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Editorial

Mineral fibres and mesothelioma

There has been considerable recent interest in the suggestion that mineral fibres other than asbestos might be associated with mesotheliomas in the pleural and peritoneal cavities. Compared with the wealth of information on the consequences of exposure to asbestos, information about the effects of other fibrous minerals is sparse and much of it is of a preliminary nature. In this editorial the relationship between fibrous minerals and mesothelioma will be considered under the following headings: (1) asbestos minerals of commercial value; (2) asbestos minerals as potential environmental contaminants; (3) naturally occurring fibrous minerals as potential environmental contaminants; (4) synthetic mineral fibres.

Asbestos minerals of commercial value

Asbestos is now considered to consist of six naturally occurring minerals: chrysotile, crocidolite, amosite, anthophyllite, tremolite, and actinolite. Chrysotile is a member of a group of minerals referred to as serpentines and it is composed almost exclusively of magnesium in combination with silica. It has a sheet structure that curls to produce hollow, tube like fibres. The other five members, belonging to the mineralogical group referred to as the amphiboles, are very similar in crystal structure, being chain silicates, but they differ in chemical composition. Crocidolite and amosite are iron rich varieties, anthophyllite is a magnesium rich mineral, and tremolite and actinolite contain a large amount of calcium together with magnesium.

The world production of asbestos in 1976 was 5000 million kg; of this, 97% was chrysotile and the remainder was crocidolite and amosite. The commercial production of the other three amphiboles has been minimal in the past but they are important as contaminants of other minerals and of agricultural soil, as will be discussed later. Chrysotile is widely distributed, with the largest commercial production in the Ural mountains in Russia, Quebec Province in Canada, Zimbabwe and Swaziland in Southern Africa, the Italian Alps, and Cyprus. Crocidolite is now mined almost exclusively in Cape Province in South Africa and, until recently, in Western Australia. Amosite is exploited only in the Transvaal, but deposits have been discovered in South India.

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Asbestos has over a thousand uses,[1] so the number of occupations in which exposure may have occurred is large. Crocidolite, because of its resistance to acids and sea water, was used extensively in naval insulation and fireproofing, as insulation for steam locomotive boilers, and later for soundproofing in passenger coaches. A large amount was used in the insulation of buildings. The use of crocidolite and its importation into Britain has been severely limited since 1969.[2] Amosite has been used for thermal insulation, in floor tiles and in the superstructure of ships. Chrysotile has been used for all other purposes, but particularly in asbestos cement products, insulation, and fireproofing and in the manufacture of friction materials such as brake linings and clutch plates. Chrysotile is still the main fibre used in textiles, but this is no longer a major section of the asbestos industry. The destruction or demolition of buildings, ships, and railway rolling stock is a source of environmental pollution.

Asbestos minerals as potential environmental contaminants

ASBESTIFORM MINERALS CONTAMINATING BANDED IRONSTONES

Although banded ironstone deposits frequently contain seams of fibrous silicates; most of these are small but occasionally large deposits occur. These large deposits are the source of the amphibole asbestos fibres that are exploited in the southern hemisphere. Other deposits are of no commercial value—for example, the amphibole fibres in the iron ore Mesabi Range on the shores of Lake Superior. Although iron ore mining in this region has resulted in contamination both of the atmosphere and of the water of the lake, no evidence of a hazard to man has been established. All the fibres are less than 5·0 μm long.

TREMOLITE AND ACTINOLITE AS CONTAMINANTS OF OTHER MINERAL DEPOSITS

Tremolite and actinolite, members of the amphibole fibre group, are friable and of little economic importance but are contaminants of industrial talc. These fibres also occur as contaminants in chrysotile deposits and are released when these materials are milled. Tremolite has been used as material for stuccoing of domestic dwellings in certain villages in Turkey,[3] Cyprus, and elsewhere in the eastern Mediterranean. In Turkey villagers collect it from quarries that have been used for generations. This was also the case in the vicinity of the chrysotile asbestos mine in Cyprus. In Korea there are mines producing tremolite for which a market is being sought.

