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ASBESTOS AND OTHER NATURAL MINERAL FIBRES

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observed in patients with asbestosis. On the basis of these observations, it has been concluded that asbestos can trigger immunological mechanisms that are involved in lung fibrosis (Huuskonen et al., 1978; Lange, 1980). A decrease in the number of T cells (Kang et al., 1974; Kagan et al., 1977a), defects in cell-mediated immunity, and a deficiency of the generation of the migration inhibition factor (MIF) have also been shown in persons with asbestosis (Lange et al., 1978). It has been suggested that changes in T-cell subpopulations affect immunoregulatory phenomena with a resulting decrease in T-cell-mediated immunity and increase in B-cell activity. This could explain the known increased production of autoantibodies, hypergammaglobulinaemia, and increase in immune complexes noted in patients with asbestosis (Salvaggio, 1982).

A detailed review of immunological changes associated with asbestosis and a discussion of the important role of alveolar macrophages in the etiology of this disease has been published by Kagan (1980).

The immunological status of individuals with asbestos-related cancers has been described in only a limited number of reports (Ramachander et al., 1975; Haslam et al., 1978). These studies indicate that the mitogenic lymphocyte response is impaired in such patients.

8.1.2 Para-occupational exposure

8.1.2.1 Neighbourhood exposure

Pleural calcification has been associated with exposure to asbestos in the environment. An increased prevalence of pleural calcification was observed in a Finnish population residing in the vicinity of an anthophyllite mine (Kiviluoto, 1960), and similar observations were made in populations living in the vicinity of an anthophyllite mine in Bulgaria (Zolov et al., 1967), an actinolite mine in Austria (Neuberger et al., 1982), and an asbestos factory in Czechoslovakia (Navratil & Trippe, 1972).

There is some evidence, mainly from case series and retrospective case-control studies, that the risk of mesothelioma may be increased for individuals who live near asbestos mines or factories; however, the proportion of mesothelioma patients with neighbourhood exposure to asbestos varies markedly in different series. In an early review, of 33 cases of mesothelioma in the Northeast Cape province of South Africa (Wagner et al., 1960), approximately 50% were individuals with no occupational exposure who had lived in a crocidolite-mining area. In 1977, Webster further reported that, of 100 cases of mesothelioma in South Africa with no

identified occupational exposure, 95 had been exposed to crocidolite and only 1 to amosite (Webster, 1977). Newhouse & Thompson (1965) observed 11 otherwise unexposed cases (30.6% of patients in the series) who had lived within 0.8 km of an "asbestos factory" using mixed amphiboles in London. Data on cases of mesothelioma observed in the neighbourhood of shipyards were reviewed by Bohlig & Hain (1973), who reported 38 cases of "non-occupational" mesothelioma, which occurred during a 10-year period in residents in the vicinity of a Hamburg asbestos plant. However, in a study conducted in Canada, excluding individuals with occupational or household exposure to asbestos, only 2 out of the 254 (0.75%) cases of mesothelioma recorded in Quebec between 1960 and 1978 lived within 33 km of the chrysotile mines and mills (McDonald, 1980). In addition, in a systematic investigation of all 201 cases of mesothelioma and 19 other pleural tumours reported to the Connecticut Tumour Registry, between 1955 and 1977, and 604 randomly-selected decedent controls, there was no association between incidence and neighbourhood exposure (Teta et al., 1983).

Few data are available on the length of residence of the patients in the vicinity of the plants in these studies. Out of 413 notified cases of mesothelioma in the United Kingdom in 1966-67, 11 individuals (2.7%), who were not asbestos workers and who did not have household exposure, had lived within one mile of an asbestos factory for periods of 3 - 40 years. In a review of cases of mesothelioma in 52 female residents of New York state, diagnosed between 1967 and 1968, three otherwise "unexposed" patients (5.8%) lived within 3.6 km of asbestos factories for 18 - 27 years (Vianna & Polan, 1978). In most of the studies, there were few data concerning the type of asbestos to which neighbourhood residents were exposed.

