National Institute for Occupational Safety and Health
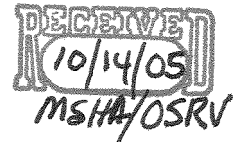
NIOSH

Comments to DOL

Comments of the
National Institute for Occupational Safety and Health
on the
Mine Safety and Health Administration
Proposed Rule on Asbestos Exposure Limit

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Department of Health and Human Services
Public Health Service
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

October 13, 2005

AB24-Comm-103

The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Mine Safety and Health Administration (MSHA) proposed rule *Asbestos Exposure Limit* published in the *Federal Register* (FR) on July 29, 2005 [70 FR 43950]. NIOSH concurs with the proposal to reduce the MSHA permissible exposure limit (PEL), making the regulation consistent with the Occupational Safety and Health Administration (OSHA) PEL. NIOSH also concurs with the proposal to incorporate reference to Appendix A of OSHA's asbestos standard [29 CFR 1910.1001], specifying a phase-contrast microscopy method (PCM) for analyzing airborne asbestos samples.

Below is a comment on the regulatory definition of asbestos followed by specific technical comments on the FR notice.

A. Regulatory Definition of Asbestos

MSHA notes on page 43972 that *"Substantive changes to the definition of asbestos are beyond the scope of this proposed rule."* MSHA has thus retained the current definition of asbestos as the six asbestos minerals, chrysotile, amosite (cummingtonite-grunerite asbestos), crocidolite, anthophylite asbestos, tremolite asbestos and actinolite asbestos. NIOSH remains concerned that the regulatory definition of asbestos should include asbestiform mineral fibers such as winchite and richterite, which were of major importance as contaminants in the Libby, MT vermiculite [NIOSH 2001; 2002]. NIOSH recognizes that the scope of this issue has implications that encompass numerous federal agencies and should be addressed in a coordinated manner.

MSHA notes on page 43953, "*Although we have received comments regarding the hazards associated with cleavage fragments, we do not intend to modify our existing definition of asbestos with this rulemaking.*" NIOSH agrees with MSHA's decision not to modify its definition of asbestos within this particular rulemaking. NIOSH is presently re-evaluating its definition of asbestos and nonasbestiform minerals, and will work with other agencies to assure consistency to the extent possible.

B. Specific Technical Comments

Page 43952, B. Where Asbestos is Found at Mining Operations. *"In some cases, visual inspection can detect the presence of asbestos."*

This statement may create the impression that confirmation by a trained analyst is not necessary. Knowledge about the geology of the mine site is useful for determining the possible presence of asbestos. If the mineralogy of the mine site indicates the potential for asbestos, then a more comprehensive assessment (e.g., bulk sample analysis, settled dust sample) might be warranted to assess whether workers may be at risk of exposure. As noted on page 43977, the collection and analysis of bulk and settled dust samples can be useful in

ascertaining the presence of asbestos. However, the collection of airborne samples is the only reliable means of determining worker exposure to asbestos.

Page 43957, A. Summary of Asbestos Health Hazards. *"Asbestos-related diseases typically have long latency periods commonly not producing symptoms for 20 to 30 years following initial exposure."*

Acute pleuritis can occur relatively early following exposure [Rudd R 2002]. NIOSH suggests the following revision: *"Most asbestos-related diseases typically have long latency periods, commonly not producing symptoms for 20 to 30 years following initial exposure."*

Page 43958, B.3. Fiber Characteristics. *"Baron (2001) reviewed techniques for the measurement of fibers and stated, '...fiber dose, fiber dimension, and fiber durability are the three primary factors in determining fiber [asbestos] toxicity..."*

The cited sentence from Baron [2001] refers to mechanisms for the toxicity of fibers in general, not just for asbestos fibers as implied. The word "asbestos" added to the quotation should be removed.

Page 43959, C.1. Lung Cancer. *"NIOSH (May 2003) identified over 10,000 lung cancer deaths in the United States during 1999 based on only 20 Census Industry Codes (CIC). This sum was computed from 'selected states,' not the entire United States. NIOSH (May 2003) also identified 300 lung cancer deaths among coal miners from 15 selected states."*

As a point of clarification, NIOSH identified many additional lung cancer deaths among other CICs not listed in the May 2003 NIOSH reference; their associated proportionate mortality rates did not meet the criteria for inclusion in the tables. The last sentence appears to be erroneous: there were 19 states for which data were obtained by NIOSH to generate a finding of 327 lung cancer deaths in 1999 where the decedent's industry was identified as coal mining. [See Table 13-1 in the May 2003 NIOSH reference and the list of states for the year 1999 in Appendix E of that same reference.]

NIOSH's National Occupational Respiratory Mortality System (NORMS) provides online interactive access to national mortality data based on information from death certificates (see http://webappa.cdc.gov/ords/norms.html). NORMS output indicates that from 1985 to 1999, there were a total of more than 2,300,000 lung cancer deaths among U.S. residents age 15 and older. For a limited subset of these deaths (from 26 states), data on decedents' usual industry is available for analysis. Analysis of this subset reveals 9,798 lung cancer deaths among decedents whose usual industry was reported as mining, out of about 500,000 decedents with reported usual industry (i.e., about 2%).

Page 43959, C.2. Mesotheliomas. *"NIOSH found that most mesothelioma deaths were included with the categories of 'all other industries' (56 percent) or 'all other occupations' (57 percent).*

The 56% and 57% figures are taken from Tables 7-5 and 7-6 in the NIOSH [2003] reference, which lists the top ten industries/occupations in terms of frequency of associated mesothelioma deaths. The "all other" categories represent the residual deaths with designated industries and occupations that were not the ten listed industry/occupation categories. Without specifying the industries and occupations that are in the top ten, the figures are not useful. It would be helpful also to specify the limited nature of the subset of data analyzed to produce these figures; as stated in the NIOSH reference, the data is limited to selected states.

"For those death certificates that included a Census Industry Code (CIC), the most frequently recorded was 'construction.'"

It is inaccurate to state that death certificates have a CIC. Death certificates have only a literal description of the decedent's usual industry. Codes for the literal description are included in electronic data mortality files. Also, this sentence doesn't seem useful because it relates to the construction industry.

It may be more informative to replace the two sentences noted in this section with the following: "NIOSH's National Occupational Respiratory Mortality System (NORMS) provides online interactive access to national mortality data based on information from death certificates (see http://webappa.cdc.gov/ords/norms.html). NORMS output indicates that, in 1999, there were a total of 2,485 mesothelioma deaths among U.S. residents, age 15 and older. For a limited subset of these deaths (from 19 U.S. states), data on decedents' usual industry is available for analysis. Analysis of this subset indicates that there were 3 mesothelioma deaths in 1999 among decedents whose usual industry was reported as mining, out of 480 mesothelioma decedents with reported usual industry (i.e., about 0.6%)."

Page 43959, C3. Asbestosis. *"Steenland et al. (2003) estimated that there were about 400 deaths from asbestosis in 1997, and that 100% of these asbestosis-deaths were due to occupational exposure."*

NIOSH suggests the following revision: "Steenland et al. estimated that, based on an analysis of underlying cause of death, there were about 400 deaths from asbestosis in 1997, and assumed that 100 percent..." The clarification that the Steenland et al. [2003] paper was based only on underlying cause makes the 400 deaths comparable to the data given in the preceding statement in the preamble. Steenland et al. [2003] assumed that all asbestosis deaths were occupational; they did not estimate the 100% attributability.

