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Health Implications of Environmental Exposure to Asbestos

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The health impact of environmental pollution resulting from the industrial use of asbestos can be assessed in three ways. First, there are the direct epidemiological surveys. These indicate that domestic exposure has been responsible for cases of mesothelioma and possibly lung cancer and radiological changes in family contacts of asbestos workers. Exposure in the neighborhood of crocidolite mines and factories has also resulted in cases of mesothelioma but no similar evidence exists for chrysotile or amosite. Neither air nor water pollution has been directly incriminated as a cause of either respiratory or digestive malignancies.

Second, a few attempts have been made to extrapolate from exposure response findings in industrial cohorts. For several reasons, even for lung cancer, this approach is dubious: the observed gradients have a 100-fold range in slope; the equivalences of dust, fiber and gravimetric measures are largely guesswork; and the carcinogenic potential of mineral fibers, particularly for the pleura, varies enormously with fiber type and/or dimensions. No adequate exposure-response observations have been made for mesothelioma.

A third approach makes use of the differing incidence of mesothelioma in men and women. Data from several countries indicate that, until the 1950s (i.e., 30–40 years after significant industrial use of asbestos began), the rates were similar in both sexes. Since then, the incidence in males has risen steeply—in the U.S. and U.K. at about 10% per annum. In females, on the other hand, there has been little or no convincing increase. These data suggest that the "background" level of mesothelioma in both sexes is and has been about 2 per million per annum and that—as at least some mesothelioma cases in females are directly or indirectly attributable to occupational exposure—there is little room left for any contribution from the general environment. It is recommended that mesothelioma surveillance, backed by appropriate epidemiological inquiries, offers an effective method of monitoring the health impact of asbestos air pollution.

Introduction

Fibrous mineral silicates are a common constituent of the earth's surface. Fibers of natural origin are present to a greater or lesser extent in air and water almost everywhere and probably always have been. The industrial value of certain of these minerals, collectively known as asbestos, was recognized at the end of the last century. Production and use increased enormously, with periods of acceleration related to both world wars (Fig. 1). Occupational exposure in asbestos production, manufacturing and user industries has reflected the conflicting trends of use and control. Since 1950, the number of workers exposed has greatly increased while their intensity of exposure has steadily decreased. Assuming a latent period of 30 to 40 years for malignant diseases to manifest themselves, we would expect to see the first effects, at least occupationally, in the 1950s, which is what actually happened. Industrial exploitation has lead to contamination of the general environment, the nature and extent of which is more difficult to document. Gross pollution in the immediate neighborhood of mines, factories and shipyards was commonplace 30 to 50 years ago but far less today. On the other hand, the general level of asbestos fibers in air, water, and food is probably higher than it was and may still be rising. Building construction and demolition have been responsible for much of this; for example, see Woitowitz and Rodels-

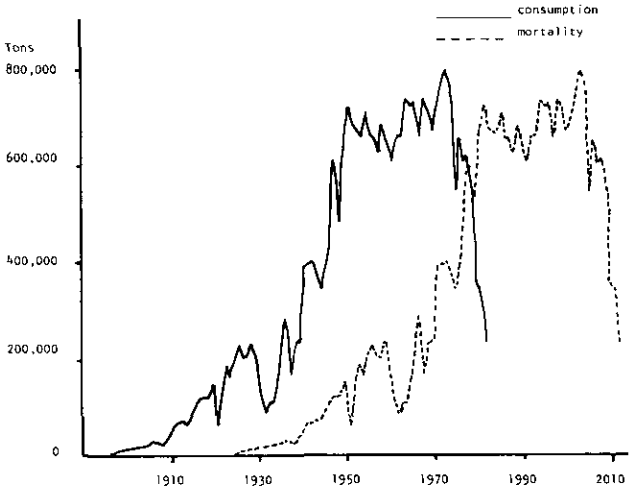

FIGURE 1. Asbestos consumption in the U.S. (*41*) showing probable pattern of related cancer mortality.

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berger (*1*). The control of occupational exposure in these industries has been slow and relatively ineffective with correspondingly great and continuing impact on the general environment, especially in cities. In addition, there is the widespread distribution and accumulation of a variety of asbestos-containing materials and products which gradually wear and deteriorate.

The health implications of this general picture are complicated by three additional factors. First, asbestos is not one but several materials, each of distinct chemical, physical, and biological qualities. In particular the amphiboles—crocidolite, amosite, anthophyllite, and tremolite—almost certainly differ from the serpentine mineral, chrysotile, in their health effects. Second, dimensions, durability, respirability, retention, and surface reactivity have considerable biological relevance, and, in different circumstances, the same mineral may vary enormously. Third, interaction between asbestos exposure and cigarette smoking is important in determining the risk of respiratory tract cancer, and unidentified factors may well play a role in the gastrointestinal tract.

This paper will attempt to assess the health impact of environmental pollution resulting from the industrial use of asbestos. Occupational exposure will be considered only to the extent that it can help to quantify the risk. So far as possible, the contribution of "natural" nonindustrial pollution will be excluded from the total. Although no precise geographical or temporal definitions are possible, the focus will be on North America (USA and Canada) in the 1980s. Nonoccupational exposures may be either respiratory or by ingestion and vary considerably both in duration and intensity. Air pollution has thus to be separated from contamination of water supplies; it can be further subdivided into three or four different grades. Domestic, indirect occupational, and bystander exposures have often been very high; neighborhood exposures in the vicinity of asbestos mines, plants, shipyards, etc., were also considerable. General urban pollution is much lower than any of these but a far larger proportion of the population is at risk. The order of magnitude of these exposures is shown in Table 1.