Four ecological[a] epidemiological studies have been conducted to investigate the relationship between exposure to asbestos in the environment and disease (Fears, 1976; Graham et al., 1977; Pampalon et al., 1982; Siemiatycki, 1983). On the basis of the analysis of cancer incidence data from the Quebec Tumour Registry, the risk for residents of asbestos-mining communities was from 1.5 to 8 times greater than that for those in rural Quebec counties, for 10 different cancer sites among males, and for 7 sites among females. The higher risks in males were attributed, in part, to occupational exposure. There was increased risk of cancer of the pleura in both sexes, which decreased with increasing distance of resi-

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[a] For the purposes of this document, an ecological epidemiological study is one in which exposure is assessed for populations rather than individuals.

dence from the asbestos mines. The authors emphasized the limitations of their study and recommended that information concerning other exposures and lifestyle factors should be considered in more powerful case-control studies.

An additional ecological study has been completed (Pampalon et al., 1982; Siemiatycki, 1983). Mortality between 1966 and 1977 in agglomerations (several municipalities) around the asbestos-mining communities of Asbestos and Thetford Mines was compared with that of the Quebec population. A statistically-significant excess of cancer among males in these agglomerations was attributed to occupational exposure. A telephone survey indicated that 75% of the men in these communities had worked in the mines (Siemiatycki, 1983). For women, whose exposure had been confined to the environment or, in some cases, to environmental exposure and family contact, there were no statistically-significant excesses of mortality due to all causes (standard mortality rate[a], SMR = 0.89), all cancers (SMR = 0.91), digestive cancers (SMR = 1.06), respiratory cancers (SMR = 1.07), or other respiratory disease (SMR = 0.58). Similarly, there were no significant excesses when the mortality rate at age less than 45 was considered or when the reference population was confined to towns of similar size. Unfortunately, very few causes of mortality were examined in this study, and the classes were fairly broad. The authors concluded that the results were consistent with the hypothesis of no excess risk, though an SMR of 1.1 - 1.4 for lung cancer could not be ruled out in such a study.

In a recently-completed study, no significant differences in the incidence of cancer of the lung or stomach were found in two Austrian towns, one near natural asbestos deposits and one with an asbestos-cement production plant, in comparison with local and national population statistics (community size and agricultural index were taken into consideration) (Neuberger et al., 1984).

In another ecological study conducted in the USA, in which there was some attempt to control for the urban effect, geographical gradient and socioeconomic class, there was no correlation between general cancer mortality rates and the location of asbestos deposits (Fears, 1976).

Ecological studies such as those described above are considered to be insensitive, because of the large number of confounding variables, which are difficult to eliminate. In addition, true excess cancer risk is probably underestimated in such studies, because of population mobility over a latent

[a] Ratio of the number of deaths observed to the number of deaths expected if the study population had the same structure as the standard population.

period of several decades (Polissar, 1980). Case-control and cohort studies are generally more powerful than ecological epidemiological studies, because exposure and outcome are assessed for individuals rather than for populations. One relevant cohort study has been conducted. Mortality data for men who lived within 0.5 miles of an amosite factory in Paterson, New Jersey in 1942 were compared with data in 5206 male residents of a similar Paterson neighbourhood with no asbestos plant (Hammond et al., 1979). All men who worked in the factory were excluded. Approximately 780 (44% of the "exposed" population) and 1735 (46% of the "unexposed" population) died during the 15-year period 1962-76. With respect to total deaths, deaths from cancer (all sites combined), and lung cancer, mortality experience was slightly worse in the "unexposed" population during this period. Therefore, there was no evidence of increased risk attributable to neighbourhood exposure.

In summary, available data indicate that the risk of pleural plaques and mesothelioma may be increased in populations residing in the vicinity of asbestos mines or factories. However, there is no evidence that the risk of lung cancer is increased in similarly-exposed populations. However, it should be noted that, in the past, airborne fibre levels near asbestos facilities were generally much higher than they are today. For example, Bohlig & Hain (1973) mentioned that before the second World War, there was "visible snowfall-like air pollution" from an asbestos factory in Germany. It is also claimed that, 20 years ago in Quebec mining communities,"snow-like films of asbestos" accumulated regularly (Siemiatycki, 1983).

8.1.2.2 Household exposure

Measurements made by Nicholson et al. (1980) in the homes of miners and non-miners in a chrysotile-mining community in Newfoundland, showed that fibre concentrations were several times higher in the former than the latter. Studies of both Newhouse & Thompson (1965) in the United Kingdom and of McDonald & McDonald (1980) in North America showed more cases of household exposure in mesothelioma patients than in controls, after exclusion of occupation. Two further epidemiological surveys have specifically addressed the question. Vianna & Polan (1978) studied the asbestos-exposure history of all 52 histologically confirmed fatal cases of mesothelioma in females in New York State (excluding New York City), in 1967-77, with matched controls. Excluding 6 cases exposed at work, 8 others had a husband and/or father who worked with asbestos; none of their matched controls had a history of domestic exposure whereas the reverse was true in only one

pair. Information on latency was not given, but 2 of the 8 whose husbands were asbestos workers were aged only 30 and 31 years, respectively.

