

EPIDEMIOLOGY OF ASBESTOS CANCERS

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1. Historical Aspects

Asbestos was used in prehistoric and classical times to strengthen pots (Noro, 1968) and to make fire-resistant cloth in which to preserve the ashes of the eminent. The modern industry dates from about a hundred years ago when large deposits of chrysotile were discovered almost simultaneously in the Province of Quebec, Canada, and in Russia near Sverdlovsk. There has been a very rapid expansion of the use of asbestos, particularly since the Second World War (see Table I).

Asbestosis, the characteristic fibrosis of the lung caused by inhaling asbestos, was first detected at the turn of the century in France and Britain, but it was not until the early 1930's that asbestosis was shown to be a major occupational hazard in the asbestos-textile industry (Merevether & Price, 1930). It was in this industry, which was built up on the experience gained in spinning and weaving cotton, that asbestos was mainly used until its value as a reinforcing agent in cement was discovered.

TABLE I. World asbestos production

Date	Amount produced (tons*)		
	Chrysotile	Crocidolite	Amosite
1924	300 000	5 000	3 000
1964	3 000 000	120 000	80 000

* 1 ton = 1016 kg.—ED.

The first warning that there might be an additional hazard—bronchial cancer—came from pathologists in Britain and the USA in 1935. Shortly afterwards a report from Germany (Wedler, 1943) indicated that pleural cancers might also be associated with asbestos, but this attracted little interest. In Britain in 1947, the Chief Inspector of Factories (Minister of Labour and National Service, 1949) reported that about 15% of all death-certificates for males on which asbestosis was mentioned recorded that death had occurred from bronchial cancer, but the association between asbestosis and bronchial cancer was doubted in other countries. Confirmation of the excess risk came in 1955 from a study by Doll of workers in "scheduled" occupations in a textile factory in the north of England. ("Scheduled" occupations are processes which were scheduled under the Asbestos Industry Regulations of 1931 as being dusty.) Men employed before 1930—when improvements in dust control were introduced—had a death-rate from lung cancer ten times the expected rate. Women were also affected. A few years later, a study of asbestos miners in the Province of Quebec (Braun & Truan, 1958) showed a much smaller excess risk of bronchial cancer, despite the dustiness of the mills having been exceptionally high in the past. The epidemiological techniques used in this survey have been criticized (Mancuso, 1965), but an additional lesson to be learnt from the apparent conflict of evidence is the need to pay more attention to the type of asbestos to which exposures had occurred and to the physical state of the respirable fraction of the dust. The nature of the dust in mining and textile processes differs considerably (Timbrell & Holmes, 1970). The studies of asbestos cancers have emphasized the need for a multi-disciplinary approach by geologists, physicists, chemists, pathologists, epidemiologists and clinicians.

By 1955, when Doll's study had also shown that those exposed only to the improved conditions in the factory had little or no excess risk of bronchial cancer and that the risk of asbestosis had been materially reduced, it looked as though the problem had been largely solved. But a year later, Wagner and his colleagues discovered the first of a large group of pleural and peritoneal tumours—mesotheliomata—apparently related to exposure to crocidolite, the blue type of asbestos mined in the north-west of Cape Province, South Africa. His paper (Wagner, 1960) published in the proceedings of the Johannesburg Pneumoconiosis Conference of 1959 stimulated a world-wide interest in the problem.

2. Types and Uses of Asbestos

It is becoming increasingly clear that the different types of asbestos are not all equally hazardous. Thus, in any new epidemiological studies it is essential to have knowledge both of the type of asbestos to which exposure has occurred and of the circumstances—mining and milling, textile manufacture, insulation, building and so on—in which the individual has been principally exposed to the dust. Much of the recent work has attempted to solve this problem and obtain at least approximate relative risks of different exposures to different types of asbestos in different occupations. As there are over a thousand uses of asbestos (Hendry, 1965), the number of occupations in which exposures may have occurred is large.