Three main methodologies will be considered and the results compared. First, there is the possibility of direct epidemiological investigation, by means of population-based studies—cohort or case-referent in type. The problem with the former is that adequate sensitivity for detection of low level risks is almost impossible to achieve; the problem with the latter is that reliable estimates of past exposure and source are even more difficult to determine. A second methodological approach depends on extrapolation from exposure–response data obtained from industrial cohorts to exposure levels observed or estimated in the general environment. The difficulties here include environmental measurement at very low fiber concentrations, the wide range of risks calculable from the few available sets of exposure–response data and the questionable validity of any extrapolation of this kind. A third approach entails the estimation of the overall impact of asbestos exposure on mortality followed by partition into occupational and nonoccupational components. Several methods of doing this have been used with results which are at best quite approximate. We shall suggest that an improved estimate can probably be obtained from examination of trends in male and female mesothelioma mortality. Even now, relatively few cases in women are attributable to occupation, and statistics for the past—before the development of a male excess—provide some indication of the natural background incidence.

Table 1. Current North American levels of exposure to airborne asbestos.

Type of exposure	Approximate level, ng/m^3
Occupational	10,000–>50,000
Neighborhood/domestic	100–10,000
Urban	1–100
Rural/background	<1–2

Estimates of Health Impact

For the purpose of this paper, it seems reasonable to assume that only diseases for which there is evidence of causation in occupational studies deserve consideration in relation to nonoccupational exposure. This limits our concern to asbestosis, respiratory tract cancers, malignant mesothelioma tumors, and gastrointestinal tract cancers. As occupational studies suggest that even a lifetime at nonoccupational levels of fiber concentration would seldom, if ever, cause disability or death from pulmonary fibrosis, this response will be considered only to the extent that it provides evidence of significant past exposure. Laryngeal cancer will not be considered *per se*. It is an uncommon cause of death, and the etiological contribution of asbestos is still unclear. So far as air pollution is concerned, the major emphasis must be on lung cancer and mesothelioma, since the estimation procedures available are very crude and other diseases could only have a marginal effect. Cancers of the gastrointestinal tract will be discussed only in relation to drinking water.

Epidemiological Surveys

Neighborhood Exposure. There are several well-documented reports indicating the occurrence of mesothelioma cases in the vicinity of crocidolite mines and factories. The initial report by Wagner et al. (*2*) of the high prevalence of this disease around the crocidolite mines in the Cape Province, Republic of South Africa, included cases without occupational exposure. The case-control studies of Newhouse and Thompson (*3*) in Barking (London) and of Hain et al. (*4*) in Hamburg indicated

an excess in the immediate neighborhood of factories which processed asbestos, mainly from the same South African mines. On the other hand, no similar cases were seen near the amosite or chrysotile mines of South Africa nor, by extensive case-control studies, near the chrysotile mines of Canada or the U.S. (*5,6*). Also negative was an analysis of mortality in persons residing within half a mile of an amosite asbestos factory in Patterson, NJ (*7*). The employees of this plant had experienced high rates of both mesothelioma and lung cancer (*8*) and appreciable numbers of amosite fibers were still present in dust collected in the attics of neighboring houses. One doubtful case only was reported in the vicinity of the Balangero chrysotile mine in Italy (*9*) and no case has ever been reported from the Russian chrysotile mining area of Sverdlovsk (*10*).

In an early uncontrolled study of 42 cases in Pennsylvania (*11*), two lived close to asbestos plants and six others had worked next to an asbestos plant. A systematic investigation of all 201 cases of mesothelioma and 19 other pleural tumors reported to the Connecticut Tumor Registry, (1955–1977) and 604 randomly selected decedent controls found no evidence of risk from neighborhood exposure (*12*). In Northwest England, Whitwell et al. (*13*) examined lung tissue by phase-contrast optical microscopy from 100 cases of pleural mesothelioma, 100 cases of lung cancer and 100 controls who had died from conditions other than industrial lung disease or lung cancer. They found that the number of asbestos fibers was related to the occupational and not to the home environment. Subjects who had lived near probable sources of atmospheric asbestos pollution had no higher counts than those from further away. In this review of data on pleural mesothelioma in England and Wales, Gardner (*14*) commented on the highly localized geographical distribution "in which occupational and occupationally related exposure has been critical."

Several investigations have been made into the possible effects of environmental pollution on the resident populations of Thetford Mines and Asbestos, Québec, the two main centers of chrysotile production in the Western world. Geographical analyses by Graham et al. (*15*) of cancers reported to the Quebec tumor registry showed higher incidence rates for tumors of the pleura, lip, salivary gland, and small intestine in males and, additionally, of kidney and skin (melanoma) in females. However, no account was taken of occupational or domestic exposure. Pampalon et al. (*16*) did much the same thing using mortality statistics. Among women, there was no excess mortality; in men, mortality from respiratory cancer was raised in Thetford Mines (SMR 1.62) and from nonmalignant respiratory diseases in the town of Asbestos (SMR 1.53). In a later report (*17*), Siemiatycki showed that, as about 75% of the older male population of these towns had been employed in the mining industry (over 50% for 30 years or more) the raised SMRs could well be explained by occupational exposure—a possibility subsequently confirmed by Liddell (*18*).

Household Exposure. Despite the scarcity of environmental data, it is likely that household contacts of asbestos workers are much more heavily exposed than others who simply live in the area. Measurements made by Nicholson (*19*) in the homes of miners and nonminers in a chrysotile mining community in Newfoundland suggest that fiber concentrations were manyfold higher in the former than the latter. Three of the 42 cases of mesothelioma in Pennsylvania, mentioned above (*11*), were in the household contacts, and the studies of both Newhouse and Thomson in England (*3*) and of McDonald and McDonald (*5*) in North America all showed more frequent domestic exposure in cases than controls, after exclusion of occupation. Two further epidemiological surveys have specifically addressed the question. Vianna and Polan (*20*) studied the asbestos exposure history of all 52 histologically confirmed fatal cases of mesothelioma in females in New York State (excluding New York City), 1967–1977, with matched controls. Excluding six cases exposed at work, eight 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 two of the eight, whose husbands were asbestos workers, were only 30 and 31 years of age.

