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WITH COMPLIMENTS

Enclosed is a report by Dr. Kevin Browne on the medical evidence presented to the Advisory Committee on Asbestos, whose report was recently published.

AIA/1/7/POL

10 December 1979

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(8)

Directors: Mr. E. van der Rest (Belgium); Dr. R. Gaze; Sir Neville Stack (Secretary)
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Sir Neville Stack,
Asbestos International Association,
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LONDON,
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5th December 1979

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Dear Sir Neville,

For circulation to the MAP and to the Member Companies of the AIA I enclose an excellent synopsis produced by Dr. Kevin Browne on the medical evidence presented to the Advisory Committee on Asbestos whose report was recently published in the U.K.

I feel that this report cannot be improved upon. I would only add to Dr. Browne's final paragraph the caveat that we are likely to be faced with some of the biological effects of inhalation of asbestos dust for many years after the use of asbestos has either been closely controlled or eliminated. So great is the latent period between exposure and disease that many years must elapse before Dr. Browne's expectations are fulfilled.

Yours sincerely,

Dr. W.J. Smither

Enc.

cc. Dr. Kevin Browne

"THE ILL EFFECTS OF ASBESTOS ON HEALTH"

The Advisory Commitee on Asbestos asked Professor Acheson, one of its members, to provide a review of the available scientific evidence on the ill effects of asbestos in man, together with a critical commentary. His review appears under the above title and in fact constitutes more than half of the total report.

Asbestosis, Mesothelioma and Lung Cancer

Asbestosis is defined as fibrosis or scarring of the lungs to such an extent as to interfere with their ability to function normally. Three points are made; firstly that there is a wide range of individual susceptibility, secondly that there is a time lag of several years before any ill effects appear, and thirdly, in a proportion of patients asbestosis progresses even if the employee leaves the industry.

Mesothelioma is a very rare type of cancer which has been known for more than two hundred years, and which is often very difficult to diagnose with any certainty. While about one person in four in this country dies of cancer nowadays, only one in every two thousand dies of mesothelioma. Of these, perhaps four fifths occur in people who have at some stage in their lives been in close contact with asbestos, while for the remaining one fifth, as with so many cancers, no reason can be found. Because of the long time lag between first exposure and the appearance of the tumour - forty years is mentioned as an average interval - the incidence of mesothelioma is still rising (there were about 300 cases in this country in 1977) and the peak is not expected to be reached until the 1980's or perhaps even later.

Lung cancer is accepted as occurring more often in asbestos workers than in the general population, although as the report states, because lung cancer is so common in the population as a whole, individual cases related to asbestos exposure are almost impossible to recognise with certainty. But the part played by smoking is very important. The question whether a non-smoking asbestos worker is more liable to develop lung cancer than a non-smoker elsewhere is still not settled. But all the series studied are in agreement that if there is a risk it is exceedingly small - one estimate quoted suggests that a non-smoking worker exposed to 1 fibre/cc of chrysotile all his working life ran the same risk as he would if he smoked three quarters of a cigarette per week. For smokers, however, the risk is appreciably increased at the sort of exposure level which prevailed 20 years ago, and estimates varying between two and eight times the risk for smoking non-asbestos workers are quoted.

Crocidolite, Amosite or Chrysotile

In the USA, it is generally held that there is not much to choose between the three types of fibre in terms of their harmful effects, and the report draws attention to this fact.

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In this country, on the other hand, crocidolite has for 10 years been regarded more adversely, and the report gives much attention to evidence distinguishing between the effects of the three types. A table sets out mortality figures from all the important published studies and relates them to the fibre types used in the industries to which they relate for asbestosis. Professor Acheson interprets them as suggesting that chrysotile may be the least harmful, crocidolite the most harmful and amosite in between, but he points out that differences in the quantity of dust inhaled may render these comparisons invalid. On equally uncertain evidence the same ranking is given for the relative risk of inducing lung cancer. For mesothelioma, however, the evidence is much stronger. The first major paper linking asbestos with mesothelioma was based on observations on crocidolite miners in Cape Province. The crocidolite miners in Western Australia also produced a high proportion of mesothelioma cases, as did gas mask assemblers both in this country (at Nottingham) and in Canada who worked with crocidolite filters. By contrast a search for mesothelioma cases at the Rhodesian chrysotile mines was unsuccessful; the same was true of the Ural mines, and among Canadian chrysotile miners less than one death in a thousand was attributable to mesothelioma. In manufacturing also mesothelioma seems rarer among chrysotile workers; a study is quoted of 20,000 T & N workers at Rochdale who entered after 1933, and among whom 10 mesothelioma cases were found - and even here some crocidolite had been used, raising the possibility that it could be responsible for the cases which occurred.