All types of asbestos are chain silicates, but they occur in two main groups that are of commercial value: chrysotile (white), and the amphiboles of which there are distinct varieties, crocidolite (blue), amosite (brown), and anthophyllite (white).

TABLE II. Chemical composition of some commercial varieties of asbestos

Variety	Composition (%)				
	Si	Fe	Mg	Na ₂ O	H ₂ O
Chrysotile (white)	40.0	2.0	38.0	0.25	13.3
Crocidolite (blue)	50.0	40.0	—	5.0	2.0
Amosite (brown)	50.0	40.0	—	0.1	2.3
Anthophyllite (white)	58.0	6.0	29.0	—	2.2

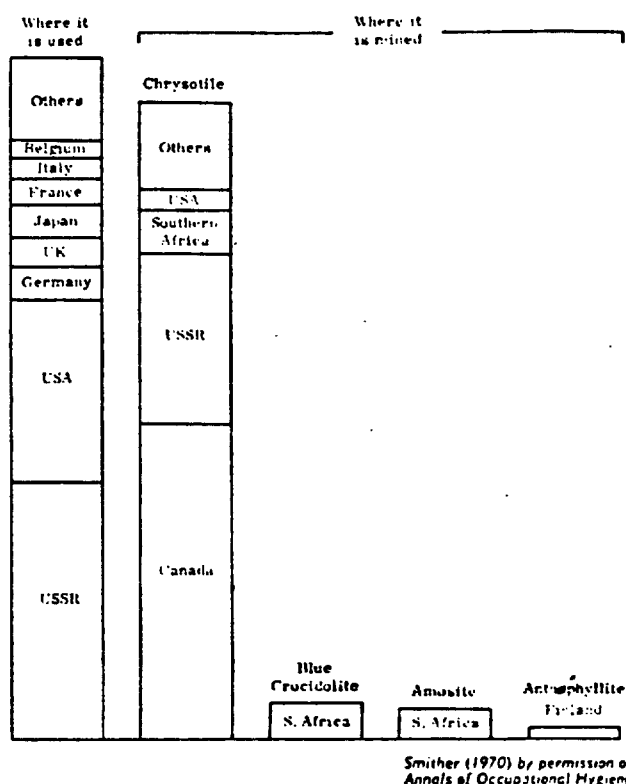
Table II shows the colour and approximate chemical composition of the principal commercial varieties. Figure 1 shows the sources and output of the principal mining areas and where the mineral is used. Chrysotile is much the most widely used. The long fibres are used for asbestos textiles but, on a weight basis, these products now form a small fraction of the total of this type of fibre. Most of the shorter-fibred material goes into cement asbestos products: frictional materials such as brake-shoes and clutch-plates, and also material for floor-tiles and building-boards. Chrysotile is thus very widely distributed in all industrialized communities. The acid resistance of crocidolite has been exploited as a filling in battery cases, but it has been also used extensively for spraying on to bulkheads and under decks in naval vessels, especially during and since the Second World War. It is also used mixed with chrysotile to improve the rate of production of asbestos cement products. The long springy fibres of amosite, too brittle to weave, are used for thermal insulation of pipes and machinery, and in the superstructure of ships. The production of crocidolite and amosite has been increasing rapidly during the last ten years. On account of its wide-spread use and indestructibility, asbestos is a potential contaminant of the general atmosphere. Confirmation of this has come from a number of studies stimulated by observations in South Africa (Thomson, Kaschula & MacDonald, 1963). These authors showed that, in a consecutive series of adult necropsies, asbestos bodies could be demonstrated in 25% of cases. This was done by using a relatively crude technique. These findings have now been confirmed by similar studies in the USA, Canada, Italy and Britain, with results varying from 20% to 50%.