In a study by Anderson et al. (*21*), over 3100 household contacts of 1664 surviving employees of the Patterson amosite asbestos plant were identified in the period, 1973–1978. 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 rather more frequent than parenchymal. The readings were made by five experienced readers and although 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 methodology has not yet been adequately described but at least three cases of mesothelioma and excess mortality from lung cancer have been reported (*22*).

General Environmental Exposure. 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 tumors undertaken by our group (*5*) in Canada, 1960–1975, and in the U.S., 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 neighborhood exposure, the places of residence of women were examined for the period 20 through 40 years 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 differ-

ences could easily be due to chance, quite apart from the greater likelihood of case recognition in urban than rural areas and the contribution of exposure in the immediate neighborhood of plants, such as that in Patterson.

Exposure by Ingestion. It has been postulated that asbestos fibers in drinking water, and perhaps also in food, could conceivably increase the incidence of alimentary cancers in populations exposed over many years. For several reasons, this question will be only discussed briefly in this paper. In the first place, excepting mining areas, the occurrence of fibers in drinking water is usually the result of contamination from natural sources rather than from industrial processes and products. Second, even in industrial cohorts, the association of asbestos exposure with alimentary cancer is irregular (*23*) and not wholly convincing (*24*); also, the risks are small compared to lung cancer and largely confined to the most heavily exposed workers. Even so, water supplies are often carried in asbestos–cement pipes, mining and quarrying activities have led to heavy water pollution, and urban air pollution from asbestos plants and construction may well contaminate water and food.

There have been 13 analyses of cancer incidence and/or mortality by site in relation to estimated concentrations of asbestos fibers in drinking water in six areas of North America. In five of these—Connecticut, Quebec, San Francisco Bay area, Utah and Puget Sound area—the contaminating fibers were chrysotile in concentrations ranging from below detection to 10^6 fibers per liter. In the sixth population—Duluth—exposure was to an amphibole mineral in a similar range of concentrations, although to what extent the particles were truly fibrous is unclear. In all such studies, the main difficulty is to allow correctly for socioeconomic, occupational, nutritional, and other confounding variables. The results of all 13 studies were reviewed by Marsh (*25*) at a recent Summary Workshop sponsored by the U.S. Environmental Protection Agency (*26*). After exclusion of one study which did not give results by cancer site, eight providing independent data were included in a binomial probability analysis designed to test the degree of agreement between them. Despite the low level of agreement between male and female results, positive finds for esophagus, stomach, pancreas, and prostate (Table 2) were unlikely to be due to chance alone, although not necessarily to water supplies. As the first two of these sites are those for which there is also the strongest evidence of an association with asbestos in occupational cohorts, Marsh recommended that these specific etiologic hypotheses should be tested by case-control studies. He pointed out, however, that the detection of low level risks would require very large samples.

Extrapolation

The several inconclusive attempts to identify and interpret small differences in disease incidence in relation to fiber content of water supplies illustrates the virtual impossibility of direct epidemiological assessment of low environmental risks related to the more complicated constituents of urban air pollution. A common alternative approach is therefore to take the exposure–response relationships observed in occupational environments and extrapolate back to the much lower exposure levels recorded in the general environment. This procedure is fraught with difficulties, however, some of which are discussed below.

The Assumptions. Extrapolation is valid only to the extent that (a) some reasonable mathematical formula for the relationship exists; (b) the point of intercept on the exposure axis is known; (c) important interactions with other etiologic factors are multiplicative or additive. For lung cancer, the scanty data available are compatible with a nonthreshold linear relationship to accumulated exposure but do not exclude other models. The even more scanty data on the combined effects of cigarette smoking and asbestos exposure suggest that the interaction is more than additive but not necessarily multiplicative in all circumstances. No comparable evi-

Table 2. Drinking water and digestive cancers.[a,b]

	Duluth	Connecticut	Quebec	Bay Area, CA	Utah	Puget Sound
Fibertype	Amphibole	Chrysotile	Chrysotile	Chrysotile	Chrysotile	Chrysotile
Fiber density, million/L	1–30	0.7	1.1–1300	0.25–36	—	7.3–207
Population exposed	100,000	576,800	420,000	3,000,000	24,000	200,000
Site						
Esophagus	○			●		
Stomach	●		○	●		
Small intestine						●
Colon						
Rectum						
Biliary passage/liver						
Gallbladder						
Pancreas	●	○	○	●		
Peritoneum				●		

[a] Derived from analyses by Marsh (*25*)
[b] Key: (○) excess in males or females; (●) excess in males and females.

dence on either of these questions exists for asbestosis or mesothelioma.

Exposure–Response. Nine cohort studies in eight industrial groups (*27–35*) have been reported in which exposure to asbestos for each subject was estimated individually in duration and intensity and related to lung cancer risk. The studies are summarized in Table 3. The first eight studies shown (studies 1–8), produced linear exposure–response relationships, but of very varied gradients. With the exception of study 7, where the analysis was case-referent in type, the other studies used man-years methods primarily, with results presented as SMRs. Since, for various reasons, not all lines passed through the origin, the gradients in Table 2 are expressed in terms of relative slope, as calculated by Liddell and Hanley (*36*). The two textile plants (studies 4–6) have gradients manyfold more steep than the rest, the sharpest contrast being between the chrysotile-only textile workers and chrysotile miners and millers. Even less risk than in chrysotile production is seen in the two friction products plants, where it is quite doubtful whether there was any significant lung cancer excess. Although far below textiles, the two factories engaged mainly in the manufacture of cement and building products were severalfold above chrysotile production. The experience of American insulation workers (*37*) and of men engaged in the manufacture of amosite insulation products (*8*) are not shown in Table 2 because exposure was not assessed individually. However, with certain assumptions, especially as to linearity, it seems likely that the gradients for these two populations lay somewhere between the cement workers and the textile workers. Study 9, of asbestos cement workers in Ontario (*35*), is difficult to interpret: both chrysotile and amphiboles were used, there were relatively few lung cancer deaths, but substantial mortality from mesothelioma. Perhaps because of the small numbers and possible confusion between the two kinds of malignancy there was no systematic relationship between estimated exposure and lung cancer so no slope was calculated.