In a study by Anderson et al. (1979), over 3100 household contacts of 1664 surviving employees of the Paterson amosite asbestos plant, were identified in the period 1973-78. From over 2300 still living, 679 subjects who themselves had never been exposed to asbestos occupationally, and 325 controls of similar age distribution, were selected for radiographic and other tests. Small opacities and/or pleural abnormalities were observed in 35% of the household contacts and 5% of the controls. Pleural changes were more frequent than parenchymal changes. The readings were made by 5 experienced readers and though the interpretation was by consensus, it was made without knowledge of exposure category. The mortality experience of this population of household contacts is also under study; the method has not yet been adequately described but at least 5 cases of mesothelioma and excess mortality from lung cancer have been reported.

8.1.3 General population exposure

(a) Inhalation

Pleural calcification has been associated with exposure to mineral fibres in the environment. Increased prevalence has been observed in populations living in the vicinity of deposits of anthophyllite, tremolite, and sepiolite in Bulgaria (Burilkov & Michailova, 1970), and tremolite deposits in Greece (Bazas et al., 1981; Constantopoulos et al., 1985). However, increased prevalence of pleural calcification has also been observed in populations without any identifiable asbestos exposure (Rous & Studeny, 1970).

There is very little direct epidemiological evidence on the effects of urban asbestos air pollution. The question was addressed to some extent in analyses of the extensive surveys of malignant mesothelial tumours undertaken by McDonald & McDonald (1980) in Canada during the period 1960-75, and in the USA in 1972. Systematic ascertainment through 7400 pathologists yielded 668 cases which, with controls, were investigated primarily for occupational factors. After exclusion of those with occupational, domestic, or mining neighbourhood exposure, the places of residence of women were examined for the 20 to 40-year period before death. Of 146 case-control pairs, 24 cases and 31 controls had lived in rural areas only, and 82 cases and 79 controls had lived in urban areas only. These very small differences could easily be due to chance, quite apart from the greater likelihood of case recognition in urban than rural areas and the

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CHRYSOTILE ASBESTOS

First draft prepared by Dr G. Gibbs, Canada (Chapter 2), Mr B.J. Pigg, USA (Chapter 3), Professor W.J. Nicholson, USA (Chapter 4), Dr A. Morgan, UK and Professor M. Lippmann, USA (Chapter 5), Dr J.M.G. Davis, UK and Professor B.T. Mossman, USA (Chapter 6), Professor J.C. McDonald, UK, Professor P.J. Landrigan, USA and Professor W.J. Nicholson, USA (Chapter 7), Professor H. Schreier, Canada (Chapter 8).

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f/ml for sanding. Following clean-up and introduction of controls, levels were 0.5 to 1.7 f/ml.

There is potential for widespread exposure of maintenance personnel to mixed asbestos fibre types due to the large quantities of friable asbestos materials still in place. In buildings where there are control plans, personal exposure of building maintenance personnel in the USA, expressed as 8-h time-weighted averages, was between 0.002 and 0.02 f/ml. These values are the same order of magnitude as exposures reported during telecommunication switch work (0.009 f/ml) and above-ceiling work (0.037 f/ml), although higher concentrations have been reported in utility space work (0.5 f/ml). Concentrations may be considerably higher where control plans have not been introduced. For example, in one case, short-term episodic concentrations ranged from 1.6 f/ml during sweeping to 15.5 f/ml during cleaning (dusting off) of library books in a building with a very friable chrysotile-containing surface formulation. Most other values, presented as 8-h time-weighted averages, are about two orders of magnitude less.

Although few data on exposures among users of asbestos-containing products in industries such as construction were identified, available data clearly demonstrate the need for appropriate engineering controls and work practices for minimizing exposures to chrysotile both in production and use. It should be noted that construction and demolition operations present special control problems.

9.2.2 *General population exposure*

Sources of chrysotile in ambient air are both natural and anthropogenic. Most airborne fibres in the general environment are short (< 5 μm).

Few recent data on concentrations of chrysotile in air in the vicinity of point sources have been identified. Concentrations around the Shibani chrysotile mine in Zimbabwe ranged from below the limit of detection of the method (<0.01 f/ml) to 0.02 f/ml (fibres longer than 5 μm).