Asbestos is an invaluable material, contributing greatly to safety of buildings and ships because of its fire resistance, and in motor cars to the efficiency of brakes and clutches. These assets have to be set against the risk in its use. Present epidemiological outlook and methods are more attuned to measuring the excess hazards than the benefits from the use of industrial products. This is another example of the need, in assessing the results of epidemiological work, for a scale of risks and standards of comparison, as mentioned by Doll, p. 25 of this Bulletin.

3. Recent Epidemiological Studies of Asbestos-Related Cancers

The last ten years have seen a world-wide interest in asbestos-related cancers. A measure of co-ordination and co-operation in international studies has been achieved, especially since 1964. The first international conference entitled the "Biological effects of asbestos", sponsored by the New York Academy of Sciences and held in 1964, brought together

FIG. 1. Sources and output of asbestos, and where it is used



The annual consumption of asbestos now exceeds 3 000 000 tons

knowledge from many countries (Whipple, 1965). This was followed by a Working Group on Asbestos and Cancer under Dr Harold Stewart, sponsored by the International Union Against Cancer (UICC). The recommendations of the Working Group were widely published (International Union Against Cancer, 1965). Since then a Sub-Committee on Asbestos Cancers under the UICC and, more recently, the International Agency for Research on Cancer (IARC) have provided channels for exchange of information and support for international research. The industry, through the Asbestosis Research Council in the UK and the Institute of Occupational and Environmental Health of the Quebec Asbestos Mining Association in Canada, has assisted many aspects of the investigations.

Epidemiological studies have been of three main types: (i) prospective mortality studies of defined groups of workers in asbestos mining and manufacture; (ii) retrospective studies of occupation and residence of groups of subjects with mesothelioma of the pleura and peritoneum, taken from hospital records; and (iii) collection of cases of mesothelioma to study their geographical distribution.

The quality of the information has varied greatly, as would be expected in such retrospective studies. In the mining areas it has been possible to be fairly sure that exposures have been to only one type of asbestos, but the information about the concentrations of past dustiness has been scanty or obtained largely by guesswork, and in many instances the populations at risk cannot be well defined. In the industrialized countries

where asbestos has been used in large amounts, the information about the populations in factories or from trade union records has been more complete, but the exposures have usually been to more than one type of fibre. Some information about dustiness has been available from past records, or by extrapolation from measuring the current levels of dustiness while re-using older techniques now largely superseded.

a. Southern Africa

In Rhodesia and Swaziland, where chrysotile has been mined for about 40 years, there are no clear pointers to a marked excess risk of bronchial or pleural cancer. The incidence of asbestosis also appears small. In the north-west of Cape Province, where crocidolite has been mined for more than 50 years, more than 100 cases of mesothelioma of the pleura and peritoneum have been reported, mainly in those working or living near the mines (Gilson, 1966). The death-rate from bronchial cancer in this area was shown to be raised, in an independent study of the national statistics (Oetlé, 1964). In the Transvaal, about 400 miles north-east, where amosite and small amounts of crocidolite have been mined for over 40 years, mesotheliomata are very rare (Harrington, Gilson & Wagner, 1971). This paradox has been used as evidence against crocidolite's being the cause of mesotheliomata (Wright, 1969). A possible explanation of why there may have been a big difference in the risk in the two areas, despite the asbestos being chemically very similar, has recently been suggested by Timbrell, Griffiths & Pooley (1971) as a result of comparing the average diameter of the fibres of the mineral from the two areas. Those from the north-west of Cape Province are much finer. From a knowledge of the aerodynamic properties of fibrous particles and of factors controlling their entry into the lungs, it can be predicted that the dustiness in the north-west of Cape Province would have been greater and the chances of the fibres' gaining access to the peripheral parts of the lung greater still in the case of the Cape blue asbestos, compared to the amosite and crocidolite from the Transvaal.