The greatest question-mark hangs over amosite. A thorough attempt to find cases of mesothelioma linked with the Transvaal amosite mines revealed only 4, compared with 83 from the Cape crocidolite mines, a fact which Professor Acheson regards as 'truly remarkable' especially as up to 1951 more amosite than crocidolite had been mined. The only strong evidence against amosite comes from Selikoff's study of the New Jersey factory where among men employed during wartime 2% had died of mesothelioma by 1973. The conditions in this factory were known to be extremely bad, and there is a faint possibility that some crocidolite was also used. In most other studies of workers in manufacturing and insulation, exposure was to at least two or all three of the fibres. Selikoff is quoted as saying that only chrysotile was used up to 1930 in the USA and during the 30's only a little amosite and almost no crocidolite was imported; on the basis of a further assumption about the greater use of amosite in shipbuilding he has produced figures purporting to show that the risk of mesothelioma is the same whether insulators use amosite or chrysotile. Professor Acheson is clearly reluctant to take these at their face value. He also raises the possibility, for which there is some support in the various studies, that mixtures of fibres may carry more risk than exposure to one type alone.

Fibre Size and Dose Response

The fate is discussed of fibres after they have been inhaled. Only fibres shorter than 200μ and thinner than 3μ diameter are thought to penetrate to the depths of the lungs, and the normal clearance mechanism of the lungs appears to be able to dispose of fibres shorter than 10μ.

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Taking smoking first, although this is mentioned briefly in connection with lung cancer, its influence on the development of asbestosis is ignored, and the major part it plays in the causation of these two diseases is not at all given the emphasis it deserves. On the second point, the absence of a threshold for the dose-response to chrysotile is mentioned 'within the range experienced in industry'. But this is the one vital issue which has not been faced; the dust range experienced in the industry in the 50's and 60's, on which the statistics of asbestos related disease are based, were probably between 10 and 1,000 times those to be found in the last 10 years. It is true that much space was devoted to dose response and the possibility of a threshold dose, but estimates were still made of low dose effects based on high dose experience, and a real examination of the evidence for the lungs' capabilities for clearing and the consequences of overloading was passed over.

Yet asbestosis has never been recorded with the minimal exposure found in the environment (as would be expected on the no-threshold calculation). There is a strong suggestion from the figures that much of the disease over which there is uncertainty, such as stomach cancer, only arises when there is massive exposure by comparison with modern experience. We know too that lung cancer becomes common in another type of severe lung fibrosis unconnected with asbestos but implying that at a certain stage a qualitative change may take place in the body's defences. This is also in keeping with what we know about the way the body's defences - the immune system - react. The system itself is extremely complex, but the analogy with a material which is stressed to breaking point is still applicable.

With all this in mind, and better evidence of true dose exposure from electron microscope studies, we can reasonably expect that modern control limits will relegate asbestos-related disease altogether to the past.

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Similarly, a lung cancer risk is considered unlikely in ordinary circumstances. The mesothelioma risk is dealt with in more detail owing to reports which arise from time to time that it has occurred following extremely brief exposure. There are certainly a small number of cases attributable to domestic exposure dating from the days when wives brushed the dust off their husband's overalls, and there does seem to have been a higher incidence in the neighbourhood of shipyards, perhaps for the same reason. But it is concluded cautiously that with modern practice no danger exists.

Asbestos fibres have also been found in drinking water and manufactured food and drink. The main evidence on which any conclusion can be based comes from Duluth, on the banks of Lake Superior, where the water supply was contaminated with waste asbestos fibres dumped in the lake. No excess of cancer deaths has been found. Similarly, animal experiments in which quantities of asbestos were eaten did not suggest any harmful effect.

Conclusion

The advisory committee's final recommendations are based closely on the conclusions of Professor Acheson's report, and do not need to be repeated here. But it is worth setting down the basis on which his figure was arrived at. He points out that in the case of occupational exposure in ionising radiation a health standard has been set (5 rems per year) which, if it was reached annually for 50 years, it was calculated would lead to an increase in cancer mortality in the exposed workers from 20% (the "natural" cancer incidence) to 22%. This is a decision which has been made and which has been accepted by society in general both in this country and internationally. If asbestos is accepted as a parallel situation, and if for chrysotile it is accepted that about half the mortality is due to lung cancer and half to asbestos, a 2% excess mortality (as for ionising radiation) would, on the basis of estimates containing "very considerable uncertainties", result from fibre levels in the range from 5 to 0.4 fibres per cc. And out of this range he suggests 1 fibre/cc, nearer the lower end, as an acceptable compromise.

Comment

Professor Acheson's review was, I believe, substantially completed nearly two years ago, and there have been a few minor research developments since then. Tremolite is beginning to be regarded with much more suspicion, occurring as it does as a contaminant of some chrysotile mines, and the high proportion of mesothelioma cases in a Turkish village due to a form of zeolite, a naturally occurring non-asbestos mineral fibre, has given further impetus to research on how this type of tumour is caused. Cancer of the larynx is not now considered to be asbestos-related. As far as asbestos in food and drink is concerned, further careful animal studies have produced no ill effects. And finally the election mircoscope is beginning to make a big impact on studies of the type and quantity of asbestos in the lung, and in analysis of environmental exposure.

But the two aspects of asbestos-related disease, over which the report is most deficient have not been changed by new evidence. These are the influence of smoking and changes in industrial practice in this country.

