United States
Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

Research and Development

EPA/600/S8-84/003F Apr. 1991

EPA **Project Summary**

Airborne Asbestos Health Assessment Update

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Data developed since the early 1970s, from large population studies with long follow-up, have added to our knowledge of asbestos-related diseases and strengthened the evidence for associations between asbestos and specific types of health effects. Lung cancer and mesothelioma are the most important asbestos-related causes of death among exposed individuals. Cancer other than lung has also been associated with asbestos exposure. The accumulated data suggest that the excess risk of lung cancer from asbestos exposure is proportional to the cumulative exposure (the duration times the intensity) and the underlying risk in the absence of exposure. The risk of death from mesothelioma is approximately proportional to the cumulative exposure to asbestos and increases sharply with time since onset of exposure.

Animal studies confirm the human epidemiological results and indicate that all major asbestos varieties produce lung cancer and mesothelioma, with only limited differences in carcinogenic potency. Some measurements demonstrate that asbestos exposures exceeding 100 times background occur in non-occupational environments. Currently, the most important of these non-occupational exposures is the release of fibers from asbestos-containing surfacing building materials or from sprayed asbestos fireproofing in high-rise buildings.

Extrapolations of risks of asbestos cancers from occupational circumstances can be made, although numerical estimates in a specific exposure circumstance have a large (approximately tenfold) uncertainty. Because of this uncertainty, calculations of unit risk values for asbestos at low concentrations must be viewed with caution and are subject to the following limitations: 1) variability in the exposure-response relationship at high exposures; 2) uncertainty in extrapolating to exposures 1/100 as much; and 3) uncertainties in conversion of optical fiber counts to electron microscopic fiber counts or mass determinations.

This Project Summary was developed by EPA's Environmental Criteria and Assessment Office, Research Triangle Park, NC, to announce key findings of the research project published in 1986 that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

The principal objective of this document is to provide the U.S. Environmental Protection Agency (EPA) with a sound scientific basis for review and revision, as appropriate, of the national emission standard for asbestos, 40 CFR 61, subpart B, as required by the 1977 Clean Air Act Amendments, Sections 111 and 112. The health effects basis for designating asbestos as a hazardous pollutant and minimizing emissions via the original 1973 National Emissions Standard for Hazardous Air Pollutants was scrutinized, at that time, during two public hearings and a public comment period. Once a pollutant has been

designated as a "hazardous" air pollutant, the burden of proof is placed on proving that designation wrong.

The original health effects basis for designating asbestos as a hazardous air pollutant was qualitative evidence establishing asbestos-associated carcinogenic effects. However, insufficient bases then existed by which to define pertinent quantitative dose-response relationships; i.e., unit risk values could not be credibly estimated. The main focus of the update document is to describe asbestos-related health effects developments since 1972 and to determine if new data warrant the specification of unit risk values for asbestos. The document forms part of the basis to perform a risk assessment.

The National Academy of Sciences (NAS) in 1983 suggested a definition of risk assessment as the use of the factual data base to define the health effects of exposure of individuals or populations to hazardous materials, such as asbestos. Therefore, the update document is mainly concerned with the excess risk of cancer from inhalation of asbestos fibers, with emphasis placed on the literature published after 1972, and on those reports that provide information on the risk from low-level exposures, such as those encountered in the non-occupational environment.

Occupational Exposure

The International Agency for Research on Cancer (IARC) lists asbestos as a group 1 carcinogen, meaning that exposure to asbestos is carcinogenic to humans. EPA's proposed guidelines would categorize asbestos as Group A, human carcinogen.

