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Biological Effects of Ingested Asbestos

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Introduction

The NIEHS is conducting a series of studies on the effects of ingested asbestos. These studies are part of the NIEHS commitment that is directed by the recently established National Toxicology Program. The Environmental Protection Agency has contributed approximately 10% of the total funding. A summary of the evolution of the study is to be found in Appendix A. A paper, given at a Workshop on Asbestos, Gaithersburg, Maryland, July 1977, detailing the studies' design and implementation is attached (Appendix B).

Current Status

Test Materials - Two samples of chrysotile, and single samples of amosite and crocidolite asbestos plus a tremolite material are being tested. A repository of these materials was established and has also served as a source for other scientific studies on asbestos.

Each material has been extensively characterized as to physical and chemical properties. The fiber size characterization performed by the Illinois Institute of Technology Research Institute (IITRI), Chicago, Illinois, has been completed and a final report received. The chemical and physical property characterization performed by the U. S. Bureau of Mines is also completed.

Hamster Studies

Three asbestos materials are being studied at IIT Research Institute, Chicago, IL. The lifetime exposure phase of these experiments has been completed. There was no indication of major differences in the mortality rate between the hamsters receiving the asbestos diet or the control diet. Histopathologic examination of tissues from female hamsters has been completed. The contractor has reported that a preliminary analysis of the hamster data indicates that no carcinogenic or cocarcinogenic effect was observed. A standard independent quality review of the pathology results has been completed for the female hamster. A similar review of the male hamsters is in progress and is expected to be completed in March 1981. Analyses of the verified data and preparation of the draft report is in progress. The report is expected to be completed and submitted to the NTP Board of Scientific Counselors' Technical Report Subcommittee for independent public peer review in May 1981.

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Rat Studies

Five test materials are being studied in this species at the Hazleton Laboratories, Vienna, Virginia. In addition, a subset of two studies includes neonatal as well as lifetime oral exposure to asbestos. The lifetime exposure phase of the study has been completed. Although data has not yet been statistically analyzed, it appears that longevity was not affected by exposure to the various types of fibers, although the known carcinogen (DMH) did significantly shorten lifespan. The histopathologic phase of the study is in progress and is projected to be completed in October 1981--there are a total of 5,158 rats to be examined. The histopathologic evaluation is to be completed by group and then subjected to pathology quality review. Sequential issuance of final reports by asbestiform type is being considered with the first reports projected to be available for public peer review in December 1981.

From: Biological Effects of Mineral Fibres
(Effets biologiques des fibres minérales)
Volume 2, Ed.: J.C. Wagner,
International Agency for Research on Cancer
Scientific Publications No. 30, Lyon,
1980: 587-601.

ASBESTOS-RELATED DISEASE: AN EPIDEMIOLOGICAL REVIEW

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INTRODUCTION

Epidemiology is concerned with disease incidence, etiological evidence and evaluation of control measures. This review will examine what has been achieved in these three fields, focussing on recommendations on asbestos and cancer made to the UICC in 1964 (UICC Working Group on Asbestos Cancers, 1965) and to the IARC in 1972 (Bogovski et al., 1973). Five of the six points which the epidemiological recommendations of 1964 comprised were repeated in 1972. Why the sixth, which related to the effects of exposure under different industrial and environmental conditions, was omitted is unclear, since it remains unanswered. The main concern in both lists was etiological, with some reference in 1964, and rather more in 1972, to questions of social impact and effectiveness of control.

It was natural that asbestos-related cancers should figure prominently in reports to the UICC and IARC. Epidemiological surveys of mortality, case-control or cohort, are more straightforward and easier to interpret than those required for the chronic and insidious manifestations of asbestosis. Certainly the information now available on the asbestos cancers is relatively more complete and so provides the main theme for this review. However, asbestosis will not be ignored, if only because its detection underlies several approaches to the prevention of both types of disease.

