies which suggest that there are major differences between them.

A pressing aspect of the problem is the need to determine the effects of exposure to man-made mineral fibre. Much new evidence on this subject was presented at a WHO Conference in Copenhagen in April 1982, yet to be fully published. The data, some of which will be briefly mentioned, are still not sufficient to allow any firm conclusion one way or the other. Because of the enormous social and economic importance of mineral fibres, control will certainly be difficult and will remain a scientific challenge for some time.

Laboratory Research

The biological activity of chrysotile and amphibole fibres was reviewed recently by Bignon and Jaurand² and of other natural and man-made mineral fibres by Wagner.³ In tests of reactivity with red blood cells, macrophages and proliferative cells, *in vitro*, chrysotile has generally been found more active than the amphiboles. Treatment with acids and phospholipids appears to decrease the reactivity and toxicity of chrysotile and increase that of the amphiboles. In short term sub-cellular tests on bacteria and in mammalian cells, neither chrysotile, amphiboles nor other mineral fibres have been convincingly demonstrated as mutagenic. On

the other hand, the cellular reactivity of fibres, especially chrysotile, by accelerating cell proliferation could be expected to promote tumour growth.

In laboratory animals, we can distinguish experiments in which fibres are implanted or injected (usually into the pleura or peritoneum), from those in which there is exposure by inhalation. Prominent in the first group are the studies of Stanton,⁴ Pott,⁵ Wagner⁶ and their various co-workers; these have clearly demonstrated that, after pleural implantation, the incidence of malignant mesenchymal neoplasms is related to the durability and dimension of the fibres — long ($>8 \mu\text{m}$), thin ($<0.25 \mu\text{m}$) fibres being the most carcinogenic, regardless of other physico-chemical properties. As most fibres in this range are not detected by light microscopy, they will not be counted in normal environmental control procedures. It was noted by Stanton *et al*⁴ that these findings may simply reflect the more efficient removal of short and thick fibres as compared with the 'negligible phagocytosis of long, thin fibres'.

The results of inhalation experiments have been less consistent. In general, there is little to suggest that chrysotile is less fibrogenic or less carcinogenic than the amphiboles. Recent work by Davis and others⁷ indicated, in fact, that chrysotile produced far more fibrosis and tumours than other asbestos types at the same fibre concentrations assessed by light microscopy. By electron microscopy, however, the chrysotile clouds contained many more long fibres ($>20 \mu\text{m}$). Mesothelial tumours have proved very difficult to induce by inhalation. In a still unfinished study, Wagner³ reported a high incidence of pleural mesothelioma in rats exposed to erionite from the State of Oregon (a similar mineral to that found in Karain, Turkey). No other mineral fibre, natural or man-made, has ever produced anything like the same frequency of mesothelial tumours in experimental animals. Part of the explanation may lie in the earlier observations of Timbrell⁸ that fine straight fibres reach the peripheral airways much more easily than coarse or curly fibres which have a high effective diameter.

The laboratory evidence thus suggests that all mineral fibres are probably capable of causing fibrosis and malignancy, with chrysotile at least as pathogenic as other fibres. However, as penetration, retention and phagocytosis are affected by size and shape, and reactivity and durability by physicochemical properties, we cannot expect all mineral fibres to have the same health effects under all conditions of environmental exposure. It will be seen that this is borne out by the epidemiological findings. A further complication in which there has been experimentation concerns the question of interaction between mineral fibres and other factors, smoking in particular. Since, for asbestos at least, the main role

of fibres in the etiology of lung cancer may be to promote rather than initiate, the parameters of the interactive mechanism need to be established in the laboratory, as it will be very difficult epidemiologically. A recent report by Woodworth *et al*⁹ that explanted metaplastic human bronchial mucosa, resulting from cigarette smoking and maintained in hamster trachea cultures, selectively allowed the passage of long asbestos fibres, indicates one possible mechanism.