Diseases considered to be associated with asbestos exposure include asbestosis, mesothelioma, bronchogenic carcinoma, and cancers of the gastrointestinal (GI) tract, including the esophagus, stomach, colon, and rectum. Lung cancer is associated with exposure to four principal commercial varieties of asbestos fiber: amosite, anthophyllite, crocidolite, and chrysotile. Excess risks of bronchogenic carcinoma are documented in mining and milling, manufacturing, and end product use (application of insulation materials). Mesothelioma is a cause of death among factory employees, insulation applicators, and workmen employed in the mining and milling of crocidolite. A much lower risk of death from mesothelioma is observed among chrysotile or amosite mine and mill employees, and no cases are associated with anthophyllite exposure. The IARC Advisory Committee suggests that the risk of death from mesothelioma is greatest with crocidolite, less with amosite, and still less with chrysotile. This suggestion was based on the association of disease with exposures. No unit exposure risk information existed prior to 1972.

Information on exposure-response relationships for lung cancer risk among various exposed groups was scanty. Data from Canadian mine and mill employees clearly indicated an increasing risk with increasing exposure, measured in terms of millions of particles per cubic foot-years (mppcf-y), but data on the risk at minimal exposure were uncertain because the number of expected deaths calculated using adjacent county rates suggested that all exposure categories were at elevated risk. A study of retirees of the largest U.S. asbestos manufacturer showed lung cancer risks ranging from 1.7 times that expected in the lowest exposure category to 5.6 times that expected in the highest. Exposures were expressed in mppcf-y, and information on conversion of mppcf to fibers per milliliter was available only for textile production. Despite the paucity of data, the 1973 report of the Advisory Committee on Asbestos Cancers to the IARC stated, "The evidence . . . suggests that an excess lung carcinoma risk is not detectable when the occupational exposure has been low. These low occupational exposures have almost certainly been much greater than that to the public from general air pollution." Limited data existed on the association of GI cancer with asbestos exposure, but the "excess is relatively small compared with that for bronchial cancer."

The prevalence of asbestosis, particularly as manifested by X-ray abnormalities of the pleura or parenchymal tissue, had been documented more extensively than the risk of the asbestos-related malignancies. In part, this documentation resulted from knowledge of this disease extending back to the turn of the century, whereas the malignant potential of asbestos was not suggested until 1935 and not widely appreciated until the 1940s. Asbestosis had been documented in a wide variety of work circumstances and associated with all commercial types of asbestos fibers. Among some heavily exposed groups, 50 to 80 percent of individuals employed for 20 or more years were found to have abnormal X-rays characteristic of asbestos exposure. A lower percentage of abnormal X-rays was present in lesser exposed groups.

Company data supplied to the British Occupational Hygiene Society (BOHS) on X-ray and clinical abnormalities among 290 employees of a large textile production facility in Great Britain were analyzed in terms of a fiber exposure-response relationship. The results were utilized in establishing the 1969 British regulation on asbestos. These data suggested that the risk of developing the earliest signs of asbestosis was less than 1 percent for accumulated fiber exposure of 100 fiber-years/ml (f-y/ml), e.g., 2 fibers/milliliter (f/ml) for 50 years. However, shortly after the establishment of the British standard, additional data from the same factory population suggested a much greater prevalence of X-ray abnormalities than was believed to exist at the time the British standard was set in 1972. These data resulted from use of the new International Labour Office (ILO) standard classification of X-rays and the longer time from onset of employment. Of the 290 employees whose clinical data were reviewed by the BOHS, only 13 had been employed for 30 or more years; 172 had less than 20 years of employment. The progression of asbestosis depends on both cumulative exposure and time from exposure; therefore, analysis in terms of only one variable can be misleading.