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The comment is made in the report that there has been a trend since the war to mill chrysotile to a greater extent than previously (for all purposes except asbestos cement), thereby producing fibres with a smaller mean diameter, and that if this were continued the reduction is risk associated with chrysotile may be lost.

Animal Experiments

Animal experiments have been carried out since before the war in an attempt to shed more light on asbestos effects in man. It has been found possible to produce lung fibrosis, lung cancer and mesothelioma in rats by exposing them to inhalation of asbestos dust. The early experiments encountered the same difficulties of variations in fibre count and fibre size of different samples, and current experiments are attempting to control these.

In these animal inhalation studies chrysotile has shown itself consistently to be at least as likely as crocidolite to produce asbestosis, lung cancer and mesotheliomas, while amosite consistently comes off best. Davis' conclusion is quoted that for a given average diameter, samples with the highest proportion of fibres $> 20\ \mu$ in length are the most dangerous, and it is suggested again that fibre size rather than type may be the decisive factor. But these experiments have all exposed the animals to massive doses (measured in hundreds or thousands of fibres per ml) and have raised more problems than they have answered.

Other Cancer Risks

There have over the years been several reports of increased mortality in asbestos workers from cancer of the stomach, bowel, larynx, ovary and breast and these are listed and discussed in some detail. Again the results of various studies are not consistent and again it is Selikoff's series in which the important increases in mortality occur. The report concludes that while the information available is sketchy and other explanations for the figures can be given, a true increase in cancer of the stomach, bowel and larynx remains a possibility in insulation workers exposed to a mixture of fibres; chrysotile miners and manufacturing workers do not appear to run any extra risk, and evidence of excess risks for other organs is inconsistent.

Environmental Exposure

Such measurements as have been made suggest that levels of asbestos fibre in the general atmosphere, even in the dust of cities, are very low - less than one thousandth of the current 2 fibre/ml standard for industrial workers. Higher concentrations may be expected inside buildings in which asbestos has been used in the construction. Even here, however, in most circumstances fibre levels were almost always less than one hundredth of the current standard. Higher levels were reported where sprayed asbestos was exposed to wear and tear, and further studies are recommended. Asbestos cement, on the other hand, seems to be associated with even less risk of release of fibre to the environment.

Reviewing the evidence for actual health damage, the report considers it unlikely that the public is at risk from asbestosis (although one or two cases of pleural thickening may have occurred, these are certainly known to occur in areas in Europe where mineral fibre occurs naturally in the soil).

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Experiments in which fibres of varying chemical structure, length and diameter were injected into the pleural space outside the lung in animals showed that the degree to which they were capable of producing malignant tumours was related to the proportion of fibres in the size range 10-80μ with diameters less than 2.5μ. The curious coincidence by which the size range of fibre which is aerodynamically able to penetrate to the alveoli, the air sacs where blood is oxygenated, is almost identical with that which will produce malignant tumours when implanted in the pleural cavity outside the lungs in animals is passed over without comment. But attention is drawn to the fact that the ability to produce mesothelioma in animals extends to fibres with diameters as low as .01μ. The ordinary light microscope will not detect fibres much smaller than .3μ, so that current methods of counting may not provide a good estimate of the levels of potentially dangerous fibres in the environment. A return is made to this point in discussion of Pooley's election microscope studies of post-mortem lung tissue of Canadian chrysotile miners. He found tremolite in large quantities in the lungs of men diagnosed in life as suffering from asbestosis, and raised the question whether contamination by tremolite or other inorganic fibres may not be responsible for some of the disease attributed to chrysotile (or amosite?). It seems certain that the election microscope will in future have to play a much larger part in fibre counting.

The difficulties in establishing a precise relationship between the quantity of fibres inhaled and resultant disease are discussed in detail. Dust counts, which in any case do not go back for very many years, were at first carried out on midget impingers and thermal precipitators before the present membrane filter came into use on any scale about 10 years ago and each method gives a different type of result. In addition, methods of counting have changed, so that a dust concentration reported as 2f/ml in 1968 would now be reported as between 4 and 10 f/ml.

There is good evidence for each of the three asbestos related diseases that, as common-sense would suggest, the more dust you inhale the more risk you run. But the question whether there is a threshold dose, i.e. a dose below which no risk is incurred, is less readily answered. Professor Acheson believes that the balance of probabilities is against there being a threshold dose in each case. However, he qualifies this in the case of asbestosis by adding that he believes there is a simple relationship between dose inhaled and risk within the range experienced in industry. This is a very important qualification to which I will return later.

A large number of studies are listed which provide evidence on dose relationship. Almost all are agreed that the relationship exists, but great discrepancies exist between estimates of the size of the risk incurred at any given dose. It is made clear that the dose response depends not only on the fibre count, but the method by which this is measured, the type of fibre, the presence of contaminants (such as tremolite), the amount of cigarette smoking (in the case of asbestosis and lung cancer but not mesothelioma) and lastly the diameter range of the fibre. It has been shown that crocidolite from Cape Province where many cases of mesothelioma have been found, is very fine, the size range being 0.09-0.8μ, while Transvaal Blue, which seems to have been responsible for far fewer cases, has a size range of 0.2-2.5μ.

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