b. Britain

More epidemiological studies of the asbestos cancers have been made in Britain than elsewhere. All the groups of mesothelioma with case controls have shown a significant association with definite or probable exposure to asbestos. The more complete the information about the cases, the more clear-cut the association, but not all cases of mesothelioma are asbestos-related. In about 10-15% of cases where the information has apparently been complete, no history of exposure to asbestos has been recorded and few or no asbestos bodies have been detected in the lung. These studies have shown the need to take the most detailed occupational history to exclude possible exposures to asbestos. For example, a small group of cases of mesothelioma occurred in women who worked in a bag-cleaning factory. Detailed inquiry showed that some of the bags had been previously filled with asbestos. Paper and plastic disposable bags are now used for the transport of fibre. In another group of cases, exposure had occurred during the Second World War while gas-masks with asbestos filter-pads were being assembled (J. S. P. Jones, personal communication, 1957). In other patients, exposure has occurred owing to the abrasion of asbestos insulation near their place of work.

A further follow-up of workers in the scheduled areas of asbestos-textile factories that were using mostly chrysotile

(Knox, Holmes, Doll & Hill, 1968) confirmed the earlier reports of a great reduction in the risk of bronchial cancer in those who worked only in the improved conditions introduced in about 1933. But a small number of cases of mesothelioma had occurred. In some, exposure had been short but the interval between first exposure and death long.

In another asbestos factory making textiles and insulating materials where exposure had been to chrysotile, amosite and crocidolite, there was a marked excess risk of bronchial cancer in workers followed up for 16 or more years and who had been intensively exposed to asbestos. In those with less intensive or moderate exposure the risk was not raised. Length of exposure was apparently less important than expected, since the excess risk was almost as large in those with short (less than two years) intensive exposures as in those with intensive exposures over a longer period (Newhouse, 1969). A review of the pathological evidence showed that the number of mesotheliomata had been under-estimated. Peritoneal tumours were commoner than pleural ones in the most intensively exposed groups.

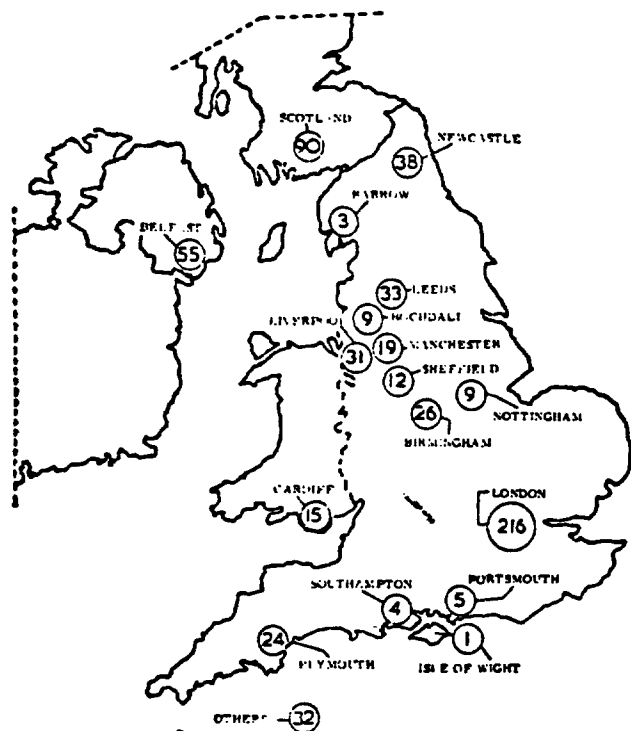
In Britain, the dust conditions in the asbestos-textile factories improved after 1930. Much less improvement or protection occurred in the insulating industry, or in the dockyards. In Northern Ireland, a marked excess of deaths from lung cancer in ladders and many cases of mesothelioma, mainly pleural, were discovered from a study of union records and a follow-up of union members (Elmes, 1966). In Devonport dockyard, intensive exposures to asbestos occurred in the late 1940's and early 1950's during spraying of crocidolite under decks and on bulkheads, and also during refitting of naval vessels, but a proportional mortality study of deaths in Plymouth between 1959 and 1968 showed no excess deaths from asbestos-related cancer in past employees of the dockyard (Harries, 1968). A number of cases of mesothelioma have occurred since, related to asbestos exposure in the dockyard. It is probable that the long period that elapses between first exposure and the occurrence of mesotheliomata, which is a characteristic of these tumours, will lead to a rise in the numbers in the future. Plans are being made to plot the course of future changes in mortality and check the efficiency of the major changes in the procedures for using asbestos and substitution of other materials introduced by the Royal Navy in the last three years.