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Page 43960, C.3. Asbestosis, Last paragraph. *"Most asbestosis deaths were classified under "all other industries" (45 percent) and "all other occupations" (57%)."*

The 45% and 57% figures are taken from Tables 1-6 and 1-7 in the 2003 NIOSH report, which lists the top ten industries/occupations in terms of frequency of associated asbestosis deaths. The "all other" categories represent the residual deaths with designated industries and occupations that were not the ten listed industry/occupation categories. Without specifying the industries and occupations that are in the top ten, the figures are not useful. It would be helpful also to specify the limited nature of the subset of data analyzed to produce these figures: as stated in the NIOSH reference, the data is limited to selected states.

"The death certificates for most individuals who died from asbestosis lacked the Census Industry Code (CIC) and the Census Occupation Code (COC)...For those death certificates that included a CIC and a COC, the most frequently recorded industry and occupation were "construction" (CIC=060) and "plumbers, pipefitters, and steamfitters" (COC=585), respectively."

It is inaccurate to state that death certificates have a CIC or COC. Death certificates have only a literal description of the decedent's usual industry. Codes for the literal description are included in electronic data mortality files. Also, this information doesn't seem useful because it does not relate to the mining industry.

It may be more informative to replace the three sentences noted in this section with the following: "NIOSH's National Occupational Respiratory Mortality System (NORMS) provides online interactive access to national mortality data based on information from death certificates (at http://webappa.cdc.gov/ords/norms.html). NORMS output indicates that from 1985-1999, there were a total of 14,507 asbestosis deaths among U.S. residents age 15 and older. For a limited subset of these deaths (from 26 states), data on decedents' usual industry is available for analysis. Analysis of this subset reveals 28 asbestosis deaths among decedents whose usual industry was reported as mining, out of 3,445 asbestosis decedents with reported usual industry (i.e., about 0.8%)."

Page 43960, C.5. Reversible Airways Obstruction (RAO). This section relates to fixed (irreversible) obstruction as much as reversible obstruction. NIOSH suggests deleting "Reversible" from the heading.

Page 43960, C.6. Other Nonmalignant Pleural Disease and Pleural Plaques. It would be useful to delete "and Pleural Plaques" from the heading because "pleural plaques" are a form of "nonmalignant pleural disease." Inserting the word "diffuse" before "pleural thickening" in the text in this section would more clearly distinguish "diffuse pleural thickening" from (localized) "pleural plaques."

NIOSH also recommends that MSHA mention in this section that acute pleuritis is known to be associated with asbestos exposures [Rudd R 2002].

Page 43960, C.7. Asbestos Bodies. "These collections of coated fibers, found in sputum or broncho-alveolar lavage (BAL) fluid, are called asbestos bodies or ferruginous bodies. Like pleural thickening and pleural plaques, these bodies indicate prior asbestos exposure."

It is not technically accurate to refer to asbestos bodies as "collections" of coated fibers. Also, not all ferruginous bodies are asbestos bodies, as implied in the above language. Finally, asbestos bodies can also be found in lung tissue, not just in sputum or BAL fluid [Craighead et al. 1982]. NIOSH recommends revising these sentences as follows: "These coated fibers, found in sputum or broncho-alveolar lavage (BAL) fluid, are called ferruginous bodies, or more specifically, asbestos bodies. When found in sputum or BAL fluid, these bodies provide evidence of prior asbestos exposure, and their abundant presence in lung tissue is one of the criteria that serve to support a pathologic diagnosis of asbestosis."

Page 43961. A. Determining Asbestos Exposures in Mining. "Several factors complicate the evaluation of personal exposure levels in mining. Non-asbestos particles collected on the filter can hide the asbestos fibers (overloading) and, as discussed earlier (see section II.C.2), mining samples may also contain intermediate fibers that are difficult to classify."

NIOSH method 7400 and OSHA method ID-160 require all fibers to be counted; when performing PCM analysis, fibers are not classified. NIOSH suggests deleting reference to classifying fibers in the above paragraph.

Page 43962. 2. Methods of Reducing or Avoiding Miners' Exposures to Introduced (Commercial) Asbestos. When intact asbestos-containing building materials (ACBM) are left intact, documenting, labeling, and monitoring the ACBM may limit the likelihood of future worker exposure if that ACBM becomes friable or is disturbed.

Page 43963. 2. Summary of MSHA's Asbestos Sampling and Analysis Results. "Available data from death certificates in 24 states confirm that there is asbestos-related mortality among miners."

The footnote for this sentence cites Appendix E of the NIOSH Work-Related Lung Disease (WoRLD) Surveillance Report [2003]. However, Appendix E only lists the 26 states for which NIOSH obtained industry and occupation information on deaths for analyses presented in the 2003 WoRLD Surveillance Report. Appendix E provides no information on asbestos-related deaths among miners.

NIOSH suggests replacing the sentence with the following: "Available death certificate data confirms the occurrence of asbestos-related mortality among decedents whose usual industry was reported as mining (National Occupational Respiratory Mortality System, http://webappa.cdc.gov/ords/norms.html)."

Page 43970, Table VI-5--Selected Studies Involving Miners Exposed to Asbestos. The major findings for Amandus et al., 1987, Part I, and Amandus et al., 1987, Part III, are reversed. Part I is the exposure document, and Part III is the radiographic findings document.

Page 43972, VII. Section-by-Section Discussion of Proposed Rule. NIOSH commented that ... should be counted as asbestos if they meet the counting requirements for a fiber (3:1 aspect ratio and >5 μm in length).

This statement should be corrected to reflect the counting requirements for a fiber recommended by NIOSH: an aspect ratio of 3:1 <u>or greater</u> and >5 μm in length [NIOSH 1980].

Page 43980, VIII.1. c. Benefit of the Proposed 0.1 f/cc 8-hour TWA, Full-Shift Exposure Limit. "We estimate that there would be from 0.5 to 13.1 lung cancer deaths avoided, 0.2 to 4.4 mesothelioma deaths avoided, and 0.1 to 1.3 gastrointestinal cancer deaths avoided....we expect a reduction of between 1 and 19 deaths avoided due to lowering the 8-hour TWA PEL to 0.1 f/cc."

This paragraph gives estimated numbers of deaths avoided, but does not indicate over what period of time these numbers of deaths would be avoided. It would be useful if the time period is specified.

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WORKPLACE EXPOSURE TO ASBESTOS
Review and Recommendations

DHHS (NIOSH) Publication No. 81-103

NIOSH-OSHA
Asbestos Work Group
April 1980

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

U.S. DEPARTMENT OF LABOR
Occupational Safety and Health Administration

November 1980

AB24-COmm-103-A

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MEMORANDUM FOR: *Dr. Eula Bingham*
Assistant Secretary for
Occupational Safety and Health

Dr. Anthony Robbins
Director, National Institute for
Occupational Safety and Health

FROM: *Asbestos Work Group*

SUBJECT: *The Updated Scientific*
Information on Asbestos and
Recommended Occupational
Standard for Asbestos Exposure

    In the fall of 1979, a NIOSH/OSHA committee was formed at the direction of Dr. Eula Bingham, Assistant Secretary of Labor for Occupational Safety and Health, and Dr. Anthony Robbins, Director of the National Institute for Occupational Safety and Health (NIOSH), to review the scientific information concerning asbestos-related disease and assess the adequacy of the current OSHA occupational health standard of 2,000,000 fibers per cubic meter greater than 5 μm in length (2Mf/m^3). Since the 1972 promulgation of this 2,000,000 f/m^3 standard, OSHA, in 1975, proposed lowering the standard to 500,000 f/m^3; NIOSH, in 1976, recommended lowering the standard to 100,000 f/m^3; and the British Advisory Committee on Asbestos, in 1979, recommended lowering its occupational exposure standards. The NIOSH/OSHA committee has reviewed the most recent scientific information, including documents concerning the above developments and the 1977 International Agency for Research on Cancer (IARC) review of the carcinogenicity hazards of asbestos, and presents the following major conclusions and recommendations. A detailed updating of significant scientific literature since the 1976 NIOSH Criteria Document and the 1977 IARC Monograph is attached.