The main issues to be considered are (1) whether or not asbestos exposure is a causal factor in the disease in question, (2) whether all fibre types are equally implicated, and (3) whether any other factors, personal or environmental, significantly modify the link between cause and effect. These three facets are interrelated and cannot be

considered in isolation. The nature of exposure-response relationships is basic to any consideration of etiology; however, evidence aimed at precise quantification will be left to Professor Donald Acheson[1].

ASBESTOS-RELATED DISEASES

Lung cancer

On the central question of whether asbestos causes lung cancer there can now be little doubt. There is direct epidemiological evidence for the carcinogenicity of chrysotile, crocidolite, amosite and anthophyllite (IARC, 1977); all the usual criteria have been met (J.C. McDonald, 1980); and the view that the risk was confined to smokers is no longer tenable (Hammond et al., 1979; McDonald et al., 1980). The relative potency of the different fibre types is less clear, however, as is the form of interaction with tobacco smoking.

Fibre type

All discussions on this subject are bedevilled by the problem of comparing like with like. Thus, even in the same industrial process at apparently similar dust/fibre levels, the distribution of particles by length and diameter may well vary with different types of asbestos. Add to this the extreme paucity of epidemiological surveys in which there are any data whatever on dust or fibre concentrations, and it will be evident that only substantial differences in observed risk have much meaning. Moreover, for obvious reasons, similar industrial processes are seldom carried out with different types of asbestos or different mixtures.

Mining and milling (i.e., fibre production) have therefore been of particular interest; but, until recently, there have been no findings reported for comparison with Quebec chrysotile workers. Thus, the reports on crocidolite mining in Wittenoom, Western Australia, by Hobbs et al.[2] and in the Cape Province, South Africa, by Talent et al.[3] are especially welcome. As the South African study was cross-sectional in type, only the Quebec and Australian findings can be compared directly, and then with some difficulty. The populations studied differed socially, in entry criteria and in the mortality to date - 41% in Quebec and 8% in Western Australia. A comparison of those employed one year or more and followed at least 15 years from first employment (Australia),

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[1] See p. 737

[2] See p. 615

[3] See p. 723

or 20 years (Quebec), appears to show that the lung cancer experience of the crocidolite miners was several times worse than that of men who produced chrysotile: the standardized mortality ratio (SMR) in Quebec miners was 1.28 and that in miners in Western Australia, 2.47. However, this comparison takes no account of environmental conditions, fibre concentrations, type and duration of work, etc.

Within the industries which work with asbestos, the position has, with few exceptions, been obscured by the use of mixtures. Despite very short periods of exposure to Australian crocidolite - seldom in excess of 2½ years - the Nottingham and Canadian gas-mask workers (Jones et al.[1]; A.D. McDonald & J.C. McDonald, 1978) both had about twice the number of lung cancer deaths expected. Amosite factory workers and several cohorts exposed to amphibole-chrysotile mixtures have also suffered very severely from this disease (IARC, 1977).

Enterline & Henderson (1973) and Hughes & Weill[2] both attempted the difficult task of separating the effects of different fibre types in factories where more than one was used. To the extent that this was achieved, their studies also point to lower risks after exposure to chrysotile only, than after exposure to amphiboles or amphibole-containing mixtures.

Apart from two small cohort studies reported by Elwood & Cochrane (1964) and Weiss (1977), there has been no information on factory workers exposed to chrysotile only. In the first-mentioned where, in fact, some crocidolite had been used, there were seven cases compared with 3.02 expected; in the latter, the SMR for lung cancer was 0.93 (but only 0.61 for 'all causes').

The mortality of men 20 or more years after first employment in the Rochdale textile plant (Peto[3]) may eventually provide more comparable data. At face value, the textile workers experienced a much higher excess mortality from lung cancer (30 deaths observed, 15.47 expected) than Quebec chrysotile miners at similar exposure levels (J.C. McDonald et al.[4]). However, crocidolite was also used at Rochdale, and there is still uncertainty about the fibre concentrations to which the men were exposed.