There were at least two possible explanations for the variation, first, that some of the exposure estimates were seriously incorrect. If so, the error was systematic or the response relationships would have been lost. Second, and I believe more likely, neither the original dust particle measurements nor the usual conversions to fibers, countable with the optical microscope, adequately reflected the biological hazard. Experimental work on fiber size and the dynamics of penetration and retention all suggest that this could be an important part of the explanation, perhaps all of it. Indeed, fibers wide enough to be seen with the light microscope have little carcinogenic effect (J.C. Wagner, personal communication).

Fiber Type and Mesothelioma. Differences between the various types of asbestos fiber can probably be ignored in predicting risks of lung cancer and asbestosis, but mesothelioma is another matter. The evidence that virtually all peritoneal and most pleural cases are attributable to amphibole exposure, rather than to chrysotile, has been reviewed elsewhere (*24,38*). Although not conclusive, the data are sufficiently persuasive for most countries—U.S. excepted—to have made a basic distinction as to fiber type in their control policies and legislation (*39*). In the present context, this major

Table 3. Exposure–response for lung cancer in male cohorts where exposure estimates were made for each subject individually.

Study no.	Type of industry	Study	Place	Fiber type	Number in cohort	Total deaths	Lung cancer expected cases	Relative slope per mpcf-yr
1	Mining and milling	McDonald (*24*)	Quebec	Chrysotile	10,939	3,291	184	0.164
2	General manufacture	Henderson and Enterline (*25*)	U.S.	Chrysotile Crocidolite Amosite	1,075	781	23.3	0.353
3	Cement products	Weill (*26*)	New Orleans	Chrysotile Crocidolite	5,645	601	49.2	0.658
4	Textiles	Dement (*27*)	S. Carolina	Chrysotile	768	191	7.5	6.896
5	Textiles	McDonald (*28*)	S. Carolina	Chrysotile	2,543	857	29.6	5.863
6	Mainly textiles	McDonald (*29*)	Pennsylvania	Chrysotile Amosite Crocidolite	4,137	1,392	50.5	5.101
7	Friction products	Berry and Newhouse (*30*)	England	Chrysotile Crocidolite	9,113	1,640	139.5	'effectively zero'
8	Friction products	McDonald (*31*)	Connecticut	Chrysotile	3,641	1,267	49.1	'effectively zero'
9	Cement products	Finkelstein (*32*)	Ontario	Chrysotile Crocidolite	536	138	5.4	not calculated

uncertainty is further compounded by the lack of adequate exposure–response information for mesothelioma. In none of the nine cohorts shown in Table 3, with individual measurements of exposure in terms of both intensity and duration, was the relationship of mesothelioma to "dose" examined. The relatively small number of cases and the confounding effects of fiber type discouraged such analyses. Despite this, some recent reports (*40,41*) suggest that an indication of risk can be obtained from a small number of other cohort studies, in which only average group exposure had been roughly estimated. All the cohorts used for these reports were exposed to pure amphibole or to amphibole–chrysotile mixtures and generally excluded from consideration were those in which the mesothelioma risk was low. Indeed, if the 18 cohorts so far reported with 200 or more deaths are listed in order of proportional mortality from this cause, those selected for these studies ranked as numbers 1,2,3,5, and 7.

Conversion. All the available exposure–response data from occupational cohorts are based on total respirable dust measurements made by impinger methods and expressed in millions of particles per cubic foot (mpcf). Determination of the equivalence of these measurements in terms of fibers (> 5 μm long) per milliliter (f/mL) is a difficult and dubious operation. Even in chrysotile mining and milling, the range of conversion ratios is at least 40-fold (*42,43*). A problem of similar magnitude concerns the equivalence in fiber terms of measurements made in the general environment, nearly all of which are gravimetric and usually expressed in nanograms per cubic meter (ng/m^3). These questions have been discussed by several authors with various conclusions; Nicholson (*40*) considered that the conversion factor relating mass to optical fiber concentration had a range of 5 to 150 and probably varied with fiber type.

On taking these many uncertainties into account, the range of possible error in any estimates made by extrapolation must be very wide indeed. Taken together, variations in exposure–response gradient and conversion factors for ng/m^3, mpcf, and f/mL could conceivably lead to estimates with a range of five orders of magnitude. Even this would not take account of such questions as sampling error in environmental measurement, fiber type, or fiber size distributions. Nevertheless, a few courageous estimates of environmental impact by extrapolation have been made. The results are not so widely disparate, at least for lung cancer, mainly because similar approaches on averaging have been used.

In a paper by Enterline in 1981 (*44*), estimates of lung cancer deaths, based on extrapolation from linear and curvilinear exposure–response models, were made. Using conversion factors of 3 for f/mL per mpcf and 40 × 10^3 for f/mL per ng/m^3 and linear extrapolation from his own exposure–response data (SMR = 100 + 0.658 mpcf-yr), he estimated that continuous lifetime exposure at 5 ng/m^3 (approximately the average outdoor level in urban areas of the U.S.) would result in 4.6 lung cancer deaths per million population. On the other hand, a curvilinear model, for which there is experimental but not epidemiological support, would result essentially in zero deaths. In a later paper (*45*), Enterline speculated on the apparent discrepancy between occupational exposures where excess lung cancer mortality generally exceeds that due to mesothelioma (*46*) and the nonoccupational situation. In the general population of the U.S., with average outdoor exposure at about 1.5 ng/m^3, the lifetime lung cancer risk was estimated by Enterline to be about 2 per million. Using data on mesothelioma incidence, however, he concluded that the lifetime risk of this disease was at least 100 per million. However, as discussed at the end of this paper, this latter estimate is probably not correct.