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1. *Definition of Asbestos*. Having considered the many factors involved in specifying which substances should be regulated as asbestos, the committee recommends the following definition:

> Asbestos is defined to be chrysotile, crocidolite, and fibrous cummingtonite-grunerite including amosite, fibrous tremolite, fibrous actinolite, and fibrous anthophyllite. The fibrosity of the above minerals is ascertained on a microscopic level with fibers defined to be particles with an aspect ratio of 3 to 1 or larger.

2. *Sampling and Analysis of Airborne Asbestos*. The committee concludes that the membrane filter-phase contrast microscopy method represents the only technique available that can reasonably be used for routine monitoring of occupational exposures and sampling for compliance purposes. However, the committee recognizes the lack of specificity of this method for fiber identification, and recommends the use of supplementary methods such as electron microscopy for fiber identification in cases of mixed fiber exposures. In recommending the primary use of light microscopy, the committee also wants to stress the inability of this method to detect short asbestos fibers to which workers are exposed. The toxicity of asbestos fibers shorter than the 5-micrometer detection limit of light microscopy cannot be dismissed on the basis of current scientific information.

3. *Biologic Effects of Exposure to Asbestos*. Animal studies demonstrate that all commercial forms and several noncommercial forms of asbestos produce pulmonary fibrosis, mesothelioma, and lung neoplasms. Chrysotile is as likely as crocidolite and other amphiboles to induce mesotheliomas after intrapleural injection, and also as likely to induce lung neoplasms after inhalation exposures.

Human occupational exposures to all commercial asbestos fiber types, both individually and in various combinations, have been associated with high rates of asbestosis, lung cancer, and mesothelioma. While significant excesses of cancer of several other sites have been observed in exposed workers, presently available information is insufficient to determine the role of specific fiber types.

On the basis of available information, the committee concludes that there is no scientific basis for differentiating between asbestos fiber types for regulatory purposes. Accordingly, the committee recommends that a single occupational health standard be established and applied to all asbestos fiber types.

Available data show that the lower the exposure, the lower the risk of developing asbestosis and cancer. Excessive cancer risks, however, have been demonstrated at all fiber concentrations studied to date. Evaluation of all available human data provides no evidence for a threshold or for a "safe" level of asbestos exposure. Accordingly, the committee recommends that, to the extent uses of asbestos cannot be eliminated or less toxic materials substituted for asbestos, worker exposures to asbestos must be controlled to the maximum extent possible.

4. Inadequacy of Current 2,000,000-Fiber Occupational Standard. The committee concluded that a variety of factors demonstrates that the current 2,000,000-fiber standard is grossly inadequate to protect American workers from asbestos-related disease. First, the 2,000,000-fiber standard was designed in 1969 by the British Occupational Hygiene Society (BOHS) for the limited purpose of minimizing asbestosis. Disease prevalence data from the BOHS study population collected subsequent to 1969 strongly suggest that this standard is insufficient to prevent a large incidence of asbestosis. Second, all levels of asbestos exposure studied to date have demonstrated asbestos-related disease, and a linear relationship appears to best describe the shape of the dose-response curve. These considerations led the committee to conclude that there is no level of exposure below which clinical effects do not occur. Third, the absence of a threshold is further indicated by the dramatic evidence of asbestos-related disease in members of asbestos-worker households and in persons living near asbestos-contaminated areas. These household and community contacts involved low level and/or intermittent casual exposure to asbestos. Studies of duration of exposure suggest that even at very short exposure periods (1 day to 3 months) significant disease can occur.

Although various models can be and have been fashioned to postulate possible dose-response relationships involving asbestos, the committee believes that the limited current data preclude the creation of any one empirical curve to describe *the exact* dose-response relationship. Over the last three decades, measurement techniques for asbestos have changed in several crucial respects, and there have been no suitable methods available to date to compare the results of prior techniques to current methods.

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In addition, no adequate epidemiological information is available on the disease experience of workers exposed below the current standard and followed for a sufficient period to identify long latent effects. Consequently, the committee cannot present a precise dose-response relationship for the variety of asbestos-related diseases. However, the committee firmly believes that compelling evidence demonstrates that prevention of asbestos-related diseases requires that an occupational standard minimize all asbestos exposures, and definitely be set far below the current 2,000,000-fiber standard.

5. *Recommended Occupational Standard for Asbestos Exposure.* Given the inadequacy of the current 2,000,000-fiber standard, the committee urges that a new occupational standard be promulgated which is designed to eliminate non-essential asbestos exposures, and which requires the substitution of less hazardous and suitable alternatives where they exist. Where asbestos exposures cannot be eliminated, they must be controlled to the lowest level possible. A significant consideration in establishing a permissible exposure limit should be the lowest level of exposure detectable using currently available analytical techniques. At present this level would be 100,000 fibers greater than 5 μm in length per cubic meter averaged over an 8-hour workday. Regardless of the choice of a permissible exposure limit, the best engineering controls and work practices should be instituted, and protective clothing and hygiene facilities should be provided and their use required of all workers exposed to asbestos. Respirators are not a suitable substitute for these control measures. The committee also reiterates its judgment that even where exposure is controlled to levels below 100,000 fibers, there is no scientific basis for concluding that all asbestos-related cancers would be prevented.

6. *Medical Surveillance Program.* Appropriate medical surveillance is crucial to detect and minimize the progression of some asbestos-related diseases. Considerable emphasis should be placed on baseline medical examinations for all workers potentially exposed or who have been exposed to asbestos at any level. These examinations should include the following: (1) a 14" x 17" postero-anterior chest X-ray; (2) spirometry including forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1); (3) a physical examination of the chest including auscultation for the presence or absence of rales, rhonchi,

and wheezing; (4) an assessment of the presence or absence of finger clubbing; and (5) a history of respiratory symptoms and conditions including tobacco smoking.

An occupational history should include a history of exposure to asbestos and exposure to other substances of real or potential medical significance. Performance criteria for these procedures, including the periodicity of subsequent medical surveillance, should be developed by NIOSH in consultation with OSHA and professional societies and organizations concerned with the diagnosis and prevention of respiratory diseases. The committee does not recommend comprehensive annual medical examinations as presently required. Sputum cytology should be evaluated in the development of an improved medical surveillance program. The committee believes that sputum cytology may prove to be a valuable supplement to X-ray evaluation.

It is also crucial that all required medical surveillance be promptly evaluated and the results reported to the employee. Furthermore, the standard should provide for periodic reporting of aggregate medical information concerning an employer's entire workforce. Results at a minimum should be displayed in a non-identifiable, aggregate format so that the employer, employees, and OSHA can see the prevalence of abnormalities possibly associated with asbestos-related disease, and also see how this prevalence has changed over time.

The committee recognizes that OSHA's recent lead standard contains a multiple physician review mechanism whereby workers can get independent medical evaluations by physicians of their choice. The lead standard also contains a medical removal protection program whereby workers can obtain special health protection where necessary, accompanied by appropriate economic protection. The committee feels that these programs are relevant to asbestos workers and should be considered as part of a new occupational asbestos standard.

Medical records generated due to the standard's medical surveillance program should be maintained for at least 40 years or for 20 years after termination of employment, whichever is longer.