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[1] See p. 637

[2] See p. 627

[3] See p. 829

[4] See p. 811

Smoking

In 1977, Saracci (1977) reviewed the nature of the asbestos-smoking interaction, as it affected the occurrence of lung cancer. He identified three simple models, though recognizing that there could be others of greater complexity; these were: (1) that the effects are independent and simply additive; (2) that asbestos and tobacco act synergistically, perhaps even multiplicatively; and (3) that asbestos produces lung cancer only in those who smoke.

With the data then available to him, he had some difficulty in discarding model 3, found nothing to support the additive model, and tentatively concluded that the multiplicative model appeared the most plausible. It should be noted that in none of the reports at his disposal were both asbestos exposure and smoking adequately quantified. Since then two further sets of results bearing on the question have become available. One based on the large cohort of North American insulation workers (Hammond et al., 1979) gave relative risks which agreed perfectly with the multiplicative model, as below:

	Asbestos exposure	
	Never	Ever
Never smoked	1	5.17
Ever smoked	10.85	53.24

The other set of data, based on our most recent findings for Quebec chrysotile miners and millers (J.C. McDonald et al., 1980), appear more than additive but less than multiplicative:

	Asbestos exposure		
	Little	Moderate	Heavy
Nonsmokers	1	2.0	6.9
Moderate smokers	6.3	7.5	12.8
Heavy smokers	11.8	13.3	25.0

It may be too much to expect that a single biostatistical model will apply exactly in all circumstances. However, both studies agree on two important points: (1) that the *relative risk* for nonsmokers exposed to asbestos is at least as great as that for smokers and (2) that in *absolute* terms most asbestos-related lung cancers occur in those who have smoked.

Mesothelioma

Since Wagner and his colleagues (1960) reported a concentration of cases of mesothelioma in the crocidolite mining area of the Cape Province, South Africa, epidemiological interest has focussed on the importance of fibre type. This led to parallel research by physical and experimental scientists (see, for example, Pooley, 1973; Timbrell, 1973; Wagner & Berry, 1973), which has added greatly to the understanding of factors that influence the penetration of fibrous particles and the critical importance of shape and size. It was hardly a surprise that malignant mesothelial tumours would eventually be found associated with other mineral fibres of the required dimensions (Baris et al., 1978, 1979). Clearly, asbestos substitutes must be viewed with fresh caution.

In recent reviews of all cases of malignant mesothelioma reported to the end of 1975, including those in industrial and community surveys (J.C. McDonald, 1978; J.C. McDonald & A.D. McDonald, 1977), the following conclusions were drawn:

(1) The geographical distribution was uneven, with concentrations near dockyards and certain large asbestos plants. Elsewhere the incidence was low, perhaps approaching the 'background' level present before the commercial exploitation of asbestos.

(2) Exposure to airborne crocidolite in man had clearly proved far more hazardous than that to chrysotile, although, in animal experiments, the carcinogenic potential of all types of asbestos and other mineral fibres seemed similar.

(3) The status of amosite was uncertain; the substantial incidence of mesothelioma in amosite factory workers conflicted with the apparent infrequency among amosite miners. From 1930 on, amosite had been used for insulation materials in the USA; and from about 1950 it had become the major constituent. Possibly, this explained the high incidence among American insulators.

Papers submitted to this conference bring much further evidence on these issues. The cohort survey by Hobbs et al.[1] of Australian crocidolite miners identified 30 cases of mesothelioma, 17 (3.3%) among 519 ascertained deaths. The authors note an unusual absence of peritoneal tumours and, indeed, a deficit of abdominal tumours of all types. With only 8% of the cohort dead, it is too soon to estimate the eventual impact of mesothelioma. At a comparable stage in the Quebec chrysotile mining cohort study there had been no deaths from mesothelioma.