Table 4. Estimated lifetime risks per million population from nonoccupational exposure to asbestos.

	Lung cancer	Mesothelioma
Enterline (*42*)	2	100[a]
Schneiderman (*45*)	3–32	4–24
Nicholson (*40*)	12–18	6–24
NRC Committee (*46*)		
Smokers, male	64–320	
Smokers, female	23–120	
Nonsmokers, male	6–29	9–46
Nonsmokers, female	3–15	

[a]This figure should probably have been about 50 (see text).

Several other estimates of current and lifetime risk of lung cancer and mesothelioma for the U.S. population have been made purely by extrapolation. A simplified comparison of these estimates is set out in Table 4. To achieve a measure of comparability, some liberties were taken with the published data, and the figures shown are therefore approximate. Having regard for the enormous range of uncertainty, it is remarkable that the four estimates are as close as they are. The differences between the lung cancer estimates are mainly due to the idiosyncratic selection of exposure–response data from industrial cohorts. The NRC committee (*41*) used three of the nine cohorts included in Table 3 and added six others, in all of which only group estimates of exposure had been made. Schneiderman (*47*) used only two of the nine and included three of the six added by the NRC committee. Nicholson (*40*) used four of the nine cohorts and not the other five. The greater similarity of the mesothelioma figures is due to the fact that, apart from Enterline, whose figure was not obtained by extrapolation, the others used the same information (or lack of it) on exposure–response—all, however, from the cohorts at highest risk.

In the light of these critical comments, it is fair to ask whether anything better can be done. Until the explanation of the 100-fold difference in gradient of slopes for the eight or nine satisfactory sets of exposure–response data is explained, and better evidence on the equivalence and mass and fiber concentration measurements is obtained, any extrapolation is, in my view, pure guesswork. However, the possibility that mesoth-

elioma may be a more serious potential hazard than lung cancer, especially for nonsmokers is real. The theoretical basis for this view has been presented by Peto (*48,49*). His mathematical models are compatible with the evidence available, but his equations for lung cancer and mesothelioma both include constants which depend on fiber dimension and type and which may differ between the two diseases and in different circumstances.

Sex Differences in Mesothelioma Mortality

If the total number of deaths attributable to asbestos exposure were known or could be calculated, it might then be possible to partition them by causal type of exposure. We took this approach at the Banbury Conference in 1980 in trying to discover what proportion of cancer was attributable to occupational asbestos exposure (*46*). Three types of information were used: first the estimated incidence of fatal cases of mesothelioma; second, the ratio of mesothelioma to other types of cancer from all available cohorts (then numbering 24); and third, the proportion of mesothelioma related to occupation from case-referent surveys in Canada, 1960–1972, and in the United States, 1972 (*5*). At that time, our best estimates for North American males in 1975 were an annual mesothelioma incidence of 8.0 per million; 75% of cases attributable to occupational asbestos exposure; and a ratio of mesothelioma to excess mortality from other cancers of 3.3 (2.4 for respiratory plus 0.9 for digestive). The corresponding figures for females were 2.5 per million, less than 10% attributable, and a lower but undefined ratio to other cancers (especially respiratory). Our best indicator of mesothelioma incidence was the SEER Program of population-based cancer registries in five states and five city areas, for which data are now available for 1973–1980 (Biometry Branch, NCI, unpublished). The number of usable cohorts has also risen, from 24 to 32, with little change in median ratios of mesothelioma to excess respiratory cancer (males, 2.5; females, 1.25). We have not yet recalculated the ratio for digestive cancer.

Returning to the problem in hand, if a similar approach were adopted, we might have estimated that, in 1975, nonoccupational causes were responsible in males for about 2.0 per million cases of mesothelioma and 5.0 per million excess lung cancers. In females, the mesothelioma figure would be fairly similar and the lung cancer excess about 2.5 per million. These nonoccupational rates would then have to be apportioned between domestic, neighborhood and general environmental exposures on the one hand and background causes on the other. For mesothelioma, this approach seems reasonable, though difficult, but the extrapolation to lung cancer, empirically acceptable for the occupational estimate, is considerably more dubious for the nonoccupational component. However, the first task is to consider mesothelioma and, for this purpose, it may be useful to examine the theoretical model illustrated in Figure 2.

If there is a background incidence of mesothelioma, unrelated to the industrial exploitation of asbestos (although quite conceivably to mineral fibers), there is no reason to believe that the levels would be different in males and females. Consideration of Figure 1 and the usual latency for mesothelioma (30–40 years) suggests that, as stated earlier, we might begin to see the effects of asbestos in the 1950s, especially in men. The trend in male incidence might then parallel the increased industrial use of asbestos, reaching a peak in about year 2000 and, hopefully, falling some 40 years after that. In females, on the other hand, a much smaller effect would be expected from occupational exposure and any increased incidence would reflect more specifically the impact of domestic and environmental exposure.