Environmental Exposure

Several research groups had shown that asbestos disease risk could develop from other than direct occupational exposures. Various researchers in 1960 have shown that a mesothelioma risk in environmental circumstances existed in the mining areas of the Northwest Cape Province of South Africa. Of 33 mesotheliomas reported over a 5-year period, roughly half were from occupational exposure. However, all but one of the remainder resulted from exposure occasioned by living or working in the area of the mining activity. Another study in 1965 that showed an extra-occupational risk investigated the occupational and residential background of 76 individuals deceased of mesothelioma in a London hospital. Forty-five of the decedents had been employed in an asbestos industry; of the remaining 31, 9 lived with someone employed in asbestos work and 11 were individuals who resided within half a mile of an asbestos factory. In 1973, investigators identified environmental asbestos exposure in 38 mesothelioma cases without occupational exposure who resided near an asbestos factory, further defining residential risk. A final study, which is particularly important because of the size of the population implied to be at risk of asbestos disease from indirect occupational exposure in the shipbuilding industry, was conducted in 1968. It described the presence of asbestosis in 13 individuals and mesothelioma in 5 others who were em-

ployed in a shipyard but were not members of trades that regularly used asbestos. Rather, they were exposed to the dust created by other employees placing or removing insulation.

Evidence of ubiquitous general population exposure and environmental contamination from the spraying of asbestos on the steel-work of high-rise buildings was established by 1972. Asbestos was commonly found at concentrations of nanograms per cubic meter (ng/m^3) in virtually all United States cities, and at concentrations of micrograms per liter (μg/l) in river systems of the United States. Concentrations of hundreds of nanograms per cubic meter were documented at distances up to one-quarter of a mile from fireproofing sites. Mesothelioma was acknowledged by the Advisory Committee to be associated with environmental exposures, but it suggested that "the evidence relates to conditions many years ago .... There is no evidence of a risk to the general public at present."

Analytical Methodology

During the late 1960s and early 1970s, significantly improved methods were developed for assessing asbestos disease and quantifying asbestos in the environment. In 1971, a standardized methodology was established. It provided a uniform criterion for assessing the prevalence of asbestos-related X-ray abnormalities.

Significant advances were also achieved in the quantification of asbestos aerosols. In the late 1960s, the membrane filter technique was developed for the measurement of asbestos fibers in workplace aerosols. While this procedure has some limitations, it did establish a standardized method, using simple instrumentation, that was far superior to any that existed previously. This method subsequently allowed epidemiological studies to be done that based exposure estimates on a standardized criterion. Experimental techniques in the quantification of asbestos at concentrations of tenths of ng/m^3 of air and tenths of μg/l of water were also developed, extending the sensitivity of exposure estimates approximately three orders of magnitude below those of occupational aerosols and allowing assessment of general population exposures. Finally, techniques for the analysis of asbestos in lung and other body tissues were developed. Tissue digestion techniques and the use of electron microscopy to analyze fibers contained in the digest and in thin sections of lung tissue showed that asbestos fibers were commonly present in the lung tissue of general population residents as well as individuals exposed in occupational circumstances.

Experimental Studies

Experimental animal studies using asbestos fibers confirmed the risks of lung cancer and mesothelioma from amosite, crocidolite, and chrysotile. In each case, the establishment of a risk in animals followed the association of the malignancy with human exposure. For example, a causal relationship between lung cancer and asbestos exposure in humans was suggested in 1935 and confirmed in the late 1940s but was not described in the open literature in animals until 1967. Mesothelioma, reported in an asbestos worker in 1953, was produced in animal experimentation in 1965. Other animal experimentation showed that combinations of asbestos and other carcinogenic materials produced an enhanced risk of asbestos cancer. Asbestos exposure combined with exposure to benz(a)pyrene was demonstrably more carcinogenic than exposure to either agent alone. Additionally, organic and metal compounds associated with asbestos fibers were ruled out as important factors in the carcinogenicity of fibers. Lastly, in 1973 experimentation involving the application of fibers onto the pleura of animals indicated that the important factor in the carcinogenicity was the length and width of the fibers rather than their chemical properties. The greatest carcinogenicity was related to fibers that were less than 2.5 μm in diameter and longer than 10 μm.

