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# CURRENT OPINIONS ON THE ASBESTOS CANCER PROBLEM

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NUMEROUS opinions on the asbestos cancer problem were expressed at the Pneumoconiosis Conference held in Johannesburg in 1969, the proceedings of which are now available (SHAPIRO, 1970). A review of the epidemiological studies (WAGNER *et al.*, 1971) and a general summary of the present situation (WAGNER, 1971) have appeared recently, and this is a synopsis of these two articles.

Epidemiological studies undertaken in countries producing and processing the various types of asbestos have been organised on an international basis under the sponsorship of the INTERNATIONAL UNION AGAINST CANCER (1965) and the International Agency for Research on Cancer. In this way, it was possible to initiate international epidemiological surveys, develop a new radiological classification (UICC COMMITTEE, 1970), organise international and national pathology panels, and prepare, characterise and distribute reference samples of asbestos dust for experimental work (TIMBRELL, 1970a).

It has been decided to reconvene the Working Party in October 1972, to consider how successfully the recommendations have been implemented and to consider what studies remain to be done.

Meanwhile, preliminary information is available on several aspects of the problem. A large survey of the Quebec asbestos miners (MCDONALD *et al.*, 1971) has shown a slight excess of lung cancer in the most heavily exposed group. Despite the heavy general air pollution by chrysotile dust over many years, the crude death rates for lung cancer in the population of the two mining towns are less than the death-rate for the Province of Quebec as a whole. No mesotheliomas are recorded in the mining population. Therefore, the situation is entirely different from that in the asbestos fields of the North West Cape (WAGNER *et al.*, 1960). The other major chrysotile producing area is in the Soviet Union: at a meeting in Dresden in 1968, Professor Kogan indicated an increased incidence of carcinoma of the lung in the asbestos area near Svedlovsk. Kogan has recently compared his findings with those of McDonald and the two observers are in general agreement that the findings in the Urals are very similar to those in the Quebec Province. The situation in Rhodesia (GELFAND and MORTON, 1970) and the Italian chrysotile mining area (VIGLIANI, 1970) support these findings. Similar results have been obtained in Finland among the anthophyllite miners. No evidence of mesotheliomas have been observed in the amosite areas of the Transvaal (HARINGTON *et al.*, 1971).



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In the manufacturing countries findings vary, and pure exposures to a single type of fibre are extremely unusual. Death rates from lung cancer in the New York insulation workers were seven times those expected (SELIKOFF *et al.*, 1970). This was particularly prevalent among the heavy cigarette smokers, but there was no correlation between cigarette smoking and the development of mesotheliomas. Mesotheliomas of the peritoneum were observed among those on the Union books in 1942 but more recently employees show an increased incidence of pleural tumours. Information about the type of asbestos used in the past by these workers is incomplete, but crocidolite, if used at all, was present in very small amounts compared to chrysotile and amosite.

In contrast, mesotheliomas have been reported from the shipbuilding ports, particularly in naval dockyards in Britain, Germany, and Holland where it was known that crocidolite had been used. The whole situation was considered in Britain by a panel of experts under the Chairmanship of the Chief Medical Inspector of Factories. Their report "Problems Arising from the Use of Asbestos" (MINISTRY OF LABOUR, 1967) concluded there was sufficient evidence to suggest "other types of fibre should be substituted for crocidolite wherever possible". The law concerning the use of asbestos has been changed and since 1970 the use of crocidolite has been restricted in Britain. It is disquieting to realise that while the use of crocidolite has dropped rapidly during recent years in Britain, there has been a steady increase in its importation into the United States, Japan and Western Europe.

Possible reasons for the role of crocidolite in the production of mesotheliomas have been considered. In animal experiments, the tumours can easily be produced following intra-pleural inoculation of various types of asbestos. Tumours are induced as readily by intra-pleurally inoculated chrysotile as by intra-pleurally inoculated crocidolite fibres (WAGNER and BERRY, 1969).

The only clues have come from the physicists who have considered the aerodynamics of the different types of airborne asbestos fibres in relation to inhalation. To a first approximation the rate of fall of an asbestos fibre depends on its diameter, not its length, so that when asbestos fibres are inhaled deposition due to sedimentation is almost independent of length (TIMBRELL, 1965). This explains why long fibres (up to about 200 $\mu$m) can penetrate to the alveolar regions if they are thin enough (less than about 3 $\mu$m diameter). On the other hand deposition by interception, or wall collision, which is very important in narrow airways, depends almost entirely on fibre length. Chrysotile fibres, resembling stretched coils, are readily deposited by interception, especially at bifurcations, since the curvature increases the collision cross-section area. Amphibole fibres, which are straight, are less readily deposited by interception since they tend to turn into the direction of the streamlines in the airflow and thus have smaller collision cross-sections. In an experiment in which rats were exposed to inhalation to dust clouds generated from the UICC reference samples, the retention of amphiboles was six times greater than for chrysotile (TIMBRELL *et al.*, 1970; TIMBRELL, 1970b). A similar result was obtained when asbestos aerosols were sucked through hollow lung casts in which the airways were left open at the respiratory bronchioles (TIMBRELL, 1970c). This ratio for the different types of fibre may be substantially higher in industry. Many chrysotile mining areas are characterized by dense clouds of dust, but a substantial proportion of particles are in the form of large flocks which settle quickly and are available for inhalation only during