There are several sets of data which suggest that this general pattern is being followed. In Canada, ascertainment through pathologists has shown a steady in-

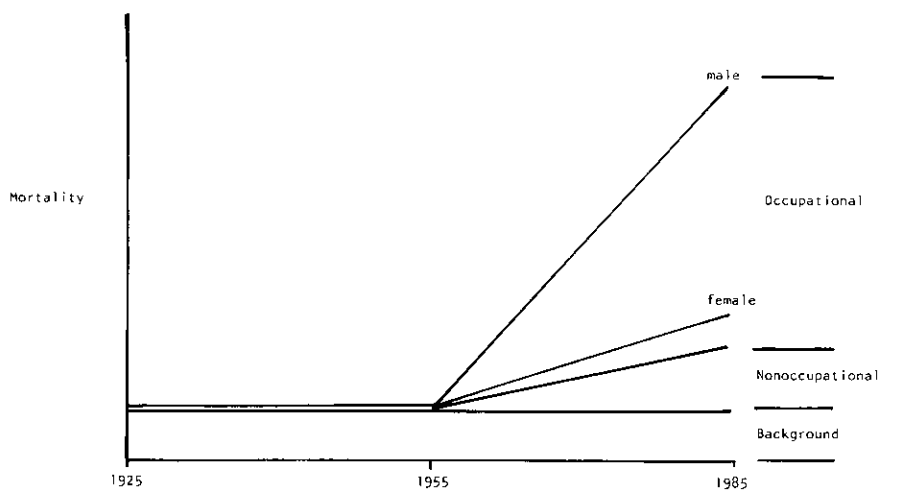

FIGURE 2. Conceptual model for mesothelioma mortality assuming complete ascertainment.

crease in male cases from about 10 in 1961 to 25 in 1974, whereas in females the annual number of cases averaged about 8 over the same period (*5*). In the U.K. (*14*), deaths from pleural mesothelioma in males have risen from 100 (4 per million) per annum in 1968 to 200 (8 per million) in 1978 (most sharply since about 1973)—a gradient of about 10% per annum. In females, the annual number of deaths has remained steady at just under 50 (2 per million). Data presented by Elmes and Simpson (*50*) tend to suggest that, in the U.K., the sex difference began to appear in about 1950. Finnish Cancer Registry statistics, 1953–1969, reported by Nurminen in 1975 (*51*) indicate that mesothelioma was equally frequent in men and women in Finland until about 1961 when they began to separate. In the U.S. data from the Connecticut Tumor Registry (*52,53*), show no sex difference until the mid 1950s, after which there was a rapid rise in the male rates. Of particular interest are the observations of Archer and Rom (*54*) on mortality by age and sex from diffuse malignant mesothelioma of the pleura in the U.S., 1950–1978. Until 1966, there was no difference between the rates for men and women in any age group. Thereafter there was a sharp divergence between the sexes, evident only after age 45 when the rate for males rose considerably and for females to a lesser extent. Below age 45, the rates for males and females continued equal and unchanged.

All these time trends are subject to the confounding effect of changes in level of diagnosis and ascertainment. Only the more recent data from the SEER program provide a reasonably complete and uniform level of ascertainment. However, the age-adjusted rates for mesothelioma, all sites, for the total period 1973–1980 are very informative. Figure 3, which also includes the essentially comparable estimate for 1970–1972, from the Third National Cancer Survey (TNCS), shows that the male rate is increasing by nearly 10% per annum whereas it is quite doubtful whether there has been any change in the female rate. These data are compatible with those of Archer and Rom and again suggest that the divergence began in the 1960s.

The conclusions seem clear enough. First, there is now good reason for believing that the background level of mesothelioma, whatever its cause, must be and has been about 2 per million in men and women for many years. Second, as there is evidence that both occupational and domestic exposure account for at least some mesothelioma cases in females, there is little or no room left for any effect attributable to environmental exposure or improved levels of ascertainment.

Finally, I return to Dr. Enterline's anomalously high estimate of 333 cases of mesothelioma in 1981 related to nonoccupational exposure—equivalent to a lifetime risk of about 100 per million (Table 4). The explanation is, first that he made no allowance for the "background" incidence and, second, that he took our estimate that 47% of male mesotheliomas in 1972 resulted from nonoccupational exposure (*44*) and applied this proportion to the much larger total number of cases in 1981. In

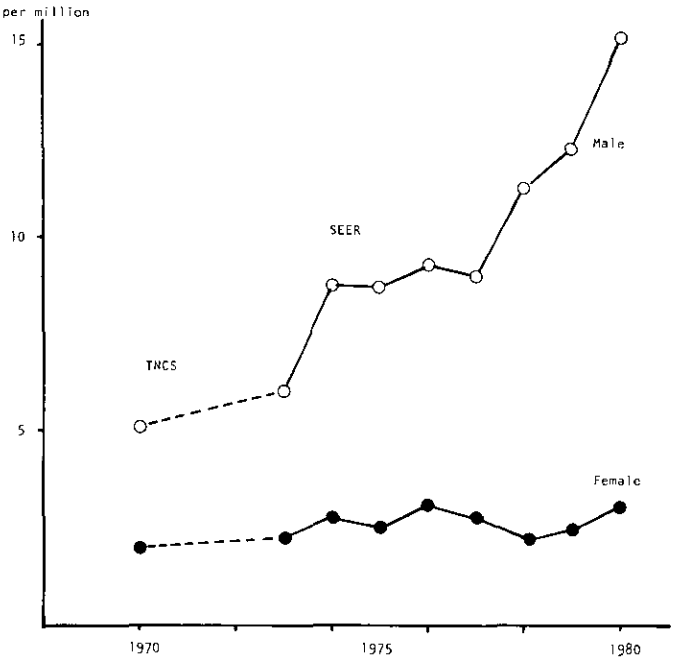

FIGURE 3. Mesothelioma incidence in the U.S., 1970–80, age-adjusted to the national population.

1970, the annual rate per million for males was 5.1 (TNCS), 47% of which is 2.4—a level similar to that shown for females in Figure 3. In 1980, we can see that nonoccupational exposure accounted for less than 20% of male cases; by the end of the century the proportion may fall to less than 10%.

Conclusion

This review does little to strengthen belief in the validity of extrapolation as a means of estimating the impact on health of urban levels of asbestos air pollution. However, the potential importance of the question and the need for prudence in matters of public health warrant the use of every available method, even this one. Linear extrapolation to very low fiber concentrations almost certainly overstates the true risk. The error may be compounded by use of inappropriate or unrepresentative exposure–response data; for example, the selection of occupational cohorts heavily exposed to amphibole fibers in estimating the risk of mesothelioma for the general population. Nevertheless, the fact remains that direct epidemiological studies may not be sensitive enough to detect very low risks.