Current Asbestos Standards

The current Occupational Safety and Health Administration (OSHA) standards for an 8-hour time-weighted average (TWA) occupational exposure to asbestos is 2 fibers longer than 5 μm in length per milliliter of air (2 f/ml or 2,000,000 f/m^3). Peak exposures of up to 10 f/ml are permitted for no more than 10 min. This standard has been in effect since July 1, 1976, when it replaced an earlier one of 5 f/ml TWA. In Great Britain, a value of 0.5 f/ml is now the accepted level for chrysotile. This standard has evolved from recommendations made in 1979 by the Advisory Committee on Asbestos, which also recommended a TWA of 0.5 f/ml for amosite and 0.2 f/ml for crocidolite. From 1969 to 1983, 2 f/ml TWA was the standard for chrysotile. This earlier British standard served as a guide for the 1972 OSHA standard.

The 1969 British standard was developed specifically to prevent asbestosis among working populations; data that would allow a determination of a standard for cancer were felt to be lacking. Among occupational groups, cancer is the primary cause of excess death among workers. Three-fourths or more of asbestos-related deaths are from malignancy. This fact led OSHA to propose a lowered TWA standard to 0.5 f/ml (500,000 f/m^3) in October 1975. The National Institute for Occupational Safety and Health (NIOSH) anticipated hearings on a new standard and proposed a value of 0.1 f/ml in 1976 in an update of their 1972 criteria document. In the discussion of the NIOSH proposal, it was stated that the value was selected on the basis of the practical limitations of analytical techniques using optical microscopy, and that 0.1 f/ml may not necessarily protect against cancer. The preamble to the OSHA proposal acknowledges that no information exists by which to define a threshold for asbestos carcinogenesis. The OSHA proposal has been withdrawn, and a new proposal was submitted on April 10, 1984. In it, OSHA proposed a TWA standard of either 0.2 or 0.5 f/ml depending upon information to be obtained in hearings (held during the summer of 1984). NIOSH reaffirmed its position on a 0.1 f/ml TWA standard.

The existing federal national emission standards for asbestos are published in Part 61, Title 40, Code of Federal Regulations. In summary, these apply to milling, manufacturing, and fabrication sources, and to demolition, renovation, and waste disposal, and include other limitations. In general, the standards allow compliance alternatives, either (1) no visible emissions, or (2) employment of specified control techniques. The standards do not include any mass or fiber count emission limitations. However, some local governmental agencies have numerical standards (e.g., New York: 27 ng/m^3), but these have little regulatory relevance.

Other Reviews of Asbestos Health Effects

Recently, several government agencies in different countries reviewed asbestos health effects. The most important of the reviews outside the United States are those of the Advisory Committee on Asbestos of the British Health and Safety Commission and the report of the Ontario Royal Commission. Each of these major reports was the result of lengthy testimony by many scientists and deliberations by selected committees over a long period of time. In the United States, the NAS has reviewed the non-occupational health risk of asbestiform fibers, and a Chronic Hazard Advisory Panel convened by the U.S.

Consumer Product Safety Commission reported on the hazards of asbestos.

There are large areas of agreement and some of disagreement between these reviews and those of the full document with regard to the spectrum of asbestos-related disease, the models describing asbestos-related lung cancer and mesothelioma, unit exposure risks in occupational circumstances, possible differences in carcinogenic potency of different asbestos minerals, and risk estimates at low, non-occupational exposures.

Summary

Lung cancer and mesothelioma are the most important asbestos-related causes of death among exposed individuals. Gastrointestinal cancers are also increased in most studies of occupationally exposed workers. Cancer at other sites (larynx, kidney, ovary) has also been shown to be associated with asbestos exposure in some studies, but the degree of excess risk and the strength of the association are less for these and the gastrointestinal cancers than for lung cancer or mesothelioma. The IARC lists asbestos as a group 1 carcinogen, meaning that exposure to asbestos is carcinogenic to humans. EPA's proposed guidelines categorize asbestos as Group A, human carcinogen.