[1] See p. 615

The survey of black South African crocidolite mineworkers by Talent et al.[1] is cross-sectional and therefore most difficult to interpret. The very existence of prevalence rates for mesothelioma, based on some 68 cases detected in various defined groups, is disturbing. A most useful figure is that four cases were found in a representative sample of 236 men examined 21 or more years after first exposure — a prevalence rate of 2%. For comparison, we estimated that the average prevalence of mesothelioma in Quebec chrysotile mineworkers during the years 1965-1977 was roughly 0.05%; and in Canadian gas-mask workers during the years 1965-1976, between 1-2%. These estimates assume that cases of mesothelioma would be detectable two years before death. It may be recalled that in the Canadian gas-mask cohort, nine (16%) of 56 deaths to the end of 1975 were probably due to mesothelioma (A.D. McDonald & J.C. McDonald, 1978); in the current paper by Jones et al.[2] on Nottingham gas-mask workers, 17 (10%) of 166 deaths to the end of 1978 were ascribed to mesothelioma.

An indication of the possible role of crocidolite is contained in the report by Rossiter & Coles[3] on mortality in naval dockyard workers. In a cohort of 6292 employees followed to the end of 1978, there was a total of 1042 deaths: 28 deaths were from mesothelioma, but only 13 deaths were from all other asbestos-related diseases. This suggests that the exposure to asbestos was not heavy but was particularly liable to cause mesothelioma. The use of crocidolite in the British Navy could well explain this pattern.

The same issue is implicit in problems identified by Peto[4] in his paper on mesothelioma in the Rochdale factory. Although the employees are described as 'chrysotile asbestos textile workers', in fact, crocidolite was also used. Without electron microscopic analyses of lung tissue, data from this survey will remain difficult to interpret.

An analysis is presented by A.D. McDonald[5] of the occupational histories of all known deaths from mesothelioma in the Province of Quebec between 1960-1968, with special attention to cases in persons exposed only to chrysotile in mines and mills and in workers employed in four factories, two of which had used crocidolite and one amosite for limited periods. There were 22 cases in the latter three factories compared with 10 cases from the mines and mills, where the workforce was some eight times larger. After exclusion of cases attributable to asbestos (almost all in men), the remaining incidence was similar in the two sexes and might conceivably have had some other etiology.

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[1] See p. 723

[2] See p. 637

[3] See p. 713

[4] See p. 703

[5] See p. 673

Lastly, two important sets of data describe results from Dr F.D. Pooley's laboratory on the mineral fibre content of lung from cases of mesothelioma and controls obtained from (a) the 1976 national survey in the UK and (b) national surveys in the US and Canada in 1972. In the first of these, reported by Jones et al.[1], 108 cases (86 confirmed) and 56 'controls' were investigated. The authors were aware that their 'controls' were unsatisfactory and may not be wholly comparable with the case series. In the North American study (A.D. McDonald[2]), 100 carefully matched case-control pairs were submitted to Dr Pooley, and the results for 37 pairs are so far available. In both studies, the laboratory examined the specimens without knowledge of their provenance.

The results from these surveys are shown side by side in Table 1. In neither is there any difference between cases and controls in the distribution of chrysotile; the levels are considerably higher, however, in the American series. In both studies amosite is present in much larger quantities in the cases than in the controls, whereas crocidolite is more in evidence in the UK. These findings reflect the relatively low levels of importation of crocidolite to North America and, indeed, the apparently lower incidence of mesothelioma on that continent (J.C. McDonald & A.D. McDonald, 1977). The figures so far available thus support the hypothesis that amosite has played an important part in the etiology of American mesotheliomas and goes some way to counter the doubts expressed by Nicholson et al.[3].

Table 1. Distribution (%) of chrysotile, crocidolite and amosite in lung tissue from mesothelioma cases and controls in North America and the United Kingdom[a]

Fibres (× 10⁶) per g dried lung tissue	Chrysotile				Crocidolite				Amosite			
	America		UK		America		UK		America		UK	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Nil	3	0	40	21	70	81	10	39	38	54	20	61
< 1	11	15	14	16	16	19	30	36	27	43	29	25
1 < 10	56	59	31	54	8	0	27	21	16	3	31	13
10 < 100	24	19	16	9	5	0	20	0	11	0	11	0
100 or more	6	6	0	0	0	0	13	4	8	0	8	2

[a] North America - 37 case-control pairs (A.D. McDonald, p. ; United Kingdom - 108 cases and 56 controls (Jones et al., p. 637)