Society thus faces something of a quandry: policies need be based on the best estimate, neither over or under, even though a decision may then be made regarding a margin of safety. One solution is to use carefully balanced extrapolation as the primary method of risk estimation, at the same time continuing to monitor the situation by direct survey methods. In this way, obvious over or under estimates of risk may be detected with least delay. The incidence of malignant mesothelial

tumors in women has great potential as an indicator of environmental asbestos exposure, especially if combined with field studies to estimate the contribution of direct and indirect occupational factors (*53*).

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REFERENCES

1. Woitowitz, H. J., and Rodelsperger, K. Asbestos emissions at the interface between workplace and environment. Institute and Policlinic of Industrial and Social Medicine, Giessen, 1982.
2. Wagner, J. C., Sleggs, C. A., and Marchand, P. Diffuse pleural mesothelioma and asbestos exposure in the North Western Cape Province. Brit. J. Ind. Med. 17: 260–271 (1960).
3. Newhouse, M. L., and Thomson, H. Epidemiology of mesothelial tumors in the London Area. Ann. N.Y. Acad. Sci. 132: 579–588 (1965).
4. Hain, E., Dalquen, P., Bohlig, H., Dahbert, A., and Hing, I. Retrospective study of 150 cases of mesothelioma in Hamburg area. Int. Arch. Arbeitsmed 33: 15–37 (1974).
5. McDonald, A. D., and McDonald, J. C. Malignant mesothelioma in North America. Cancer 46: 1650–1659 (1980).
6. Thériault, G., and Grand-Bois, L. Mesothelioma and asbestos in the Province of Quebec 1969–1972. Arch. Environ. Health 3: 15–19 (1978).
7. Hammond, E. C., Garfinkel, L., Selikoff, I. J., and Nicholson, W. J. Mortality experience of residents in the neighborhood of an asbestos factory. Ann. N.Y. Acad. Sci. 330: 417–422 (1979).
8. Seidman, H., Selikoff, I. J., and Hammond, E. C. Short term asbestos work exposure and long term observation. Ann. N.Y. Acad. Sci. 330: 61–89 (1979).
9. Rubino, G. F., Piolatto, G., Newhouse, M. L., Scansetti, G., Aresini, G. A., and Murray, R. Mortality of chrysotile asbestos miners at the Balangero Mine, Northern Italy. Brit. J. Ind. Med. 36: 187–194 (1979).
10. Kogan, F. M. Asbestos-Containing Dusts and Measures Preventing Their Noxious Effect on the Health of Workers (Russian). Mid-Ural Book Publishing Agency, Sverdlovsk, Russia, 1975.
11. Lieben, J., and Pistawka, H. Mesothelioma and asbestos exposure. Arch. Environ. Health 14: 559–562 (1967).
12. Teta, M. J., Lewinsohn, H. C., Meigs, J. W., Vidone, R. A., Mowad, L. Z., and Flannery, J. T. Occupational and geographic associations. J. Occup. Med. 25: 749–755 (1983).
13. Whitwell, F., Scott, J., and Grimshaw, M. Relationship between occupations and asbestos-fibre content of the lungs in patients with pleural mesothelioma, lung cancer, and other diseases. Thorax 32: 377–386 (1977).
14. Gardner, M. J. Tumour incidence after asbestos exposure in Great Britain with special reference to the cancer risk of the non-occupational population. VDI Ber. 475: 185–190 (1983).
15. Graham, S. Methodological problems in ecologic studies of the asbestos–cancer relationship. Environ. Res. 25: 35–49 (1981).
16. Pampalon, R., Siemiatycki, J., and Blanchet, M. Environmental asbestos pollution and public health in Quebec. Union Méd. Canada 111: 475–489 (1982).
17. Siemiatycki, J. Health effects on the general population: mortality in the general population in asbestos mining areas. Proceedings of the World Symposium on Asbestos, Montreal, 1983, pp. 337–348.
18. Liddell, F. D. K. Tumour incidence after asbestos exposure in the general population of Canada. VDI Ber. 475: 179–183 (1983).
19. Nicholson, W. J., Rohl, A. N., Weisman, I., and Selikoff, I. J. Environmental asbestos concentrations in the United States. In: Biological Effects of Mineral Fibres (J. C. Wagner, Ed.), IARC Scientific Publications, No. 30, Lyon, France, 1980, pp. 823–827.
20. Vianna, N. J., and Polan, A. K. Non-occupational exposure to asbestos and malignant mesothelioma in females. Lancet, i: 1061–1063 (1978).
21. Anderson, H. A., Lilis, R., Daum, S. M., and Selikoff, I. J. Asbestosis among household contacts of asbestos factory workers. Ann. N.Y. Acad. Sci. 330: 387–399 (1979).
22. Anderson, H. A. Family contact exposure. Proceedings of the World Symposium on Asbestos, Montreal, 1983, pp. 349–362.
23. McDonald, J. C. Mineral Fibres and Cancer. Ann. Acad. Med., Singapore 13 (Suppl.): 345–352 (1984).
24. Acheson, E., and Gardner, M. J. Asbestos: The Control Limit for Asbestos. Health and Safety Commission, HMSO, London, 1983.
25. Marsh, G. M. Critical review of epidemiologic studies related to ingested asbestos. Environ. Health Perspect. 53: 49–56 (1983).
26. U.S. Environmental Protection Agency. Summary workshop on ingested asbestos. Environ. Health Perspect. 53: 1–204 (1983).
27. McDonald, J. C., Liddell, F. D. K., Gibbs, G. W., Eyssen, G. E., and McDonald, A. D. Dust exposure and mortality in chrysotile mining, 1910–1975. Brit. J. Ind. Med. 37: 11–24 (1980).
28. Enterline, P. E., and Henderson, V. Type of asbestos and respiratory cancer in the asbestos industry. Arch. Environ. Health 27: 312–317 (1973).
29. Hughes, J., and Weill, H. Lung cancer risk associated with manufacture of asbestos-cement products. In: Biological Effects of Mineral Fibres (J. C. Wagner, Ed.), IARC Scientific Publications, No. 30, Lyon, France, 1980, pp. 627–635.
30. McDonald, A. D., Fry, J. S., Woolley, A. J., and McDonald, J. C. Dust exposure and mortality in an American chrysotile textile plant. Brit. J. Ind. Med. 40: 361–367 (1983).
31. Dement, J. M., Hams, R. L., Symons, M. J., and Shy, C. M. Estimates of dose-response for respiratory cancer among chrysotile asbestos textile workers. Ann. Occup. Hyg. 26: 869–887 (1982).
32. McDonald, A. D., Fry, J. S., Woolley, A. J., and McDonald, J. C. Dust exposure and mortality in an American factory using chrysotile, amosite and crocidolite in mainly textile manufacture. Brit. J. Ind. Med. 40: 368–374 (1983).
33. Berry, G., and Newhouse, M. L. Mortality of workers manufacturing friction materials using asbestos. Brit. J. Ind. Med. 40: 1–7 (1983).
34. McDonald, A. D., Fry, J. S., Woolley, A. J., and McDonald, J. C. Dust exposure and mortality in an American chrysotile asbestos friction products plant. Brit. J. Ind. Med. 41: 151–157 (1984).
35. Finkelstein, M. M. Mortality among long-term employees of an Ontario asbestos-cement factory. Brit. J. Ind. Med. 40: 138–144 (1983).
36. Liddell, F. D. K., and Hanley, J. Relations between asbestos exposure and lung cancer SMRs in occupational cohort studies. Brit. J. Ind. Med. 42: 389–396 (1985).
37. Selikoff, I. J., Hammond, E. C., and Seidman, H. Mortality experience of insulation workers in the United States and Canada, 1943–1976. Ann. N.Y. Acad. Sci. 330: 91–116 (1979).
38. McDonald, J. C. Asbestos-related disease: an epidemiological review. In: Biological Effects of Mineral Fibres (J. C. Wagner, Ed.) IARC Scientific Publications, No. 30, Lyon, France, 1980, pp. 587–601.
39. McDonald, J. C. Aspects of the asbestos standard. In: Occupational Lung Disease (J. B. Gee, W. K. L. Morgan and S. M. Brooks, Eds.), Raven Press, New York, 1984, pp. 139–149.
40. Nicholson, W. J. Tumour incidence after asbestos exposure in the USA: cancer risk of the non-occupational population. VDI Ber. 475: 161–176 (1983).
41. Non-Occupational Health Risks of Asbestiform Fibres. NRC Report. National Academy Press, Washington, DC, 1984.
42. Dagbert, M. Etude de corrélation des mesures d'empoussiérage dans l'industrie de l'amiante. Document 5. Québec: Comité d'études sur la salubrité dans l'industrie de l'amiante (R. Beaudry, président).
43. McDonald, J. C., Gibbs, G. W., and Liddell, F. D. K. Chrysotile fibre concentration and lung cancer mortality: a preliminary report. In: Biological Effects of Mineral Fibres (J. C. Wagner, Ed.),