POSSIBLE CONTAMINATION IN AGRICULTURE

Fibrous mineral contamination in agriculture has been appreciated only during the last few years and may be shown to be important. So far evidence is fragmentary. The only confirmed instance of asbestos contamination is in Bulgaria, where pleural plaques have been found in people who work in the tobacco fields, which have tremolite and anthophyllite in the soil.[4 5] Huge calcified pleural plaques have been reported from Finland[6]; anthophyllite was recovered from the lung tissue. More recently, tremolite has been discovered in lungs in similar cases from Greece.[7]

Sequelae of exposure to asbestos dust

There have been many descriptions of the lesions resulting from exposure to asbestos dusts.[8] Briefly, they are as follows: (1) asbestos bodies in the sputum; (2) pleural plaques and diffuse pleural fibrosis; (3) interstitial pulmonary fibrosis (asbestosis); (4) an increased incidence of carcinoma of the lung; (5) diffuse mesothelioma of pleura and peritoneum; and (6) an increased incidence of gastrointestinal tumours and a possible increase in incidence of carcinoma of the larynx. On detailed investigation, each of these findings has provided problems that not only apply to asbestos exposure but also have to be considered in the wider assessment of the other mineral fibres.

The evidence that crocidolite (blue) asbestos is associated with the development of mesotheliomas is clear.[9] This relies on the original South African data,[10] clearly supported by the findings in Western Australia,[11] where crocidolite was produced on a relatively small scale. Mesotheliomas are occurring both in those employed in the mines and in the environmentally exposed population. Only in South Africa and Western Australia is there evidence of mesotheliomas in those living in the vicinity of the mines and mills.

In Britain, as in other manufacturing countries, it is difficult to establish a definite exposure to a single type of fibre as most industrial workers have been exposed to more than one mineral. The technique developed for the identification of mineral fibres in lung tissue,[12] is the most successful method available for identifying the individual exposures but this has emphasised the complexity of the problem. For example, the gas mask workers investigated by Jones[13] appear to have had a pure exposure to crocidolite, but Pooley's analysis of lung tissue confirmed the presence of an appreciable amount of chrysotile. This contrasts with the findings in cases of mesothelioma in Britain and the United States, in which the amount of chrysotile found in the lungs of those with the tumours is of the same order as that in the lungs of controls. The difference is that in the British cases there is an association with crocidolite.[14] In the American cases amosite is present as well as crocidolite and is found in larger quantities.[15] The whole problem has been further complicated by the finding of tremolite in those who were previously thought to have been exposed only to chrysotile. Doll and Peto[16] say that "The conclusion that chrysotile is carcinogenic to humans can be questioned only on the grounds that it is commonly contaminated by small amounts of tremolite (an amphibole). Any distinction between the effects of chrysotile and tremolite is, however, academic unless tremolite can be removed from chrysotile or supplies can be obtained which are tremolite free."

Importance of fibre size

The first evidence[17] of the importance of fibre size indicated that fibre diameter is the major factor and length the minor factor in deposition, while a later study[10] again emphasised that the ultimate diameters of crocidolite and amosite were essential in assessing the probability that the fibre would be associated with mesothelioma development. Animal experiments[18-20] in which asbestos and other mineral fibres were implanted into the pleural and peritoneal cavities of rats gave similar results. From all these investigations we can now conclude that the fibres responsible for mesotheliomas have a diameter of less than 0.25 μm and probably a length greater than 5.0; μm. Fibres of up to 3.0 μm in diameter that are inhaled and retained in the peripheral airways are associated with pulmonary fibrosis; and the effective length of at least 10 μm suggested by Timbrell in 1968[21] has not been challenged, although there is no agreement on the maximum fibre length that might be associated with disease. The result of these experiments and the emphasis on fibre size thus led to the important finding that fibres of the correct size other than asbestos could cause mesotheliomas.

In an attempt to clarify the importance of fibres in tissue, a detailed examination of a large series of cases is being undertaken. Included in the investigation are cases of mesothelioma from the United Kingdom,[22] the United States, and Canada[23]; fewer cases of mesotheliomas from Cyprus and Central Turkey; cases of asbestosis from the United Kingdom and elsewhere; and a large number of lungs from adults who have had no industrial exposure as a comparable group.