[1] See p. 187

[2] See p. 681

[3] See p. 823

Other malignancies

Gastrointestinal cancers.- Since those who inhale asbestos fibres may well swallow even more, it is reasonable to suppose that this might lead to malignant disease of the gastrointestinal tract. In some industrial populations a substantial risk has been demonstrated, e.g., in insulation workers in Belfast and in North America and in American amosite factory workers; in other groups, however, there has been no excess, e.g., in London factory workers, Finnish anthophyllite miners and Rochdale textile workers. The studies of Quebec chrysotile miners and millers have also been difficult to interpret; for example, there was substantial excess mortality from cancer of the oesophagus and stomach in the most heavily exposed men, but no systematic exposure-response relationship; and differences between the two main mining areas were not readily explained by dust exposure.

In a careful review of the subject, Miller (1978) concluded that, despite irregularities and inconsistencies, the weight of evidence pointed to a causal relationship, affecting all sites in the gastrointestinal tract. He doubted whether further data of the kind anticipated would clarify the situation. There appear to be unrecognized factors of importance, perhaps in the diet, which are not being taken into account: it is as though the effects of asbestos on the respiratory tract were being studied in ignorance of tobacco. Identification of the missing link could have similar importance.

Laryngeal cancer.- Some studies have shown an association between asbestos exposure and cancer of the larynx; others have not. In the cohort of insulation workers studied by Selikoff et al. (1979), nine deaths were recorded, compared with 4.7 expected. In London factory workers (Newhouse & Berry, 1973), there were two cases and 0.4 expected. In Quebec chrysotile workers (J.C. McDonald et al., 1980), 17 cases were observed and 16.1 expected; however, there was a direct relationship here with smoking. An excess of laryngeal cancer in Italian chrysotile miners is difficult to interpret as the mine is located in a province with a very high incidence of the disease (Rubino et al., 1979). A case-control study in Liverpool by Stell & McGill (1973) showed a very high relative risk (14.5), but the inquiries were not made blind, and it is difficult to accept that only 3% of control subjects in that city had been exposed occupationally to asbestos. In a smaller case-control study in Toronto by Shettigara & Morgan (1975), also not made blind, an association was found with both asbestos exposure and smoking. Newhouse et al.[1] now report the results of a substantial case-control survey from the London area, based on living subjects. Neither patients nor interviewer were aware of the diagnosis at the time of the inquiry, and the control series seems particularly appropriate. The cancer patients smoked more heavily than the controls but had not been any more frequently exposed to asbestos.

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[1] See p. 687

Other sites.- In the most recent report by Selikoff et al. (1979) on North American insulation workers, 922 deaths from cancer were recorded on death certificates, compared with 319.7 expected. Of the 602.3 excess, 472.2 were ascribed to mesothelioma or to cancer of the respiratory or alimentary tracts. There thus remained an excess of 130.1 deaths from malignant disease at other sites (SMR, 1.9). Review of 'best available information (autopsy, surgical, clinical)' reduced the ratio to 1.4, but the effect of similar review of all death certificates in the US, from which the 'expected' figures were calculated, is of course unknown. Indeed, it may be questioned whether national rates for a large country, such as the USA, provide a fair basis of comparison for a specific and unevenly distributed occupational group such as insulation workers. In our own cohort study of chrysotile miners and millers the comparable mortality from cancer at other sites was: observed, 304; expected, 285.8 (SMR, 1.06). Whether there are other organs in which malignant disease is induced by asbestos must be considered, but the diagnostic problems (see Selikoff et al., 1979) seem well-nigh insuperable and the pathogenic mechanisms correspondingly obscure.