Data from a study of U.S. insulation workers allow models to be developed for the time and age dependence of lung cancer and mesothelioma risk. Thirteen other studies provide exposure-response information. The accumulated data suggest that the excess risk of death from lung cancer from asbestos exposure is proportional to the cumulative exposure (the duration times the intensity) and the underlying risk in the absence of exposure. The time course of lung cancer is determined primarily by the time course of the underlying risk. However, the risk of death from mesothelioma increases very rapidly after the onset of exposure and is independent of age and cigarette smoking. As with lung cancer, the risk appears to be proportional to the cumulative exposure to asbestos in a given period. The dose and time relationships for other asbestos cancers are uncertain.

Values characterizing lung cancer risk obtained from different studies vary widely. Some of the variability can be attributed to specific processes. Chrysotile mining and milling, and perhaps friction product manufacture, appear to have lower unit exposure risks than chrysotile textile production and other uses of asbestos. Other variability can be associated with the uncertainties of small numbers in epidemiological studies and improper estimates of exposures in earlier years. Some differences between studies may be related to differences in fiber type, but these are much less than those associated with specific processes.

Four studies provide similar quantitative data on the unit exposure risk for mesothelioma and six additional studies provide corroborative, but less accurate, quantitative data. The same factors that affect the lung cancer unit exposure risk appear to affect that of mesothelioma, as the ratio of a measure of mesothelioma risk to excess lung cancer risk is roughly constant across the ten studies. However, in other studies the ratio of number of mesothelioma deaths to lung cancer deaths among groups exposed to substantial quantities of crocidolite is two to four times higher than among groups exposed predominantly to other fibers. Further, the risk of peritoneal mesothelioma appears to be less from exposure to chrysotile than to either crocidolite or amosite, but this suggestion is tempered by uncertainties associated with the greater possibility of misdiagnosis of the disease.

Animal studies confirm the human epidemiological results. All major asbestos varieties produce lung cancer and mesothelioma with only limited differences in carcinogenic potency. Implantation and injection studies show that fiber dimensionality, not chemistry, is the most important factor in fiber-induced carcinogenicity. Long (>4 μm) and thin (<1 μm) fibers are the most carcinogenic at a cancer-inducible site. However, the size dependence of the deposition and migration of fibers also affects their carcinogenic action in humans.

Measurements demonstrate that asbestos exposures exceeding 100 times the background occur to individuals in some non-occupational settings. Currently, the most important of these non-occupational exposures is from the release of fibers from asbestos-containing surfacing building materials, or from sprayed asbestos-containing fireproofing in high-rise buildings. A high potential exists for future exposure from maintenance, repair, and removal of these materials.

Extrapolations of risks of asbestos cancers from occupational circumstances can be made, although numerical estimates in a specific exposure circumstance have a large (approximately tenfold) uncertainty. Because of this uncertainty, calculations of unit risk values for asbestos at the low concentrations measured in the environment must be viewed with caution. The best estimate of risk to the United States general population for a lifetime continuous exposure to 0.0001 f/ml is 2.8 mesothelioma deaths and 0.5 excess lung cancer deaths per 100,000 females. Corresponding numbers for males are 1.9 mesothelioma deaths and 1.7 excess lung cancer deaths per 100,000 individuals. Excess GI cancer mortality is approximately 10-30 percent that of excess lung cancer mortality. These risks are subjective, to some extent, and are also subject to variability in the exposure-response relationship at high exposures, uncertainty in extrapolating to exposures 1/100 as much, and uncertainties in conversion of optical fiber counts to electron microscopic fiber counts or mass determinations.

Recently, several government agencies in different countries reviewed asbestos health effects. Areas of agreement and disagreement between various reviews are presented in the full document. A comparison of the different risk estimates is also provided.

☆U. S. GOVERNMENT PRINTING OFFICE: 1991/548-028/20206

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The complete report, entitled "Airborne Asbestos Health Assessment Update," (Order No. PB86-242864/AS; Cost: $31.00, subject to change) will be available only from:
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