Based on surveys conducted before 1986, concentrations (fibres > 5 μm in length) in outdoor air measured in five countries (Austria, Canada, Germany, South Africa and USA) ranged between 0.0001 and about 0.01 f/ml, with levels in most samples being less than 0.001 f/ml. Means or medians were between 0.00005 and 0.02 f/ml, based on more recent determinations in seven countries (Canada, Italy, Japan, Slovak Republic, Switzerland, United Kingdom and USA).

Fibre concentrations in public buildings during normal use where there is no extensive repair or renovation are within the range of those measured in ambient air, even where friable asbestos-containing materials were extensively used. Concentrations (fibres > 5 μm in length) in buildings in Germany and Canada reported before 1986 were generally less than 0.002 f/ml. In more recent surveys in five countries (Belgium, Canada, Slovak Republic, United Kingdom and USA) mean values were between 0.00005 and 0.0045 f/ml. Only 0.67% of chrysotile fibres were longer than 5 μm.

9.3 Health effects

9.3.1 Occupational exposure

Adverse health effects associated with occupational exposure to chrysotile are fibrosis (asbestosis), lung cancer and mesothelioma. These effects have also been observed in animals exposed to chrysotile by inhalation and other routes of administration. Based on available data in miners and millers, there is an interaction between tobacco smoke and chrysotile in the induction of lung cancer which appears to be less than multiplicative. Epidemiological evidence that chrysotile asbestos is associated with an increased risk of cancer at other sites is inconclusive.

Emphasis in this evaluation is on those studies that contribute to our understanding of the health risks associated with exposure to chrysotile, especially those that characterize at least to some extent, the exposure–response relationship. It should be noted, however, that exposure–response relationships have relied upon reconstruction of historical exposures. This is often problematic, due to lack of historical exposure measurements, and changes in measurement methods that

have required use of conversion factors which are highly variable. Moreover, there are wide variations in exposure characteristics, including fibre size distributions, which are not well characterized in traditional measures of exposure.

The Task Group noted that there is an exposure–response relationship for all chrysotile-related diseases. Reduction of exposure through introduction of control measures should significantly reduce risks. Construction and demolition operations may present special control problems.

9.3.1.1 *Fibrosis*

The non-malignant lung diseases associated with exposure to chrysotile comprise a somewhat complex mixture of clinical and pathological syndromes not readily definable for epidemiological study. The prime concern has been asbestosis, generally implying a disease associated with diffuse interstitial pulmonary fibrosis accompanied by varying degrees of pleural involvement.

Studies of workers exposed to chrysotile asbestos in different sectors have broadly demonstrated exposure–response relationships for chrysotile-induced asbestosis, in so far as increasing levels of exposure have produced increases in the incidence and severity of disease. However, there are difficulties in defining this relationship, due to factors such as uncertainties in diagnosis, and the possibility of disease progression on cessation of exposure.

Furthermore, some variations in risk estimates are evident among the available studies. The reason for the variations is not entirely clear, but may relate to uncertainties in exposure estimates, airborne fibre size distributions in the various industry sectors and statistical models. Asbestotic changes are common following prolonged exposures of 5 to 20 f/ml. The risk at lower exposure levels is not known but the Task Group found no reason to doubt that, although there may be subclinical changes induced by chrysotile at levels of occupational exposure under well-controlled conditions, even if fibrotic changes in the lungs occur, they are unlikely to progress to the point of clinical manifestation.

9.3.1.2 Lung cancer

Exposure–response relationships for lung cancer have been estimated for chrysotile mining and milling operations and for production of chrysotile asbestos textiles, asbestos-cement products and asbestos friction products. Risks increased with increasing exposure. The slopes of the linear dose–response relationships (expressed as the increase in the lung cancer relative risk per unit of cumulative exposure (fibre/ml-years)) were all positive (although some not signficantly) but varied widely. Textiles produce the highest risk (slopes 0.01 to 0.03). Risks for production of cement products (slopes 0.0003-0.007), friction materials (slopes 0.0005-0.0006) and chrysotile mining (0.0006-0.0017) are lower.

The relative risks of lung cancer in the textile manufacturing sector in relation to estimated cumulative exposure are, therefore, some 10 to 30 times greater than those observed in chrysotile mining. The reasons for this variation in risk are not clear.