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a short period. Even in chrysotile mills enough fibre may reach the bronchus to cause asbestosis and carcinoma of the lung but, in general, exposure to the amphiboles is more likely to produce these diseases. The small risk of developing mesotheliomas with chrysotile may well be due to its curly nature preventing most of it reaching the pleura. Quantitative studies of the distribution of different types of fibre within the lungs following inhalation need further development.

By using the electron microscope for measurement, physicists have shown that the fibres of crocidolite mined in the N.W. Cape and in Australia are much thinner and shorter than those of the crocidolite and amosite mined in the Transvaal, and consequently have a much greater chance of reaching the pleura. This observation could account for the high rate of pleural mesotheliomas in the N.W. Cape compared to only one possible case in the Transvaal (TIMBRELL *et al.*, 1971). It is of interest to note that mesotheliomas have been associated with Australian crocidolite which is even finer than N.W. Cape fibre.

Carcinomas of the lung are associated with the moderate to severe asbestosis, but there is no evidence as yet to implicate a particular type of asbestos nor indeed any way of measuring the relative risks from exposure to one type of fibre. It would seem that excessive exposure to all types of fibre could be responsible. There is evidence to support the contention that the incidence of carcinoma can be greatly reduced by good plant hygiene (KNOX *et al.*, 1968). In contrast to this, mesotheliomas can occur after relatively brief though not necessarily light exposures and there does not seem to be any clear pattern of a dose response. Present evidence would tend to implicate crocidolite in the development of these tumours. Until the situation is clarified the use of this particular fibre should be restricted, except for the very few industrial situations where it is essential. The position of amosite is not yet clear so that a high standard of dust control is required for this fibre. The use of chrysotile may carry only a small risk when the dust control is at a level which is now practical and economic. The threshold limit values for chrysotile proposed by the BRITISH OCCUPATIONAL HYGIENE SOCIETY COMMITTEE ON HYGIENE STANDARDS (1968) has provided a valuable basis for maintaining such standards. However, there is a considerable difference between the chrysotile from various deposits, and preliminary results of current intra-pleural experiments (WAGNER, 1970) indicate that chrysotile from certain individual mines are more reactive than others. Thus the need is still urgent for further studies on the biological effects of the various types of asbestos, to find a relatively inert fibre for industry. Further work on the effect of crocidolite on mesothelial cells may provide useful information in the study of carcinogenesis.

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# DISCUSSION

DR. SMITHERS (Chairman, Asbestosis Research Committee) asked whether Dr. Wagner had any evidence that mesothelial tumours due to chrysotile were limited to those types of chrysotile of which the fibres are straight or harsh and aerodynamically similar to the amphiboles.

Dr. V. TIMBRELL (Pneumoconiosis Unit, Penarth) said that animal inhalation experiments had been performed at Penarth using several different samples of chrysotile and amphibole asbestos. There was not much difference between these samples in the length of the fibres or their aerodynamic size. The main difference was that chrysotile consists of curly fibres whereas the amphiboles are straight fibres. Since the amphiboles tend to line up with the axes of the lung airways, they have small collision cross-sections and can penetrate to the pleura where the mesothelioma tumours are produced. Chrysotile fibres have much larger collision cross-sections because of their curly shape and penetrate to the pleura much less efficiently.

Dr. SMITHERS said that one type of chrysotile produced in the centre of the Quebec field seemed to be producing more tumours than any other. He wondered if this happened to be a particularly harsh or a particularly straight fibre.

Dr. TIMBRELL said that he had never seen long straight chrysotile fibres; if the fibres were short the curvature was not obvious, but such fibres comprised only a small proportion of the total material. It would be very interesting to find a chrysotile of straight fibres. He would expect this to be very dangerous material as the fibres if inhaled could penetrate to the pleura, and injection experiments had shown that if chrysotile is applied to the pleura it can produce mesothelial tumours as readily as the amphiboles. Normally the curly shape of chrysotile prevents it from reaching the pleura except in minute quantities.

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