7. *Other Recommendations.* The committee further recommends the following: (1) Due to the widespread current and past uses of asbestos products in the maritime and construction in-

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dustries, it is vital that any new asbestos standard address these industry sectors as well as other workplaces with employees exposed to asbestos. Regulation of these industries should be structured around the principle that where work must be done using asbestos, only those employees needed to do this work should be present, and only for the minimum period of time needed to complete this work.

(2) Due to the sampling and analytical difficulties concerning asbestos, manufacturers of asbestos-containing products such as construction materials should perform detailed monitoring of exposures which could result from all foreseeable uses of their products, including misuse. This monitoring should include electron microscopy to identify fiber type mix and exposures to fibers less than 5 μm in length. This monitoring data should accompany these products downstream so the users not only know that asbestos exposures may occur, but also know the nature of potential exposures. This monitoring data could, if appropriate, avoid the need for small employers who use asbestos-containing products to have to conduct monitoring on their own.

(3) Due to the fact that other agencies regulate occupational exposures to asbestos (such as the Mine Safety and Health Administration), these agencies should be urged to participate in the development of a new standard and adopt this new standard.

(4) Because cigarette smoking enhances the carcinogenic effect of asbestos exposure on the lung, particular emphasis should be placed on this in any educational program developed under a new standard.

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Richard A. Lemen, M.S.
  Chairman of the OSHA/
    NIOSH Asbestos Work
      Group
  Assistant Chief
  Industry Wide Studies
    Branch
  NIOSH

J. William Lloyd, Sc. D.
  Senior Epidemiologist
  OSHA

David H. Groth, M.D.
  Chief
  Pathology Section
  Division of Biological
    and Behavioral Sciences
  NIOSH

Han K. Kang, Dr. P.H.
  Health Scientist
  OSHA

John M. Dement, M.S.
  Deputy Director
  Division of Respiratory
    Disease Studies, NIOSH

Robert L. Jennings, Jr., J.D.
  Special Assistant to the
    Assistant Secretary
  OSHA

Joseph K. Wagoner, S. D. Hyg.
  Senior Epidemiologist
  NIOSH

I. ASBESTOS NOMENCLATURE/DEFINITIONS.

Review

There is considerable controversy as to which mineral part-
icles should be considered "asbestos" insofar as demonstrated
health effects are concerned (Campbell et al., 1977; Ampian,
1978; Zoltai, 1978; Langer, 1979). Until recently, most environ-
mental and epidemiological studies concerning mineral fibers
were focused on occupational cohorts exposed to asbestos fibers
from commercial deposits. However, there is currently much
interest in exposures to other minerals such as submicroscopic
amphibole fibers and cleavage fragments and related health
effects. Mineralogists have voiced concern that mineralogical
terms have been used improperly, potentially classifying many
non-asbestos materials as asbestos (Ampian, 1978; Campbell et
al., 1977; Zoltai, 1978).

An important problem which exists is the basic definition
of what minerals should be called "asbestos." Various defini-
tions have been proposed or used:

National Academy of Sciences (1977):
"The name for a group of naturally occurring hydrated sili-
cate minerals possessing fibrous morphology and commercial
utility."

Bureau of Mines (1977):
"(1) A collective mineralogical term encompassing the asbesti-
form varieties of various minerals; (2) an industrial product
obtained by mining and processing asbestiform minerals." As-
bestiform minerals were further defined to be "a specific type of
mineral fibrosity in which the fibers and fibrils possess high
tensile strength and flexibility."

IARC (1977):
"Asbestos is the generic name used for a group of naturally
occurring mineral silicate fibers of the serpentine and amphi-
bole series."

Zoltai (1978):
"...a collective term referring to the unusual crystallization of
certain minerals in the form of long, strong, and flexible fibers,
aggregated in parallel or radiating bundles from which fibers
can *easily* be separated."

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The above definitions demonstrate an important problem. That is, the condition of fibers in nature as a result of crystal growth is the only criteria for distinguishing asbestos from other silicates (Langer, 1979). Most properties mentioned above can only be measured on bulk samples (megascopic properties). However, airborne fibers in the occupational setting are only observable on the microscopic level, thus not allowing measurements of such properties as tensile strength and flexibility. Langer et al. (1979) have pointed out that, using strict mineralogical nomenclature, isolated submicroscopic single fibers derived from known asbestos sources could not be termed "asbestos." In fact, among the many minerals demonstrating a fibrous habit in nature, only six minerals are commercially exploited and thus considered "asbestos." These include the serpentine mineral chrysotile and the amphiboles cummingtonite-grunerite including amosite, anthophyllite asbestos, tremolite asbestos, actinolite asbestos, and crocidolite.

In addition to problems relative to exposures to mineral fibers other than one of the six mentioned above, acicular cleavage fragments are frequently indistinguishable from mineral fibers derived from commercial asbestos sources, especially on the submicroscopic scale. Cleavage plays an important role during commutation for some amphibole minerals. Submicroscopic amphibole mineral fragments often demonstrate structural and chemical properties indistinguishable from asbestos homologues. Airborne size characteristics such as length and diameter are often similar to asbestos.

General Definition

The foregoing considerations present a fundamental question of how broad a new or revised regulation should be. Arguments can be made for inclusion of all fibrous minerals posing risks comparable to commercially exploited fibrous minerals called asbestos. On the other hand, the fibrous minerals generally called asbestos appear to form the most pressing hazards to the largest number of current workers. This effort has not attempted to recommend coverage of all fibrous minerals or analogs, but has focused on commercial materials generally considered asbestos and asbestiform contaminants common to commercially exploited materials. We recommended the following definition for regulatory purposes, pending thorough and complete regulation of the hazards of all fibrous materials.

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1. Asbestos is defined to be chrysotile, crocidolite, and fibrous cummingtonite-grunerite including amosite, fibrous temolite, fibrous actinolite, and fibrous anthophyllite.

2. The fibrosity of the above minerals is ascertained on a microscopic level with fibers defined to be particles with an aspect ratio of 3 to 1 or larger.

We also expressly adopt the following approach articulated by the recent British Advisory Committee on Asbestos (Vol. 1, p. 11):

> *Asbestos* is a generic term for the fibrous forms of several mineral silicates. These occur naturally in seams or veins, generally between about 1 and 20 millimetres (mm) in width in many igneous or metamorphic rocks and belong to one of two large groups of rock-forming minerals: the serpentines and amphiboles.
>
> We recognize the mineralogical complexities associated with the definition and identification of asbestos and asbestos fibre, but for the purposes of this report we concentrate on the fibre types with which people are most likely to come into contact as a result of their use in industry. The serpentine group contains the type of asbestos known as chrysotile ('white asbestos'), which is the only asbestiform member of this group of minerals and by far the commonest and commercially the most important type of asbestos. The amphibole group contains crocidolite ('blue asbestos'), amosite ('brown asbestos'), anthophyllite, actinolite and tremolite. Amosite is an acronym for Asbestos Mines of South Africa and is mineralogically known as cummingtonite – grunerite asbestos. Tremolite may occur as a contaminant with chrysotile and with other minerals such as talc. Crocidolite, amosite and anthophyllite have all been exploited commercially, although anthophyllite is no longer in significant quantities.

The above definitions of asbestos should not be taken to mean that fibers or mineral fragments of other minerals are without biological significance (IARC, 1977). Although epidemiologic data for other "mineral fibers" are limited at this time, prudence dictates that such substances be handled with caution.