9.3.1.3 Mesothelioma

Estimation of the risk of mesothelioma is complicated in epidemiological studies by factors such as the rarity of the disease, the lack of mortality rates in the populations used as reference, and problems in diagnosis and reporting. In many cases, therefore, risks have not been calculated, and cruder indicators have been used, such as absolute numbers of cases and death and ratios of mesothelioma over lung cancers or total deaths.

Based on data reviewed in this monograph, the largest number of mesotheliomas has occurred in the chrysotile mining and milling sector. All of the observed 38 cases were pleural with the exception of one of low diagnostic probability, which was pleuro-peritoneal. None occurred in workers exposed for less than 2 years. There was a clear dose–response relationship, with crude rates of mesotheliomas (cases/1000 person-years) ranging from 0.15 for those with cumulative exposure less than 3500 mpcm (< 100 mpcf-years) to 0.97 for those with exposures of 10 500 mpcm (300 mpcf-years).

Proportions of deaths attributable to mesotheliomas in cohort studies in the various mining and production sectors range from 0 to 0.8%. Caution should be exercised in interpreting these proportions, as studies do not provide comparable data stratifying deaths by exposure intensity, duration of exposure or time since first exposure.

There is evidence that fibrous tremolite causes mesothelioma in humans. Since commercial chrysotile may contain fibrous tremolite, it has been hypothesized that the latter may contribute to the induction of mesotheliomas in some populations exposed primarily to chrysotile. The extent to which the observed excesses of mesothelioma might be attributed to the fibrous tremolite content has not been resolved.

Epidemiological studies of populations of workers using chrysotile-containing products in applications such as construction have not been identified, although for workers with mixed exposures to chrysotile and the amphiboles, by far the greatest proportion of mesotheliomas occurs in users of asbestos-containing products rather than in those involved in their production.

9.3.2 *General environment*

Data on incidence or mortality of disease in household contacts of chrysotile workers or in populations exposed to airborne chrysotile in the vicinity of point sources reported since EHC 53 was published in 1986 have not been identified. More recent studies of populations exposed to chrysotile in drinking-water have likewise not been identified.

9.4 Effects on the environment

The impact of chrysotile/serpentine presence and degradation on the environment and lower life forms is difficult to gauge. Observed perturbations are many but their long-term impact is virtually unknown.

10. CONCLUSIONS AND RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH

a) Exposure to chrysotile asbestos poses increased risks for asbestosis, lung cancer and mesothelioma in a dose-dependent manner. No threshold has been identified for carcinogenic risks.

b) Where safer substitute materials for chrysotile are available, they should be considered for use.

c) Some asbestos-containing products pose particular concern and chrysotile use in these circumstances is not recommended. These uses include friable products with high exposure potential. Construction materials are of particular concern for several reasons. The construction industry workforce is large and measures to control asbestos are difficult to institute. In-place building materials may also pose risk to those carrying out alterations, maintenance and demolition. Minerals in place have the potential to deteriorate and create exposures.

d) Control measures, including engineering controls and work practices, should be used in circumstances where occupational exposure to chrysotile can occur. Data from industries where control technologies have been applied have demonstrated the feasibility of controlling exposure to levels generally below 0.5 fibres/ml. Personal protective equipment can further reduce individual exposure where engineering controls and work practices prove insufficient.

e) Asbestos exposure and cigarette smoking have been shown to interact to increase greatly the risk of lung cancer. Those who have been exposed to asbestos can substantially reduce their lung cancer risk by avoiding smoking.

11. FURTHER RESEARCH

(a) Research and guidance are needed concerning the economic and practical feasibility of substitution for chrysotile asbestos, as well as the use of engineering controls and work practices in developing countries for controlling asbestos exposure.

(b) Further research is needed to understand more fully the molecular and cellular mechanisms by which asbestos causes fibrosis and cancer. The significance of physical and chemical properties (e.g., fibre dimension, surface properties) of fibres and their biopersistence in the lung to their biological and pathogenic effects needs further elucidation. Dose–response information from animal studies for various asbestos fibre types is needed to evaluate the differential risk of exposure to chrysotile and tremolite.

(c) Epidemiological studies of populations exposed to pure chrysotile (i.e. without appreciable amphiboles) are needed.

(d) The combined effects of chrysotile and other insoluble respirable particles needs further study.

(e) More epidemiological data are needed concerning cancer risks for populations exposed to fibre levels below 1 fibre/ml, as well as continued surveillance of asbestos-exposed populations.