Since 1962, a register of cases of mesothelioma has been kept at the Medical Research Council's Pneumoconiosis Unit. Information on many cases is inevitably incomplete, but the geographical distribution of cases, which have in the majority been verified as mesotheliomata by one or more members of the Panel of Pathologists set up under the UICC Committee, is shown in fig. 2. There is a concentration of cases in ports and in cities with factories where asbestos has been handled in large amounts in the past. Although the number of new cases of mesothelioma has been apparently rising steeply in Britain since 1962, the geographical distribution of the cases has not markedly changed. The cumulative totals are: up to 1962, 4; to 1965, 160; and to 1969, 622; and the number of new cases that are detected each year is now about 60. Present evidence points to nearly all of these cases being occupational and not the result of contamination of the general environment.

c. United States of America

In the USA, prospective mortality studies using Social Security records showed an excess risk of bronchial cancer in workers in an asbestos-textile factory just before the Second

FIG. 2. Mesotheliomata associated with exposure to asbestos



Numerals in circles show the provisional number of cases recorded up to 1969

World War (Mancuso & El-Attar, 1967). Information on the jobs within the factory is not available with this technique and the actual risk of those significantly exposed could not be separately measured. In the insulation workers in the New York area (Selikoff, Hammond & Churg, 1970), where a high proportion of the trade union members may be presumed to have had significant exposure to asbestos, the death-rates from lung cancer (of those on the books in 1942) were about seven times those expected. Smoking habits were obtained on the survivors of the original population in 1963 and a follow-up to the end of 1968 showed that the risk of lung cancer was exceptionally high in those exposed to asbestos and cigarette smoke compared with those with no exposure to asbestos and with non-smokers. This detailed survey has emphasized that the risk of mesothelioma increases with passage of time and that there is need for a very long follow-up to detect the full extent of the risk from this cause. Information about the type of asbestos used in the past by this group of workers is inevitably incomplete, but crocidolite, if used at all, was present in very small amounts compared to chrysotile and amosite.

Occupational and residential information about individuals with mesotheliomata from hospital records has confirmed observations in the UK, Germany, and South Africa that there has in the past been a risk of asbestos-related mesotheliomata from exposure to dust outside the factories and other places of work (Lieben & Pistawka, 1967). In some cases, asbestos dust from clothing brought into the home seems a probable source of exposure. In others it is possible that

exposure occurred from dust in the immediate environment of a factory or mill (Anspach, Roitzsch & Clausnitzer, 1965; Newhouse & Thompson, 1965).

d. Canada

Since 1878, most of the chrysotile used in the Western world has been mined in the Province of Quebec at Asbestos and Thetford Mines. Until recent years, dust control was poor and the mines and their neighbourhood were noted for a snow-like appearance at all times of year! This region is being studied by McDonald, McDonald, Gibbs, Siemiatycki & Rossiter (1971). A remarkably complete follow-up of about 12000 workers, born between 1891 and 1920 and employed in the mines and mills, has shown that there is only a small (about 12%) excess death-rate from all causes in the 10% of employees who were exposed to the highest dust levels in the past. The excess death-rate from lung cancer in the highest exposed group is about five times that in the employees with the least exposure. Despite the heavy general air pollution by chrysotile dust over many years, the crude death-rates from lung cancer in the population of these two mining towns are less than the death-rate for the Province of Quebec as a whole.