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II. ASBESTOS SAMPLING AND ANALYSIS

Update on New Methods

Since the NIOSH revised recommended asbestos standard was published in December, 1976, there have been several new developments in the area of sampling and laboratory analysis. Kim et al. (1979) have developed a quick screening test for chrysotile, crocidolite, and amosite which can be used for bulk material samples. The test is based upon the formation of color complexes with Mg^{+2} and Fe^{+2} released from asbestos upon acid digestion. The Mg^{+2} from chrysotile is complexed with p-nitrobenzenazo-s-naphthol. The Fe^{+2} from crocidolite and amosite is complexed with 1,10-phenathroline. A positive test is indicated by formation of colored complex for Mg^{+2} and/or Fe^{+2}. The test by Kim et al. is not specific for asbestos; however, the detection limit is reasonable for bulk samples with 1-2 mg being detectable in any given sample. Of 70 samples tested, 52 were correctly classified as containing asbestos or not, 18 samples gave false positives, and there were no false negatives. The method has little promise for airborne samples.

Lange and Haartz (1979) have developed a method for chrysotile asbestos determinations by X-ray diffraction. The method for membrane filters involves ashing followed by re-deposition on silver membrane filters. The 7.33Å peak for chrysotile is primarily used in an integrated mode. Normalization using reflections from the silver membrane is employed along with X-ray absorption corrections. The lower limit of detection is reported to be 2 µg on a filter with good linear response to over 200 µg per filter. Minerals such as antigorite, lizardite, kaolinite, and possibly chlorite are potential interferences with chrysotile. The method has not been adapted for amphibole determinations.

Lilienfeld and Elterman (1977) and Lilienfeld et al. (1979) have developed a portable monitor capable of real-time determinations of airborne fiber concentrations. The monitor is based upon rotation of elongated particles by means of a rotating electric field of large voltage gradient. Fibers of various lengths are then detected by synchronous detection of modulated light scattered from a continuous-wave helium-neon laser beam with modulation generated by the rotating particles. Concentrations between 0.001 and 30 fibers/cc are reported to be detectable. At a concentration of 1 fiber/cc, a relative stan-

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dard deviation of 10% is reported. The minimum detectable fiber length and diameter are estimated to be 2 μm and 0.2 μm, respectively. The instrument is not specific for asbestos as other elongated particles align within the electric field, and the instrument cannot be easily used for obtaining "breathing zone" samples.

Gale and Timbrell (1979) have reported progress in development of an automated method for determining fiber density on membrane filters. The method involves first clearing the membrane filter by conventional methods followed by aligning fibers on the filter in a strong magnetic field. The sample is then placed in a specially designed microscope on a motor driven stage. Fiber density is determined by measuring light scattered from the rotating fibers. The method is not yet commercially available, but is predicted to have a lower limit of detection of about 0.1 fiber/cc based on a 4-hour sampling period.

Optical Microscopy

The phase contrast method recommended by NIOSH for compliance sampling in the occupational setting was reviewed in the 1976 NIOSH document. Since that review, Leidel et al. (1979) have reported studies to better define precision of the method at lower levels. Minor changes in fiber counting methods have also been recommended by NIOSH to correct a potential statistical bias.

Based on the most recent data available, Leidel et al. (1979) estimated the coefficient of variation for the membrane filter sampling–phase contrast counting method to be 0.11 to 0.15, given a total count of at least 100 fibers. With a reduced fiber count of 10 fibers in the analysis, the coefficient of variation is estimated to be 0.41. Statistical tests based upon these estimates of precision are recommended by NIOSH for determining compliance or non-compliance with regulatory standards (Leidel et al., 1979). Procedures are available for single full shift samples, multiple samples covering the workshift, or short "grab samples."

The phase contrast method is clearly capable of measuring airborne fiber levels down to 0.1 fibers/cc (fibers longer than 5 μm) given that due consideration is given to inherently high variability at such levels. The method is highly sensitive for detection of fibers longer than 5 μm; however, specificity of the

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method for identifying asbestos fibers may be a serious problem under certain circumstances. Fiber identification is based only upon fiber length and aspect ratio; therefore, the method is not specific in situations where a mixture of asbestos and non-asbestos fibers occur or where large numbers of other elongated particles are present. The lack of specificity becomes more serious at lower fiber concentrations, and alternate methods for identification are likely to be required. The most likely choice for fiber identification in airborne dust samples is electron microscopy, where both electron diffraction and microchemical analyses may be used to identify fibers (NIOSH, 1976). The fraction of asbestos fibers determined by these methods could then be multiplied by phase contrast determinations to arrive at asbestos fiber levels. It seems reasonable that such determinations only need be made for a statistically determined sample and not for each airborne dust sample, with subsequent determinations made only upon process or product modifications. The statistical confidence of the airborne asbestos fraction determinations should be taken into account in determinations of compliance or non-compliance.

In addition to the problem of lack of specificity for fiber identification, only a fraction of all airborne asbestos fibers are actually accounted for by the phase contrast method, which considers only fibers longer than 5 μm. The phase contrast method, therefore, can only be considered an "index" measure of fiber exposure. In fact, the fraction of airborne fibers longer than 5 μm is extremely variable, ranging from 1 to 50%, depending on fiber type and industrial operation (Dement et al., 1976). In addition to determinations of fiber identification by electron microscopy, it may also be desirable to determine airborne fiber size and specifically the fraction of airborne fibers longer than 5 μm.

III. BIOLOGIC EFFECTS OF EXPOSURE TO ASBESTOS IN ANIMALS

In Vivo

Animal studies reported since 1976, in which several types of asbestos have been utilized, further support the findings published in the NIOSH Revised Recommended Asbestos Standard. In that publication, reference was made to research which adequately demonstrated that all commercial forms and several other types of asbestos can produce mesotheliomas and primary bronchogenic neoplasms in animals.

Although mesotheliomas were most readily produced by intrapleural injections, they were also produced by inhalation exposures (Wagner et al., 1974). Since then, additional studies by Wagner et al. (1979) have shown that a commercial grade, predominantly short fiber Canadian chrysotile, which is used primarily for paint and plastic tile fillers, can induce mesotheliomas when injected intrapleurally into rats, and induce primary lung neoplasms when the animals are exposed by inhalation.

Not only is chrysotile as potent as crocidolite and other amphiboles in inducing mesotheliomas after intrapleural injections (Wagner et al., 1973), but also equally potent in inducing pulmonary neoplasms after inhalation exposures (Wagner et al., 1974). In terms of degree of response related to the quantity of dust deposited and retained in the lungs of rats, chrysotile appears to be much more fibrogenic and carcinogenic than the amphiboles (Wagner et al., 1974). The concentration of dust in the lungs of rats exposed to Canadian chrysotile was only 1.8-2.2% of the dust concentration in the lungs of animals exposed to amphiboles (after 24 months of inhalation exposures). Yet the lung tumor incidences and degrees of pulmonary fibrosis were similar in all groups. The reasons for higher incidences of lung cancer and mesotheliomas in workers exposed to amphiboles is, therefore, probably related to higher concentrations of respirable fibers during their exposures.

Research to this day has not been able to establish a fiber length below which there exists no carcinogenic potential by inhalation, the most common route of occupational exposure. This is true because of the unavailability of specifically sized fibers (Pott, 1979).

Not only were naturally occurring fibers carcinogenic, but synthetic fibers were carcinogenic as well. Pylev (1979) obtained mesotheliomas in 54% of rats injected intrapleurally with a milled synthetic hydroxy-amphibole, and primary lung neoplasms in 23% of hamsters injected intratracheally with a synthetic chrysotile. Mesotheliomas were also induced in 9/60 hamsters injected intrapleurally with glass fibers, 82% of which were greater than 20 μm in length (Smith et al, 1979).