TREMOLITE

Three phases of tremolite have been studied experimentally: (1) coarse flake like fibre; (2) fibre with a diameter of 1.0–3.0 μm; and (3) a very fine fibre with a diameter of less than 0.5. In both mammalian cell cytotoxicity tests and pleural implantations only the very fine tremolite fibre produced significant results, with appreciable cytotoxicity and a high incidence of mesotheliomas.[24]

The flake like tremolite used in the previous experiment was obtained from a talc mine in California. There is no evidence of disease among the miners and millers at this site. A coarse fibrous tremolite is also found as a contaminant of the chrysotile deposits in Quebec Province in Canada.[25] This fibre has been found in the lungs of workers from these mines and is thought to be associated with pleural plaques and pulmonary fibrosis. In talc mines in the northern part of New York State there is contamination by a coarse fibre talc, and pulmonary fibrosis and carcinoma of the lung have been reported.[26] In Eastern Turkey and Cyprus, where the tremolite is less than 0·5 μm in diameter, mesotheliomas have occurred. Elsewhere in Turkey, where the coarser fibre is used for stuccoing, large pleural plaques have been reported.

Naturally occurring fibrous minerals

The naturally occurring fibrous minerals are a miscellaneous collection. Most are silicates, but some are metal oxides such as rutile (the fibrous form of titanium dioxide), which is proving of interest because it has been recovered from the lungs of various industrial workers. The two groups of fibrous silicates of particular interest are the zeolites and the clays.

ZEOLITES

Zeolites are a complex group of silicates formed by metamorphosis in deposits of volcanic ash. They are characterised by an open lattice structure, which is useful for filtration, catalysis, and absorption in the chemical industry and in agriculture. Most of the commercially used zeolites are now synthesised and non-fibrous. Few of the natural minerals are fibrous but there are at least three: mordenite, clinoptilite, and erionite. These fibrous zeolites form hexagonal glassy rods, which may occur singly or in strands and vary in diameter from deposit to deposit. Extremely fine erionite fibres have been found in a few deposits in Oregon in the United States and in central Turkey.

The association between exposure to fine erionite fibres and the development of numerous mesotheliomas of pleura and peritoneum in three villages in the Urgup region of Anatolia in Turkey are well known, although the epidemiological evidence for a causative role of fine fibre erionite still requires strengthening—for example by demonstration of fine fibres within the lungs. Work is currently in progress that may supply this additional evidence. Examination of pleural biopsy material and some associated lung tissue and examination of the lungs of sheep (which act as suitable dust samplers) has produced preliminary evidence that fine erionite fibres are present in both human and animal lungs from the suspected villages but are absent from material from elsewhere in Turkey (unpublished observations). Additional evidence has come from intrapleural inoculation and inhalation experiments, in which animals have been exposed to (1) the erionite rock fibre mixes from Turkey, (2) a very similar pure erionite fibre from Oregon, and (3) a slightly shorter prepared fibre from near Auckland in New Zealand. The Oregon and Turkish fibres produced a very large number of mesotheliomas on intrapleural inoculation. The Oregon fibres produced mesotheliomas after inhalation in all cases[27]; no other fibre, including crocidolite, has ever produced tumours in more than 10% of cases after inhalation. Investigations are proceeding in Oregon, where no cases of mesothelioma appear to have been recorded. At the site from which our fibre was obtained, however, there is a ghost town with a very large cemetery! Examination of lung material from humans and cattle from the region would produce interesting information.

ABSORBENT CLAYS

The absorbent clays have been used for various industrial purposes for many years, particularly as oil absorbents in factories and garages and as a "gelling" agent in drilling muds for the oil industry. Recently there has been an increasing demand for absorbent clays for use as cat litter. A chance discovery showed that some of the material used for cat litter was fibrous in nature. Although these minerals appeared to consist of solid materials, when finely ground samples were examined by transmission electron microscopy they were found to contain numerous short fibres. The fibres were particularly noticeable in minerals such as attapulgite, palygorskite, and sepiolite. During the past year major industrial groups have been considering the use of absorbent clays as an asbestos substitute.

Studies of the absorbent clays are needed and some are already in progress. Animal investigations are being undertaken, as well as studies at sites of sepiolite and attapulgite production in Spain and mineralogical studies have been undertaken on attapulgite from the far west region of Spain. According to the producers this fibre, which has been used as a substitute for chrysotile, also has an excellent "gelling" effect and has been used for drilling mud by several major oil companies. Information from the industry indicates that the drilling muds are mixed dry in enclosed chambers on the rigs, producing a very dusty atmosphere. Early indications from experiments in which this material is implanted intrapleurally are that it may produce nearly as many mesotheliomas as the contaminated chrysotile it is replacing. The oil industry is now aware of this finding.