Epidemiology

Pulmonary and pleural fibrosis

Comparison between the effects of mineral fibre exposure, always difficult because of uncertainty about environmental measurement, is doubly so for pulmonary fibrosis, because of diagnostic problems. Despite efforts at standardization, symptom questionnaires, chest X-ray readings and even respiratory function tests are liable to subject and observer error. Death certificates are also unreliable because they reflect both medical preconceptions and the contribution of other causes of death. That said, there is no good evidence that asbestos fibre type *per se* influences the frequency or severity of pulmonary fibrosis but it seems likely that for chrysotile the risk may be higher in the textile industry than in mining and milling¹⁰ or in the manufacture of non-textile based friction products.¹¹ It is of more than historical interest that the first attempt in 1938 at establishing an occupational hygiene standard for asbestos in the United States assumed a threshold concept. In fact, the data available at that time and the findings of more recent studies are all compatible with a linear relationship though where the line intercepts the exposure axis cannot be defined very precisely.¹⁰

Pleural calcification

The epidemiology of these readily recognized but clinically benign changes is puzzling. In most groups exposed at work to asbestos, pleural calcification is common and usually accompanied, by signs of pleural thickening and pulmonary fibrosis. On the other hand, its occurrence appears to be related to time since first employment rather than accumulated exposure;¹² it is much more common in some localities than others;¹³ and, there are geographical areas, both extensive and focal in Finland,¹⁴ Eastern Europe,¹⁵ Greece¹⁶ and Turkey¹⁷ where calcification is highly prevalent in the general population. These areas show no consistent relationship to asbestos deposits and it seems likely that the changes are due to some other mineral commonly but not invariably associated with asbestos; coarse fibrous tremolite has been suggested (JC Wagner, *personal communications*; GW Gibbs, *personal communication*).

Malignant mesothelioma

This tumour is considered first because its occurrence appears independent of any other 'co-carcinogen'. Much of the resulting advantage from the viewpoint of epidemiological interpretation is lost nevertheless, because of the confusing effects of both fibre type and industrial process. No good exposure-response data exist for these tumours, mainly because in six of the eight studies with adequate measurements of intensity and duration, there were few mesotheliomas; in the remaining two studies the situation was seriously confounded by fibre type. However, semi-quantitative data presented by Newhouse and Berry,¹⁸ Hobbs *et al*¹⁹ and Seidman *et al*²⁰ all point to some form of systematic relationship between risk and accumulated exposure.

Without reliable information on intensity and duration of exposure *by fibre type*, the considerable weight of evidence which points to a substantial difference between chrysotile and the amphiboles (especially crocidolite) in their capacity to cause mesothelioma cannot be wholly conclusive. Nevertheless, the issue is of such immediate importance that it cannot be left open and some conclusion must be reached on the available evidence. The main points were summarized in a recent paper¹⁰ as follows:

1. Substantial concentrations of cases have occurred in naval dockyard cities where amphibole exposure, especially during World War II, was heavy.
2. Case-referent surveys in North America have shown very high risks associated with insulation work which usually entailed exposure to amosite-chrysotile mixtures.
3. Very brief exposure to pure crocidolite in the manufacture of military gas masks in Canada and the UK resulted in an extraordinarily high incidence of cases. To a lesser degree the same was true of workers in Australian and South African crocidolite mines and in an American insulation products plant which used only amosite. In contrast very few cases have occurred in chrysotile production workers in Canada, Italy, South Africa and the USSR.
4. Cohort surveys in three American plants, two of which used only chrysotile and one all three fibre types showed about a 50 fold difference in incidence. One of the chrysotile factories was the textile plant with the highest risk of lung cancer ever recorded, yet with only one case of mesothelioma.
5. Identification of cases of mesothelioma associated with four asbestos factories in the Province of Quebec showed the same association with amphibole use.
6. Electron microscopy case-referent surveys in North America and in the United Kingdom, have

shown a substantial excess of amphibole fibres in cases over controls but no difference as regards chrysotile.

Additional evidence has accumulated since this passage was written, for example:-

7. In a friction products plant studied by Berry and Newhouse²¹ which used chrysotile only (except in a well-defined area of one workshop, where for 9 years crocidolite was processed) the only excess mortality comprised 10 deaths from pleural mesothelioma, 8 or perhaps 9, in men who had worked with the crocidolite.
8. There were 5 cases of mesothelioma reported by Acheson *et al*²² among 219 deaths in women who had manufactured military gas masks (containing crocidolite) compared with 1 case among 177 deaths in women manufacturing civilian masks (containing chrysotile); this woman had also worked with crocidolite in another factory where other mesotheliomas occurred.
9. There were 5 cases of mesothelioma among 431 deaths in a London insulation products factory which used only amosite,²³ 136 of the 431 deaths were in men 20 years or more after first employment (Acheson ED, *personal communication*).