Further experimentation with fibers of differing diameters and lengths supports the previous observation that long, thin fibers are much more carcinogenic than short or thick fibers. Utilizing 16 preparations of fiberglass of differing fiber lengths

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and diameters, Stanton et al. (1977) were able to show that glass fibers with diameters less than 1.5 μm and lengths greater than 8 μm were carcinogenic in the pleura of rats, and that fibers shorter or wider than those were much less carcinogenic. For example, one preparation in which 60% of the fibers were less than 1.5 μm in diameter induced pleural sarcomas in 64% of rats, whereas another preparation in which only 16% of the fibers were less than 1.5 μm in diameter induced pleural sarcomas in only 14% of rats. Ninety-five percent of the fibers in both preparations were greater than 8 μm in length.

Besides the corroborating evidence for the carcinogenic potential of asbestos, recent results indicate a strong co-carcinogenic effect. Kung-Vosamae and Vinkmann (1979) reported a strong synergism between nitroso-diethylamine (NDEA) administered orally and chrysotile given intratracheally. NDEA given orally alone induced lung tumors in only 2% of the hamsters, whereas NDEA administered orally plus Canadian chrysotile given intratracheally induced lung neoplams in 40%. Chrysotile alone induced no lung tumors.

Additional research on the transport of fibers into tissues has confirmed that fibers reach the lymphatics shortly after oral administration (Masse et al., 1979). In view of the ability of intratracheally administered chrysotile to act synergistically with at least one nitrosamine, it is possible that ingested asbestos could act synergistically with orally administered nitrosamines to induce cancer in the gastrointestinal tract.

In Vitro

In vitro studies of all commercial forms of asbestos have been inconsistent when repeated or performed at different laboratories. Their correlation with in vivo studies has also been inconsistent and, thus, their value in studying the etiology of asbestos induced diseases is unclear at present.

IV. BIOLOGIC EFFECTS OF EXPOSURE TO ASBESTOS IN HUMANS

Amosite

Seidman et al. (1979) have extended their study of amosite asbestos workers with short-term exposures. The study group consisted of 820 men first employed between June, 1941 and December, 1945 in the production of asbestos insulation and

who were alive in 1961. Followup was through 1977, with expected deaths adjusted for age and calendar time estimated using death rates for white males in the general population of New Jersey.

Among the cohort studied by Seidman et al., 83 lung cancers were observed according to death certificate information, whereas 23.1 were expected. Among 61 men employed less than 1 month, 3 lung cancers were observed versus 1.3 expected. Although based on small numbers, excess mortality from lung cancer showed an increasing trend with employment duration. Cancer latency periods were progressively shortened with increasing employment duration. Four mesotheliomas were reported on death certificates in contrast to 14 which were identified on autopsy and other tissue diagnoses. Three in the group had less than 1 year of exposure. Although no environmental data are available for this plant, dust counts were made in another plant using the same fiber type and production process. Seidman et al. reported average exposure at this plant to be 23 fibers/cc. Further data available for this comparison plant were published by NIOSH (1972) showing mean exposures to range from 14 to 75 fibers/cc. At such concentrations, a lung cancer relative risk of 2.3 could be calculated with employment less than 1 month.

Anderson et al. (1979) evaluated the risks of non-malignant and malignant disease associated with household exposure to work-derived amosite dust. Four mesothelioma cases were reported among household contacts of former workers at a plant manufacturing amosite insulation products in Paterson, New Jersey. Anderson et al. also reported a 35.9% prevalence of radiographic abnormalities among household contacts of former employees at this same amosite plant, compared with a 4.6% prevalence among a control group. These radiographic abnormalities included pleural thickening, pleural calcification, pleural plagues, and irregular opacities. These studies raise the specter of non-occupational hazards associated with casual or low-level exposures to amosite.

Murphy et al. (1978) reported a followup to their first report (1971) of shipyard pipe coverers exposed predominantly to amosite asbestos. Workers in the original Murphy report of 1971, with "asbestosis" diagnosed by multiple criteria, had a poor prognosis as reported in the 1978 longitudinal survey.

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Chrysotile

Robinson et al. (1979) reported an additional 8 years of observation and 385 deaths to the Wagoner et al. (1973) study of mortality patterns among workers at one facility manufacturing asbestos textile, friction, and packing products. Chrysotile constituted over 99% of the total quantity of asbestos processed per year, except for 3 years during World War II. During these 3 years, amosite was selectively used to a limited extent because of U.S. Naval specifications, and accounted for approximately 5% of the total asbestos used per year. Crocidolite and amosite for the other years accounted for less than 1% of total usage in very selected areas. Exposures to these other two types may have played some role in the etiology of disease; however, due to the overwhelming exposure of the cohort to chrysotile, it is likely that the other exposures played a minor role in the overall mortality patterns. Robinson et al. confirmed Wagoner et al.'s observations of statistically significantly excess deaths due to bronchogenic cancer, suicide, heart disease, and non-malignant respiratory disease including asbestosis and a statistically non-significant excess of digestive cancer and lymphoma. Robinson et al. described 17 mesotheliomas whereas no mesotheliomas were detected in the Wagoner et al. study where observation of mortality ceased in 1967. The appearance of 17 mesothelioma in the updated study reflects latency periods of 24 to 53 years since onset of first exposure. Further analysis indicated 14 of 17 mesothelioma deaths occurred after the original study period. This observation confirms other findings that mesotheliomas are characterized by very long latency periods. Chovil and Stewart (1979) also reported latencies of 6 to 44 years, with a mean of 26.9 years.

Weiss (1977) reported no unusual mortality experience over a 30-year period for a cohort of workers employed in a paper and millboard plant stated to be using only chrysotile. The author concluded that the study results were suggestive of a minimal hazard from chrysotile. This conclusion must be viewed in light of the limitations inherent in the study. The study population was small (n = 264) and only 66 workers had died at the time of analyses. Two of these workers died of asbestosis. Moreover, the unusually low Standard Mortality Ratio (SMR) for many causes of death in the Weiss et al. paper suggests the possibility of a selection bias greater than that usually seen when contrasting industrial populations with the general population.

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McDonald et al. (1973, 1974) reported an increased risk of lung cancer among men employed in Quebec chrysotile mines and mills. The risk of lung cancer among those workers most heavily exposed was 5 times greater than those least exposed. Liddell et al. (1977) further analyzed the mortality experience of the cohort of chrysotile asbestos miners and millers previously studied by McDonald et al. and found excesses of respiratory cancer, asbestosis, and mesothelioma. These same chrysotile miners and millers of Quebec, as of 1977, had experienced nine confirmed and two suspected mesotheliomas (McDonald, 1978). The author concluded for the seven cases observed at Thetford mines that "There is therefore no good reason to doubt chrysotile exposures as the cause."

A recent study by Nicholson et al. (1979) examined the mortality of 544 Quebec chrysotile mine and mill employees which corresponded closely in terms of duration of exposure and periods of observation to cohorts of mixed fiber asbestos factory workers and insulation workers established in other studies. Among this cohort of 544 men with at least 20 years of employment in chrysotile mining and milling at Thetford Mines, Canada, 16% of the deaths were from lung cancer and 15% from asbestosis. The risk of death for asbestosis, at equal times from onset of exposure, was very similar in the miners and millers to that found in the factory workers and insulators. Lung cancer was similar among the miners and millers and in the factory workers but higher in the insulators. One death from mesothelioma was reported in this study.