Palygorskite has been obtained in small amounts as a contaminant in a quarry in the English Midlands. Unpublished experiments using this material show that it is capable of producing a high incidence of mesotheliomas after intrapleural inoculation and that it can produce severe pulmonary fibrosis in inhalation studies.

Man made mineral fibres

The synthetic mineral fibres comprise slag wools derived from industrial slag, rock wools made from volcanic rock, and also glass and ceramic wools and filaments. All are formed from a liquid melt at temperatures of 1000–1500°C, although the methods of producing the fibres vary. The fibres have a glassy structure and are thus not crystalline. Their length and diameter distributions vary considerably and are dependent on the method of production and the chemical composition. Usually commercially produced fibres are considerably coarser than asbestos fibres, although specialised samples have been produced that have diameters similar to those of asbestos. Synthetic fibres fall into three broad categories of fibre size. The first is the continuous filament glass fibres that are used in textiles and as a reinforcement for plastics and other materials; these products have fibre diameters greater than 8 μm. In the second category are insulation wools with fibres nominally 1–6 μm in diameter, although there are ends that go to 0.20 μm. The third category contains fibres smaller than 1.0 μm in diameter, which are used for specialised purposes such as the manufacture of scientific filter papers. The fibres are usually coated with binding compounds to produce fabricated shapes and forms. In the past, insulation wool binders have included bitumen, urea, and phenol-formaldehyde resin compounds. Today innovations in binding agents based on resin systems are continually being made.

Information on the potential of man made fibres for producing disease is limited. Experiments in animals in which vitreous wools used in insulation are introduced intrapleurally or inhaled[28] have failed to show any significant adverse effects. A further fibre, an extremely fine glass microfibre produced by an American company, did produce mesotheliomas under the same conditions; but fibres that were slightly coarser but otherwise identical did not.

Ceramic fibres have not been studied as comprehensively as the vitreous materials and fuller information is required. There is particular interest in a further ceramic material, mullite. Mullite was found in nature in a small deposit in the island of Mull; otherwise it is seen only as a synthetic but rare aluminium silicate fibre in refractory bricks that have been subjected to intense heat. In our studies[29] and in investigations in Europe[30] and Canada[31] the most common fibre found in human lung tissue was identified as mullite. It is now suggested that mullite is formed when coals with a high clay content are burned. Extraordinarily high mullite counts are found in lung tissue from workers in coal fired electricity power stations. Occasionally workers from these plants have mesotheliomas, with mullite as a major component of the dust found in their lungs. Most of the fibres seen in these cases are short but the possibility of selective retention of the longer fibres is under investigation.

Selective retention of fibres

The importance of selective retention of fibres has been discussed in a recent paper.[32] We are convinced that those diseases associated with exposure to mineral fibre are due to the fibres retained in the lungs. If this hypothesis is correct then the lungs are the only reliable dust sampling mechanism that is available for the recording of the lifetime exposure of an individual. In the investigations that have been studied there are instances in which the significant mineral fibre or fibres retained in the lungs have either not been recorded in the environment or are minimal components of the total sample of the environmental or occupational atmosphere. This was well illustrated in the studies of the chrysotile millers who were found to have significant quantities of tremolite in their lungs, and in the finding of erionite fibres in the lungs of the Turkish villagers. In view of these findings analysis of the fibres in the lungs would appear to be essential in the search for potential occupational hazards. Reliance on environmental dust studies can give results that may be totally misleading.

Conclusions

There is clearly an association between exposure to dust containing mineral fibre and the development of diffuse mesotheliomas of pleura and peritoneum. Combined epidemiological, pathological, and mineralogical studies indicate that any mineral fibre, if straight and having the defined length and diameter, must be regarded as a possible hazard, with the potential for causing malignant transformation of the mesothelial membranes. Most minerals studied in experimental animals react predictably in relation to their size and concentration. The response to the fine erionite fibres illustrates that there must be other factors that are as yet unknown. Future informative studies will depend on the recognition and definition of natural and synthetic fibres in the lung tissue of those suspected of having been put at risk. Unless the dimensions of these fibres are calculated with the use of transmission electron microscopy and the nature of the fibre is identified, the crucial factors may not be recognised.

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