Asbestosis

Pulmonary and pleural fibrosis have been common causes of disability, and less frequently of mortality, in asbestos workers in many countries (e.g., López-Areal Del Amo[1]). The early detection and removal from exposure of affected workers, biological monitoring systems and the definition of hygiene standards, are preventive measures which all rely on epidemiological understanding. Considerable effort has been put in recent years into the development of radiological, physiological and clinical tests for the presence of disease manifestations and into standardizing them for epidemiological surveys. Even so, problems of inter- and intra-observer error and subject variation remain enormous; the specificity and sensitivity of tests inevitably conflict; and their validity is largely unmeasured. Peto (1978), in discussing the lack of information on the prognostic significance of crepitations, states: 'if data on severe disability or death are sufficient to evaluate the significance of the sign, they will also be sufficient to assess the serious risk directly, so there may be little advantage in considering the prevalence of such a sign in framing a hygiene standard'.

This lack of information on prognostic significance applies to virtually every sign and symptom used in studies of asbestosis. The current paper by Liddell[2] is therefore something of a landmark. It summarizes results of his more extensive studies on the relation between radiological findings in Quebec chrysotile workers while still employed and their subsequent mortality. While it is true that the findings

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[1] See p. 201

[2] See p. 667

convincingly validate the UICC/Cincinnati classification (and by inference, the ILO U/C system also), they do so in a relative rather than in an absolute sense. Thus, it was the use of the classification scales by a specific group of six readers on a unique sample of chest radiographs which was validated, rather than any particular *level* of reading. Peto's reservation therefore stands: until signs and symptoms can be recorded and interpreted objectively, mortality may still be the most reliable basis for hygiene standards.

The paper submitted by Berry[1] deals with validation of another kind, that of compensation procedures under the Industrial Injuries Act in the UK. As in a similar study some years ago (McVittie, 1965), the observed mortality was between two and three times expectation: 52% of the excess was due to lung cancer, 32% to asbestosis, 14% to mesothelioma and 3% to other cancers. Despite the special nature of the study material, the very low figure for gastrointestinal and other cancers is worth noting.

The finding of pleural plaques in general populations raises analogous questions as to their significance. Localized areas of pleural thickening may or may not be calcified and calcified areas of pleura may or may not be thickened. The endemic phenomenon in question is mainly one of 'calcified plaques', and while they have certainly occurred in areas where asbestos is found, they are also found elsewhere. Indeed, the evidence that there is any causal relationship between pleural calcification and mineral fibre *per se* is unconvincing. Nevertheless, some environmental mineral, often closely associated with asbestos deposits, must surely be implicated (see for example Gibbs, 1979). We certainly need to know more about the etiology and prognostic importance of these mysterious changes.

SOME METHODOLOGICAL POINTS

Four papers in this section deal with problems which may be loosely classified as methodological. Lewinsohn et al.[2] describe preliminary phases in a study of mesothelioma cases in the Connecticut Tumor Registry, which has still to overcome serious problems of diagnostic reliability and in recording asbestos exposure. Perdrizet et al.[3] discuss the objectives and achievements of the French mesothelioma register, initiated in 1975. As a measure of disease incidence, the procedure

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[1] See p. 603

[2] See p. 655

[3] See p. 697

failed to secure the universal collaboration of French pathologists. On the other hand, it appears to be leading to a wider recognition of mesothelioma as a disease entity and to better diagnostic standardization. For all its imperfections, the authors believe that the register will enable useful etiological observations to be made, especially if backed by tissue analyses.

Di Menza et al.[1] investigated the important question of whether valid information on past asbestos exposure is obtainable from microscopic examination of lung washings. Their data showed good correlation between the presence of ferruginous bodies and a definite history of exposure. Other relationships were inconclusive. More information might be obtained if time since last exposure were taken into account.

Liddell's paper[2] on latent periods in lung cancer mortality stems from the frequent suggestion that the period between first exposure and appearance of the tumour is related inversely to dose. His analysis, based upon the experience of Quebec chrysotile workers, showed no evidence of this relationship. The question is of more than academic importance, since the presence of such a relationship would greatly complicate efforts to define exposure-response models and to establish hygiene standards.