Selikoff (1977b) surveyed 485 current employees of a chrysotile mine in Baire-Verte, Newfoundland, which had been in operation since 1963. Fifty employees (10%) had one or more radiographic abnormalities of the type commonly associated with asbestos exposure. Parenchymal abnormalities were most common, and pleural changes were detected in only 3% of the individuals surveyed. For those individuals employed less than 5 years the prevalence of abnormalities was 5%, and this increased with duration of employment. Changes occurred most commonly in those with the most intense exposures. This study was designed only to assess asbestos-related disease under more modern conditions than have previous studies (Kogan et al., 1972; Rossiter et al., 1972); thus, assessments of the effects of short duration of exposure and long latency could not be made. The interpretation of these data is further complicated

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by the lack of a control population and environmental measurements. The study does demonstrate the prevalence of chest X-ray changes in an appreciable proportion of employed workers, despite a short period since initial exposure.

Rubino et al. (1979) reported nine asbestosis deaths among chrysotile asbestos miners in northern Italy. Excess lung cancer (7 vs. 3.4) was seen only during the last quinquennium of observation, 1971-1975, that period of time after greatest latency. Also, one mesothelioma was reported in this latest period.

Studies examining lung tissue of mesothelioma cases and comparison groups have shown equivocal results as to the possible relationship of chrysotile in lung tissue and mesothelioma. Jones et al. (1979) found no evidence to indict chrysotile, while Acheson and Gardner (1979) estimated a 6-fold relative risk of mesothelioma for persons with only chrysotile in lung tissue as compared with controls with no asbestos fiber in their lungs.

Boutin et al. (1979) reported on a study of chest film abnormalities among chrysotile miners and millers in Corsica. They studied 166 ex-workers of the mines and mill closed in 1965, and compared them with 156 controls without asbestos exposure and with similar demographic variables. Chest films were read according to the ILO U/C Classification system. Compared with controls, chrysotile workers had a prevalence of all parenchymal abnormalities 2.4 times that of controls. For those with a profusion of 1/2 or more, the prevalence ratio was approximately twice the controls. Pleural changes were twice as prevalent in chrysotile workers as in controls. Exposures among this cohort were reported to have been very high, with exposure levels ranging from 85 to 267 millian parts per cubic foot (mppcf).

Crocidolite

Jones et al. (1976) reported a high incidence of mesothelioma among women who worked predominantly with crocidolite in a factory producing gas mask canisters during World War II, and have recently extended observations on this population (Jones et al., 1979). Among this group of 1,088 workers exposed only between 1940 and 1945, 22 pleural and 7 peritoneal mesotheliomas were observed. This is likely an underestimate since 373 women were lost to observation. A linear dose-response

relationship with length of employment was observed for meso-thelioma, with three mesotheliomas observed among those exposed 5-10 months.

McDonald and McDonald (1978) have also studied mortality of 199 workers exposed to crocidolite during gas mask manufacture in Canada during 1939 to 1942. This cohort was followed through 1975, and 56 deaths occurred. Out of these 56 deaths, 4 (7%) were from mesothelioma and 8 from lung cancer. It should be pointed out that an additional five mesotheliomas not reported on death certificates were diagnosed on review of pathology or autopsy material.

Mixed Fiber Types

Weill et al. (1979) and Hughes and Weill (1979) reported on the mortality experience of a cohort of 5,645 men employed in production of asbestos cement products and who had at least 20 years since first exposure. These workers were exposed largely to chrysotile, with some crocidolite and amosite. Among this group, 601 persons were identified as deceased by the Social Security Administration. Those with unknown vital status (25%) by this source were assumed to be alive, thus likely resulting in underestimation of the true risk. Death certificates were obtained for 91% of the known deaths. Dust exposures were estimated using each worker's employment history in conjunction with historical industrial hygiene data.

Weill et al. (1979) observed increased respiratory cancer mortality only among those with exposure in excess of 100 mppcf/year, where 23 cases were observed versus the 9.3 expected. The unusually low SMR for all causes in the low exposure groups suggests the possibility of a selection bias, and any interpretation of risks at low exposures should be done with caution. Two pleural mesotheliomas were reported. Separating the cohort by type of fiber exposure, the authors concluded that the addition of crocidolite to chrysotile enhanced the risk for respiratory malignancy; however, an excess risk (8 observed vs. 4.4 expected) was observed among those not exposed to crocidolite, with cumulative exposures in excess of 200 mppcf-months (16.6 mppcf-years). Both average concentration of exposure and duration of exposure were found to be related to cancer risk.

Jones et al. (1979) studied the progression of radiographic abnormalities and lung function among asbestos cement work-

ers. Chest films taken in 1970 and 1976 on 204 workers were read independently by two readers according to the ILO U/C 1971 Classification scheme. These films were read side-by-side in known order and ranked according to progression. Spirometric measurements were made in 1973 and 1976. The major findings of the Jones et al. study were: (1) the progression of small opacities was dependent upon both average and cumulative exposure; (2) significant declines in lung function were shown to result from both smoking and cumulative exposure; and (3) pleural abnormalities progressed as a function of time with little association to additional exposure. No estimates were made of the incidence of various respiratory abnormalities in relation to exposure.

Peto (1979) reported on the mortality experience of a cohort of asbestos textile workers previously studied by Doll (1955), Knox et al. (1968), and Peto et al. (1977). Data from this factory had previously been used by the British Occupational Hygiene Society (BOHS, 1968) in establishing occupational exposure standards and was subsequently studied by Lewinsohn (1972). Routine dust measurements in this factory were first made in 1951. Among the 255 males first employed after 1951, 12 lung cancers were observed, whereas only 4.65 were expected, based on national death rates. Among those with 20 or more years since initial employment, 8 lung cancers were observed versus 1.62 expected. Fiber exposures were estimated to be 32.4 fibers/cc in 1951, decreasing to 1.1 fibers/cc in 1974. These estimates are 2.4 times previously estimated values for this plant (Peto et al., 1977). Peto estimated the relative risk for cumulative exposures of 200-300 fibers/cc-year to be between 2 and 3. The cohort is too small and followup too short to estimate cancer risks at lower exposures. No mesotheliomas were observed in the cohort first employed after 1951; however, the followup period is insufficient to address this question.

Berry et al. (1979) extended their 1968 observations concerning asbestosis by including persons completing 10 or more years employment by 1972. Persons who left after June 30, 1966, were also contacted and encouraged to participate, with 68 of 113 persons eventually participating. Outcome measures studied included chest radiographs, medical examination including assessment of basal crepitations, and pulmonary function (FEV, FVC, FRC, TLC, RF, TL, $PaCO_2$). Chest films were read by four readers by the ILO/UC 1971 Classification system

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with readings being averaged. Dust exposures were estimated for each person using available hygiene data and estimates of control effectiveness.

In this study, "possible asbestosis" was diagnosed based on one or more combinations of basal rales or crepitations, radiological changes, a falling transfer factor, and restrictive lung function changes. Among these 379 men, 60 cases of possible asbestosis were diagnosed by the factory medical officer, whereas 85 cases were diagnosed by an independent clinician. Collaboration by these investigators subsequently resulted in 82 men with crepitations, 58 with "possible asbestosis," and 34 with certified asbestosis. Using the exposure data, these authors estimated the cumulative dose necessary for a 1% incidence for crepitations, possible asbestosis, and certified asbestosis to be 43, 55, and 72 fibers/cc-year, respectively. These authors pointed out limitations of the cumulative dose concept and acknowledged the imprecision of their exposure estimates. Two cases of certified asbestosis were observed among non-smokers and nine among ex-smokers. There were, in general, fewer respiratory symptoms and signs in non-smokers and light smokers than in heavy and ex-smokers.