With the notable exception of the USA, for obscure reasons, and South Africa, for obvious reasons, most advanced countries have been sufficiently persuaded by this evidence to ban the use of crocidolite and some the use of amosite. Acheson and Gardner²⁴ in their recently updated review for the British Health and Safety Commission summarize their conclusions on mesothelioma as follows:

"*Peritoneal* mesothelioma has an almost exclusive relationship with exposure to the amphiboles, crocidolite and amosite. As far as *pleural* mesothelioma is concerned, although the association is less strong than for peritoneal mesothelioma and such tumours

have been caused by exposure to chrysotile alone, all the recent publications that we have been able to find support our previous view that crocidolite is substantially more dangerous than chrysotile."

An indication of the magnitude of the difference is shown in Table I, based on the results of 30 major cohort studies in males. The proportional mortality rates for mesothelioma present a systematic pattern, that for crocidolite being 50 fold greater than for chrysotile. Whereas mesotheliomas account for nearly twice the excess mortality ascribed to lung cancer after crocidolite exposure, excess lung cancer is 10 times more frequent than mesothelioma after chrysotile. The data on women is much more scanty but the pattern is similar.

Despite this evidence, some authorities remain unconvinced. For example, Nicholson in his 1981 Criteria Document for the Swedish government²⁵ dismissed the evidence against crocidolite and the amphiboles as "limited" and perhaps related to the fact that the first environmental mesotheliomas were found near the crocidolite mines of South Africa. He went on to suggest that the differences in risk might be explained by fibre size distributions, the finer smaller fibres resulting from industrial manipulation being more likely to migrate to the pleura. Although there may be substance in this argument, it is not supported by the experience of the South Carolina Textile plant where only one mesothelioma occurred. Another point, repeatedly stressed by Robock and others, is the extreme dustiness of crocidolite, sometimes sufficient to render it difficult to handle industrially. There is probably some natural anxiety in both parties to the controversy that their particular point should not be lost: a) that despite the epidemiological appearances, chrysotile is certainly no less carcinogenic in the laboratory; and conversely, b) that despite the laboratory findings, the risk of mesothelioma (often very high) is virtually confined to persons exposed to amphiboles.

TABLE I
MESOTHELIOMA, LUNG CANCER AND FIBRE TYPE IN 30 MALE COHORTS*

Type of exposure (cohorts)	No. of deaths	No. of mesotheliomas	Rate/000	Excess lung cancer deaths	Rate/000	Ratio of excess lung cancer to mesothelioma
Chrysotile (8)	6,539	15	2.3	143.5	21.9	9.6
Amosite (2)	959	19	20.0	88.1	91.9	4.6
Anthophyllite (1)	248	0	—	8.4	33.9	—
Crocidolite (2)	279	33	118.3	19.4	69.5	0.6
Tremolite (2)	165	3	18.2	10.8	65.5	3.6
Mixtures (15)	10,728	369	34.4	624.6	58.2	1.7
Total (30)	18,918	439	23.2	894.8	47.3	2.0

*Based on Table 2 of McDonald and McDonald⁴¹, corrected and updated.

Lung cancer

While there can be little reasonable doubt that asbestos exposure is a cause of human lung cancer, the exact nature of the relationship remains poorly defined. The problem has three main components: — interaction with tobacco smoke (and perhaps other co-carcinogens), fibre type and industrial process. To unravel these inter-relationships is a complex and difficult task; the latent interval is long (usually 30–40 years) and all relevant parameters must be adequately assessed over this period. Few if any studies meet all the requirements and, to date, there are only seven working populations in which even the asbestos exposures has been estimated for each subject individually. For other natural mineral fibres, except tremolite, there are no data; for man-made fibres, the situation is rather better.