IARC Scientific Publication No. 30, Lyon, France, 1980, pp. 811–814.
44. Enterline, P. E. Extrapolation from occupational studies: a substitute for environmental epidemiology. Environ. Health Perspect. 42: 39–44 (1981).
45. Enterline, P. E. Cancer produced by nonoccupational asbestos exposure in the United States. J. Air Pollut. Control Assoc. 33: 318–322 (1983).
46. McDonald, J. C., and McDonald, A. D. Mesothelioma as an index of asbestos impact. In: Quantification of Occupational Cancer. (Banbury Report No. 9), (R. Peto, and M. Schneiderman, Eds.), Cold Spring Harbor, N.Y. 1981, pp. 73–85.
47. Schneiderman, M. S., Nisbet, I. C. T., and Brett, S. M. Assessment of risks posed by exposure to low levels of asbestos in the general environment. bga-Ber. 4: 1–27 (1981).
48. Peto, J. Dose and time relationships for asbestos-related cancers, and risk assessment in the general population. VDI Ber. 475: 309–312 (1983).
49. Peto, J., Schneiderman, H., and Selikoff, I. J. Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. Brit. J. Cancer 45: 124–135 (1982).
50. Elmes, P. C., and Simpson, M. J. C. The clinical aspects of mesothelioma. Quart. J. Med. [45] 179: 427–449 (1976).
51. Nirminen, M. The epidemiologic relationship between pleural mesothelioma and asbestos exposure. Scand. J. Work Environ. Health 1: 128–137 (1975).
52. Lewinsohn, H. C., Meigs, J. W., Teta, M. J., and Flannery, J. T. The influence of occupational and environmental asbestos exposure on the incidence of malignant mesothelioma in Connecticut. In: Biological Effects of Mineral Fibres (J. C. Wagner, Ed.), IARC Scientific Publications No. 30, Lyons, France, 1980, pp. 655–660.
53. Bruckman, L., Rubino, R. A., and Christine, B. Asbestos and mesothelioma incidence in Connecticut. J. Air Pollut. Control Assoc. 27: 121–126 (1977).
54. Archer, J. E., and Rom, W. N. Trends in mortality of diffuse malignant mesothelioma of pleura. Lancet, ii: 112–113 (July 9, 1983).
55. McDonald, A. D. Mesothelioma registries in identifying asbestos hazards. Ann. N.Y. Acad. Sci. 330: 441–454 (1979).