IMPORTANCE OF CONTROL

Faced with an environmental hazard, several strategies are possible: simple steps to minimize the effects, application of hygiene standards, or complete ban (with or without substitutes). The public and their governments make these decisions on the basis of their appreciation of what scientists tell them about various aspects of cost and benefit. Epidemiology has done much to identify and explain the health effects of asbestos - indeed few environmental problems have been studied so extensively; it has not done so well in putting the risks into proper perspective or in evaluating the control options. It would be invidious to identify the incompetent and misleading estimates and unfair to blame it all on the news media, vested interests or political pressures. The fact remains that more than 40 years after the introduction of hygiene standards and 15 years after the 1964 New York Conference, few if any industrial countries have reliable or comprehensive data on the health costs of asbestos, and there is next to no information on what control measures have achieved. There are a few exceptions; for example, Hammond et al. (1979) demonstrated that asbestos workers who gave up smoking had substantially lower death rates than those who continued. Or again, Becklake et al. (1979) studied the effect of removal of asbestos workers from further exposure, with less encouraging results. The need for better data on the importance and effectiveness of control is a challenge for epidemiological research.

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[1] See p. 609

[2] See p. 661

CONCLUSIONS

Several important etiological questions seem now to have been settled. Lung cancer is caused by all kinds of asbestos, without need for any other factor. The interaction between smoking and asbestos is at least additive and in some circumstances multiplicative. The amphiboles appear to carry a higher risk of lung cancer than chrysotile; however, there are still no comparable data on exposure-response relationships with different fibre types or in various industrial circumstances.

The risk of mesothelioma after chrysotile exposure appears small, and most asbestos-related cases are probably due to crocidolite or amosite. A low incidence of this tumour, of unknown etiology, antedated the commercial use of asbestos and probably continues. The implications of fibre size and shape, rather than type *per se*, deserve attention. The causal association with other cancers - notably of the upper gastrointestinal tract and larynx - is less consistent and suggests a role for other unidentified factors.

A major difficulty in the study of the pleural and parenchymal changes of asbestosis lies in the standardization of tests and in defining their prognostic significance. The ILO U/C radiological classification has now been validated in terms of mortality in chrysotile workers, but the findings cannot be generalized. The etiology and significance of pleural calcification is still unknown.

The present and future impact of asbestos-related disease on the community remains controversial, and few estimates are based on adequately representative data. Evidence of the effectiveness of environmental and other control measures is equally deficient.

RESUME

Il semble que plusieurs questions étiologiques importantes soient maintenant résolues. Le cancer du poumon est provoqué par toutes les variétés d'amiante sans que l'intervention d'un autre facteur soit nécessaire. Les interactions entre l'usage du tabac et l'amiante sont pour le moins additives et, dans certains cas, multiplicatives. Les amphiboles paraissent comporter un plus fort risque de cancer du poumon que le chrysotile; mais il n'existe toujours pas de données comparables sur les relations exposition-effet avec différents types de fibres ou dans diverses situations industrielles.

Le risque de mésothéliome après exposition au chrysotile semble faible, et la plupart des cas liés à l'amiante sont probablement dus à la crocidolite ou à l'amosite. Une faible incidence de cette tumeur, d'étiologie inconnue, précédait l'utilisation commerciale de l'amiante et subsiste probablement. Les effets de la taille et de la forme des fibres, plutôt que de la variété elle-même, méritent attention. L'association causale avec d'autres cancers - ceux des voies digestives supérieures et du larynx notamment - est moins régulière et laisse supposer l'intervention d'autres facteurs non identifiés.

L'une des grandes difficultés de l'étude des lésions pleurales et parenchymateuses dues à l'amiantose réside dans la normalisation des tests et la détermination de leur signification pronostique. La classification radiologique BIT U/C a maintenant été validée en ce qui concerne la mortalité des travailleurs exposés au crysotile, mais on ne saurait généraliser ces observations. L'étiologie et la signification de la calcification pleurale demeurent inconnues.

Les répercussions actuelles et futures des maladies liées à l'amiante sur la collectivité restent matière à controverse, et peu d'estimations reposent sur des données suffisamment représentatives. Les indices de l'efficacité des mesures de lutte environnementales ou autres sont également insuffisants.

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