Fibre type: It remains uncertain whether chrysotile, crocidolite and amosite differ in their capacity to cause lung cancer. Occupational exposures to these minerals usually occur under different industrial circumstances and except in production (i.e., mining and milling) mixtures are usually present. In an earlier review,¹ I mentioned that the level of excess lung cancer experienced by crocidolite miners was five times that in Quebec chrysotile miners; however, it was not known whether exposure levels or other relevant factors were comparable. Both Enterline and Henderson²⁶ and Hughes and Weill²⁷ presented evidence of the same fibre type difference in factories where both chrysotile and amphiboles were used but the circumstances did not really permit complete separation of exposures by fibre type. More recently we studied a textile plant which used only chrysotile²⁸ and another mainly textile plant which also handled amphiboles.²⁹ Exposure response expressed in relative risks, showed no difference for lung cancer although there were many more mesotheliomas in the latter. If fibre type has an effect it seems unlikely to be a major one.

Industrial process: The eight cohort studies (in seven industrial groups) where exposure to asbestos for each subject was estimated individually in duration and intensity, covered the following industries and fibre types:

- Study 1. Mining and milling in Quebec³⁰
— chrysotile only
- Study 2. Cement, textile and friction products in New Jersey²⁶
— chrysotile and crocidolite
- Study 3. Cement products in Louisiana²⁷
— chrysotile and crocidolite
- Study 4/5. Two studies of the same textile plant in South Carolina^{28,31}
- Study 6. Mainly textiles in Pennsylvania²⁹
— chrysotile, amosite and crocidolite

- Study 7. Friction products in UK²¹
— chrysotile and some crocidolite
- Study 8. Friction products in Connecticut¹¹
— chrysotile only

Two other studies of asbestos-cement workers should also be mentioned, one in Canada³² and the other in Sweden.³³ Both are difficult to interpret in terms of exposure-response for much the same reason. Both plants used chrysotile and amphiboles, had relatively small numbers of lung cancer deaths, but substantial mortality from mesothelioma; in neither was there any systematic relationship between lung cancer and exposure. Perhaps the small numbers and possible confusion between the two kinds of malignancy may be part of the problem.

In marked contrast, all eight studies^{1–8} of the seven populations produced clear linear exposure-response relationships, but of very varied gradients. With the exception of Study 7, where the analysis was case-referent in type, the other studies used primarily life-table methods with results expressed as SMRs. Since, for various reasons, not all lines passed through the origin, it is probably best to compare the slopes expressed as relative risks. For the purpose of Figure 1, the uniform calculations of Liddell and Hanley³⁴ have been used, rather than the varied methods of the individual investigators. It can be seen at once that the two textile plants have gradients many fold more steep than the rest. The

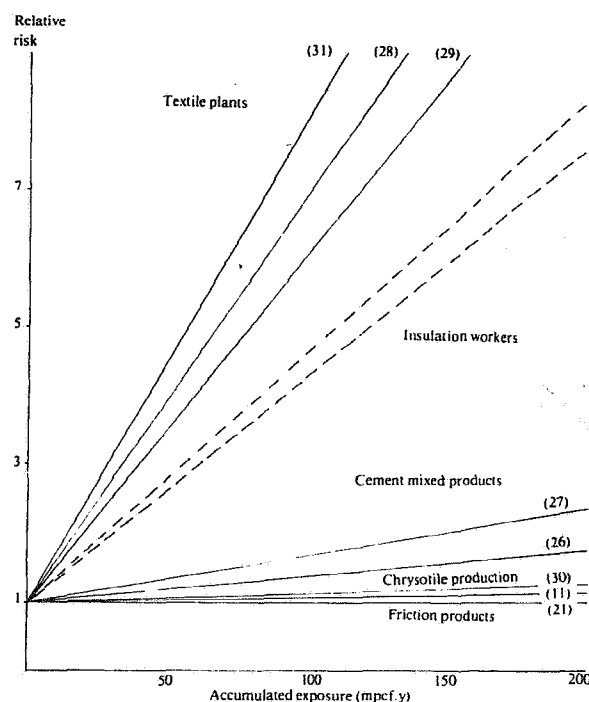


Fig. 1. Lung cancer risks and asbestos exposure in 10 occupational cohorts.

sharpest contrast is between the chrysotile only textile factory and chrysotile production. Even less risk than in production is seen in the two friction products plants, where it is quite doubtful whether there was any significant lung cancer excess. Although far below textiles, the two factories mainly engaged in the manufacture of cement products were several fold above chrysotile production. Also shown in this figure is the experience of American insulation workers,³⁵ and of men engaged in the manufacture of amosite insulation products.²⁰ In neither of these studies was exposure assessed individually but, on certain assumptions especially as to linearity, it seems likely that the gradient for these two populations lay somewhere between the cement workers and the textile workers.