Mesotheliomata are very rare in chrysotile miners, and in Canada as a whole only 165 cases were recorded by over 400 pathologists between 1960 and 1968. Of the minority of cases with a clear-cut occupational history of exposure to asbestos, mesotheliomata occurred more frequently in the manufacturing and insulating industries (where exposures are more likely to have been due to more than one type of fibre) than in the chrysotile miners.

e. Finland

Anthophyllite has been mined for many years at Paakkila, the principal source of this type of amphibole in the Western world. A prospective mortality study of the miners has shown a small excess risk of bronchial cancer (Kiviluoto & Meurman, 1971). Pleural thickening and calcification, which are recognized complications of exposure to asbestos and related minerals, are relatively common in Finland, but despite careful search over recent years no mesotheliomata associated with exposure to anthophyllite asbestos have been detected in Finland. None has been observed among the miners at Paakkila.

Death-rates from lung cancer in Finland are second only to those in the UK. In a study of 50 cases of lung cancer and matched controls without this disease, asbestos bodies were more commonly seen in the cases of lung cancer, but not significantly so. However, there was evidence that combined exposure to cigarette smoke and asbestos (as indicated by asbestos bodies) was more likely to be associated with lung cancer than were either alone (Meurman, Hormia, Isomäki & Sutinen, 1970).

f. Sweden

In Sweden there has been less interest in this problem until recently. A collection of cases of mesotheliomata and controls from the hospital records over ten years at Malmö showed a less clear-cut relation between the presence or absence of asbestos bodies and the occurrence of mesothelioma than in most other studies, but the abundance of bodies did relate to the presence of mesotheliomata (Hägerstrand, Meurman & Ödlund, 1968).

g. Holland

Mesotheliomata have been shown to be associated with shipbuilding in Flushing (Stumphius & Meyer, 1968). The relation to asbestos exposure was not clear until detailed occupational histories and studies of the lungs for asbestos bodies were made. The possibility that fumes associated with welding might be an additional factor was raised, but asbestos pads are used in shipbuilding to retain heat during welding and some welding rods are wrapped with asbestos.

h. Other Countries

From Australia, West and East Germany, the USSR, Italy, and many other countries there are reports linking asbestos exposure with bronchial cancer and mesothelioma of the pleura and peritoneum. Reports from Australia that mesotheliomata have occurred following exposure to crocidolite in the mines there add to the evidence that this type of fibre may carry a greater risk of mesothelioma than other types of asbestos, especially as the crocidolite fibres from these mines (now closed) are even smaller in diameter than those from the north-west of Cape Province (Timbrell, Pooley & Wagner, 1970).

4. Conclusions from Epidemiological Studies

The association between past exposure to asbestos and bronchial cancer and mesothelioma of the pleura and peritoneum is now well established from observations in many countries, but there are differences in the epidemiology of the two types of tumour.

The risk of bronchial cancer is more clearly related to the intensity of past exposure and to the risk of asbestosis. When the environmental control is good enough to eliminate asbestosis, the excess risk of bronchial cancer is also small. It is not known whether the type of asbestos inhaled affects the risk of bronchial cancer in man. Experiments in animals suggest that it should, because chrysotile produces less severe fibrosis than does amosite or crocidolite in equal doses. Cigarette smoking is important; the risk of bronchial cancer is exceptionally high following exposure to asbestos and cigarette smoke. More research is needed to show at what level of asbestos exposure a detectable increase of risk due to the two factors together occurs. As small amounts of asbestos are detectable in the lungs of many urban dwellers, this problem is worth further study. But prevention must be primarily through giving up cigarettes.