How does one interpret all this? There are two possibilities, first, that some of the exposure estimates were seriously incorrect. If so, the error was systematic or the linear response relationships would have been lost. Second, and I believe more likely, neither the original dust particle measurements nor the usual conversions to fibres, countable with the optical microscope, adequately reflect the biological hazard. Experimental work on fibre size and the dynamics of penetration and retention all suggest that this could be an important part of the explanation, perhaps all of it.

Co-carcinogens: Only the role of cigarette smoking has been investigated but it follows that if mineral fibres work at least in part as promoters rather than initiators of carcinogenesis, exposures other than personal smoking may also be relevant. In particular, 'passive smoking', seldom taken seriously in itself, may be far from negligible if combined with asbestos air pollution. There are still very few studies in which the interaction between asbestos and cigarette smoking has been estimated.³⁶ The most recent analysis of our own data in chrysotile miners again points to a relationship which is more than additive but less than multiplicative.³⁷

Man-made fibres: At Copenhagen in April 1982, results were presented of two major mortality studies of cohorts engaged in the manufacture of man-made mineral fibres. One of these, by Enterline and Marsh,³⁸ covered 16,730 male employees in America's 17 oldest and largest plants. The other, by Saracci *et al*,³⁹ dealt with 25,072 workers from 13 European plants. Both studies showed excess mortality from respiratory cancer, evident only 20 or more years after employment. The excess was greater in mineral wool than fibrous glass production and after a latent interval of 30 years. There was little evidence, however, that these findings were related to fibre concentration or duration of employment. On the other hand the fibre levels to which the workers had been exposed were very low indeed. In the American study, for example, the average environ-

mental concentrations were 0.04 f/ml for fibrous glass and 0.35 f/ml for mineral wool. In the European plants, the corresponding levels were fairly similar (0.006–0.02 f/ml for glass wool and 0.4 f/ml for rock wool). At these levels, only in asbestos textile factories would any lung cancer excess have been detectable; conversely, assuming linear exposure-response, the risk gradient in these man-made fibre cohorts was at least as steep as anything observed with asbestos. This kind of extrapolation is hardly justifiable but the evidence from these two cohorts is not reassuring.⁴⁰

Cancer at other sites: Whereas the associations between asbestos and mesothelioma and lung cancer are clear and strong, with other cancers they are rather dubious. The large survey of North American insulation workers reported by Selikoff *et al*³⁵ showed excess mortality at several sites, notably gastro-intestinal tract, larynx and kidney and there is some but not consistent support for these from certain other investigators.

In a recent review,⁴¹ we summarized the principal findings from all cohort mortality studies to 1981, 24 of which included figures on alimentary cancer in men. Since then, there have been six more studies.^{11,21,28,29,32,33} In 12 of the 30 data sets the number of male deaths from gastro-intestinal cancer was the same or less than expected (total deficit, 47 deaths). In 28 sets there were more deaths than expected (total excess, 167 deaths). Ninety-two of the 167 excess deaths were in four cohorts, three of insulation workers and one in a very large factory which used both chrysotile and amphiboles in the manufacture of mixed products. The incidence of mesothelioma in these four cohorts was high and some of the excess could conceivably have been due to unrecognized peritoneal cases. Although this is unlikely to be the whole story, we agree with the recent statement by Acheson and Gardner²⁴ that: "The evidence that asbestos fibre causes alimentary cancer in man is less convincing than in 1979". In neither of the major studies of man-made fibre production workers was there any excess of gastro-intestinal cancer.

A link between asbestos exposure and laryngeal cancer has also been suspected but again on limited evidence. Two general population case-control studies, one in Liverpool and the other in Toronto gave much larger relative risks than would be expected from the modest excess noted by Selikoff *et al* and Newhouse and Berry in their high risk cohorts of American insulators and London factory workers.²⁴ The hypothesis remains reasonable but is still poorly substantiated.

Conclusions

The 1964 New York Conference on asbestos was a landmark in environmental science; since then the volume of research on this theme has probably exceeded

that in any other. It is proper to ask what has been achieved, where are the gaps and how much more confidently can the community deal with the economic and health problems of asbestos and its substitutes than it could 20 years ago?

Achievements

The answer to these questions can be considered against six recommendations for epidemiological study made by the UICC Working Group after the 1964 Conference.⁴² The first recommendation dealt with fibre type, and many, but not all, would feel that despite a similar biological potential, amphiboles constitute a far more serious hazard to man than chrysotile. The second dealt with exposure-response and here the significant finding is that linear relationships predominate, with no evidence of a threshold. No 'safe' level is likely to exist or, at least, be demonstrable. The third recommendation asked for investigation of the effects of removal from exposure. This difficult question has not received much attention but there is evidence that fibrotic changes progress after withdrawal and it is abundantly clear that both lung cancer and malignant mesothelioma, which reflect accumulated exposure, usually occur years after it has ceased.

The fourth recommendation called for intensified investigation of mesothelial tumours. Much has been learned about the frequency of this sensitive indicator of mineral fibre exposure in certain countries (see for example several papers in the Banbury Report No 9.⁴³ The development of electron microscopic methods of quantitative analysis of mineral fibres in tissue has added a new dimension to biological monitoring with great potential for environmental health research. A fifth recommendation urged far wider study of asbestos-exposed populations and many more groups have been studied, but few with adequate measurement of either exposure or response. Finally, the Working Group called for the development of improved epidemiological methods. The considerable growth of occupational epidemiology, in quantity, quality and innovation, during the last 20 years has been due in large part to stimulation provided by the mineral fibre problem — as this and many other scientific conferences testify.

The gaps

For every achievement just listed, it is easy to find a mirror image of ignorance. Fundamentally the problem is lack of quantification, especially as to exposure. After 20 years it is indeed regrettable that there are but a handful of reasonably satisfactory cohort studies. The need to separate fibre-type and industrial process was stated fairly explicitly in New York but there have been few attempts to seek out occupational groups capable of resolving these questions. Despite the fact that over half

the world's asbestos is used for asbestos cement, building products and friction materials we have very little data indeed in these industries. Not only are these sectors of great socio-economic importance but they may even be relatively safe. Unfortunately there are more incentives for medical scientists to demonstrate hazards, however well recognized, than any new but negative finding.

So far as man-made fibres are concerned, the work on health effects in fibre production, at least in two major investigations, is outstanding and with time these will prove even more informative. These studies suffer, however, as a result of the very low exposure levels prevailing in this industry. As with asbestos, much higher exposures often occur in secondary and application processes. These, so far, have proved very difficult to study but the need to do so remains a priority.

Epidemiologists cannot be blamed for the lack of environmental measurement at the workplace many years ago, though they can if they fail to use what is available. This deficiency, always serious, is especially so at the present stage of mineral fibre research. We desperately need to know, not only the identity and concentration of fibres in the ambient air but also distributions by length and diameter in the *sub-microscopic range*. The problem seems well nigh insoluble, but hopefully some innovative young scientists will find the answer.

Policy issues

While knowledge is sufficient for the development of control procedures in specific situations, it is too seriously deficient on several fundamental questions to allow more generalized policies to be designed with any confidence. There now exist a number of reasonably reliable sets of exposure response data for particular industrial processes, sufficient for those concerned to seek agreement on acceptable exposure levels. It must be understood however that any important change in the process, certainly in the materials used, may well invalidate the data base. Moreover, the natural desire for a simple uniform hygiene control 'standard' is not achievable or will prove unnecessarily severe in some situations and too lax in others. Attempts to regulate asbestos without regard for fibre type may be adequate for lung cancer and asbestosis in most industries but do little to reduce the risk of mesothelioma. Indeed, such policies are not only inherently unsafe but socially unjust, in that they do more to protect cigarette smokers than non-smokers. The search for safe substitutes for asbestos — natural or man-made fibre, mineral or organic — is not hopeless but will certainly remain difficult and hazardous until the parameters of pathogenicity are fully understood.

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*Summaries of these papers can be found in "Biological effects of man-made mineral fibres. Report on a WHO/IARC meeting. EURO Reports and Studies 81. WHO, Denmark, 1983".