Mesotheliomata are less certainly ~~dose related~~. There are many examples where the exposure has been short, though not necessarily slight; information about the intensity has never been certain. These tumours apparently occur more frequently in the peritoneum than in the pleura when the exposure has been intensive, but the route of entry of the dust to the abdomen is not known. There is much clearer evidence of a difference in risk of mesothelioma varying with the type of asbestos than there is in the case of the bronchial tumours. Exposure to anthophyllite very rarely, if ever, causes mesotheliomata. Exposure to chrysotile alone is also probably a rare cause. In a majority of cases, exposure has been to crocidolite and/or amosite with or without chrysotile. Some recent evidence suggests that the fineness of the fibre of the amphibole may be an important factor in controlling the risk. Present opinion rates the risk from crocidolite higher than that from amosite. Cigarette smoking is not an important factor. The very long period that elapses between first exposure and the development

of mesotheliomata has so far prevented an estimate of what proportion of an exposed group develops these tumours. The proportion is likely to be fairly small, much less than, for example, that following exposure to some bladder carcinogens. Not all mesotheliomata of the pleura are relatable to exposure to asbestos; there are, therefore, presumably other factors. This makes the interpretation of the relationship between asbestos exposure at a low level and mesotheliomata difficult. There is a need for more information on the quantity and type of the asbestos burden in the lung and the occurrence of mesotheliomata.

Cancers of other sites—ovaries and gastrointestinal tract—may be related to exposure to asbestos, but the evidence is inconclusive. Research into this is in progress.

5. Prevention of Asbestos-Related Cancers

On many points the epidemiological evidence, though inconclusive, has given clear leads to prevention.

i. *Substitution.* Alternative materials for insulation, such as glass and rock fibre, vermiculite, calcium silicate, and for some purposes foam plastics and cork, can be used instead of asbestos. For brake-shoes and clutch-plates, and for many other purposes, asbestos is still an essential mineral. Information about the possible long-term damage from inhalation of dust from some substitutes is, however, incomplete, and it would be wise to ensure that their use is adequately observed in the future to detect any ill-effects as soon as possible. In use, some of the insulating materials with low content of asbestos have been shown not to reduce the amount of asbestos dust in the air as much as was expected.

ii. *Use of safer types of asbestos.* The epidemiological evidence is insufficiently precise, largely because of unknown historical factors, to be able to express quantitatively the relative cancer risk associated with different types of fibre. The trend of more recent research is towards increasing the estimate of the difference in risk between exposure to chrysotile alone and to crocidolite. It appears that the use of chrysotile may carry only a very small risk when the dust control is at a level which is now practicable and economic. This is fortunate, as chrysotile is much the most widely used fibre. Crocidolite is probably the one which should be eliminated wherever possible. The position of amosite is probably intermediate, but until its position is better defined the dust control should be at a high standard.

iii. *Dust control and personal protection.* Experience in asbestos-textile factories is encouraging in that it shows that the dust can be brought down to levels which are probably safe, but, in the removal and installation of asbestos insulation in ships, factories and offices, supervision and dust control are far less easy. Steps have now been taken in Britain by means of the Asbestos Regulations 1969 (Department of Employment and Productivity, 1970) and by development of codes of practice and other forms of guidance by the industry (Asbestosis Research Council) to raise the standard of hygiene wherever asbestos is used. Much asbestos is already in place in heating installations throughout the world. In the maintenance of this equipment there will be a risk for many years ahead. Personal protection by awareness of the risk, the following of codes of practice, and the use of well-fitting masks or air-fed respirators or hoods could greatly reduce the future incidence of asbestos-related cancers in this work.

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iv. *Threshold-limit values.* The evidence from epidemiological studies will gradually put the threshold-limit values on a sound basis. A start has been made by the British Occupational Hygiene Society (1968), but the evidence will need periodical review. At present this standard only applies to chrysotile.

There is a need to plan the supervision of asbestos-exposed individuals and the measurement of their environment in such a way that our successors will not find themselves without the essential information that has been a characteristic of recent epidemiological studies of asbestos cancers.

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