Elmes and Simpson (1977) have extended their earlier (1971) report to include deaths occurring since 1965 through 1975. The mortality trend has shifted from a preponderance of asbestosis and gastrointestinal cancer deaths to malignancies of the lung and mesothelioma, diseases associated with longer latent periods. These authors stated that their findings would suggest any standard based "on the prevention of asbestosis may not provide adequate protection against neoplasia."

Morbidity and mortality analysis by Lacquet et al. (1979) of workers in a Belgian asbestos cement factory revealed a strong dose-response relationship for asbestosis, and pleural and parenchymal lung changes. Pleural thickening and adhesions began occurring in the lowest dose category (0-49 fibers/cc-year). Parenchymal lung changes occurred less frequently. No cases of asbestosis were recognized in workers with less than 100 fiber-years of exposure. Asbestosis occurs more frequently and with shorter latency periods (as the exposure levels increase) and adverse mortality tends to occur at longer latency periods (as the dose decreases) (Seidman et al., 1979). Because the observation period of the Lacquet et al. study was only 15 years, it cannot be assumed that the absence of asbestosis in the low dose categories currently observed will not occur

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have been reported by others (Elmes and Simpson, 1971; Kogan et al., 1972).

Cook and Olson (1979) have recently shown that sediment in human urine contains amphibole fibers, thus providing the first evidence that mineral fibers pass through the human gastrointestinal mucosa under normal conditions of the alimentary canal.

Stell and McGill (1973) found that of 100 men with squamous-cell carcinomas of the larynx, 31 had known exposure to asbestos, compared with only 3 in matched controls. Similar associations have been reported by Morgan and Shettigara (1976); Shettigara and Morgan (1975); Rubino et al. (1979); and Selikoff et al. (1979a). Newhouse et al. (1979), however, utilizing an interview of patients at the Royal National Throat, Nose, and Ear Hospital in London, found that asbestos exposure was not more common among cases as compared to controls.

Significant increases in cancer of the buccal cavity and of the pharynx have been reported by Selikoff et al. (1979a). Among 17,800 asbestos insulation workers they observed 16 deaths due to cancer of these sites whereas 10.1 deaths would have been expected based on U.S. white male rates.

Robinson et al. (1979) reported an excess of deaths due to lymphosarcoma and malignant lymphoma among white males employed in an asbestos textile, friction, and packing products manufacturing facility. There were 7 deaths due to cancer of these sites, while 3.28 cases were expected.

V. SMOKING AND ASBESTOS

Hammond et al. (1979) recently reported the results of their 10-year followup study (January 1, 1967-December 31, 1976) of 12,051 asbestos insulation workers who had 20 or more years of work experience. They were able to obtain complete smoking histories of a large number of study subjects (8,220 workers) and compare their lung cancer mortality with that of a control population with a known smoking history. As a control population, 73,763 men in the American Cancer Society's prospective cancer prevention study were selected. These men were similar to asbestos workers in many respects. They were white males; non-farmers; had no more than a high school education; had a history of occupational exposure to dust, fumes, vapors, gases, chemicals, or radiation; and were alive as of January 1, 1967. Most of all, their smoking habits were also known.

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in these low dose categories after a longer latent period, or that pleural and parenchymal lung changes are not indicators of early lung change that can or will progress to asbestosis. The mortality portion of the study revealed asbestosis and an excess of digestive cancer, but not excesses for lung cancer or mesothelioma. This, again, is not surprising since lung cancer and mesothelioma tend to develop after latent periods greater than 15 years.

Baselga-Monte and Segarra's (1978) examination of 1,262 workers employed in four factories in the Barcelona area demonstrated a dose-response relationship based upon radiologic images. The authors demonstrated a quick response for pleural radiological changes at individual cumulative doses as low as 5 fibers/cc-years, while the pulmonary and pleuropulmonary responses tend to appear later, but not at statistically different doses. The authors were reluctant to draw conclusions because of the design of the epidemiologic evaluation, which considered only active employees. Other epidemiologic studies of worker populations would indicate that evaluation of only active employees tends to underestimate the health risk since diseased workers oftentimes tend to self-select out of the active workforce (Fox and Collier, 1976; Enterline et al., 1972; Borow et al., 1973). Baselga-Monte and Segarra concluded that "the present worldwide trend to establish more exigent hygienic criteria for exposure to asbest(os) is confirmed." Based on their working model, this level for a 50-year working life should be 0.07-0.10 fiber/cc, "(taking into account protection levels of 89 and 95%)."

Malignant Neoplasms other than Mesothelioma and Cancer of the Lung.

A number of epidemiological studies indicate less striking associations of excess risks of other types of cancers (in addition to bronchial and mesothelial) and occupational asbestos exposure. Selikoff (1977a) reported increased rates for cancer of the stomach and esophagus (20 observed vs. 6.46 expected) and cancer of colon (23 observed vs. 7.64 expected) among 632 asbestos insulation workers in the New York and New Jersey area. Selikoff et al. (1979) made similar observations among 17,800 asbestos insulation workers in the United States and Canada. They reported increased mortality from cancer of the esophagus (18 observed vs. 7.1 expected), stomach (18 observed vs. 14.2 expected), and colon and rectum (58 observed vs. 38.1 expected) among this study cohort. Similar observations

Age-standardized lung cancer mortality rates for control and asbestos workers were as follows:

Groups	Exposure to asbestos	History of cigarette smoking	Death* rate	Mortality ratio
Control	No	No	11.3	1.00
Asbestos workers	Yes	No	58.4	5.17
Control	No	Yes	122.6	10.85
Asbestos workers	Yes	Yes	601.6	53.24

*Rates per 100,000 man-years standardized for age on the distribution of the man-years of all the asbestos workers. Number of lung cancer deaths based on death certificate information.

Asbestos workers who did not smoke showed about a 5 times greater risk of dying of lung cancer when compared to the non-smoking control population. Asbestos workers who did smoke also had a 5 times greater risk of dying of lung cancer as compared to the controls who smoked. This means the relative risk associated with asbestos is about 5-fold for smokers and non-smokers alike. Therefore, the probability that their lung cancer was due to asbestos exposure is about 80% in both smokers and non-smokers.

The combined effect of smoking and asbestos exposure appears to be more than simple addition. If the combined effect were additive, one would expect death rates of 169.7 per 100,000 man-years among asbestos workers who smoked. This rate was derived from the sum of the baseline rate (11.3) plus the excess over that baseline due to asbestos (58.4-11.3=47.1) plus the excess due to smoking (122.6-11.3=111.3). The data seem rather to satisfy a multiplicative model. It was shown that smoking alone increased the death rate about 11 times, and asbestos alone increased it 5 times. Therefore, for a multiplicative model, the mortality ratio for those exposed to both asbestos and smoking would be 55 (5 times 11) times greater than those who

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were exposed neither to asbestos nor to smoking. The mortality ratio for those exposed to asbestos and to cigarettes was actually 53.24.

Liddell et al. (1977) further analyzed the mortality experience of a cohort of chrysotile asbestos miners and millers previously studied by McDonald et al. (1973, 1974) and McDonald and McDonald (1976). This cohort of 10,951 men born between 1891 and 1920, and who had at least 1 month of employment, was followed through December 31, 1973. Cause of death was ascertained for 97% of the 4,037 known deaths, whereas 1,117 (10%) were lost to followup. Smoking habits were ascertained through a questionnaire administered to those living or to relatives of deceased workers who died after 1951. Unlike previous reports on this cohort, person-years were accumulated by 5-year age groups and 5-year periods of calendar time, with expected deaths by cause calculated using mortality rates for males in the Province of Quebec.

For this cohort, the SMR for all causes was 107, and a SMR of 125 was observed for cancer of the lung and pleura. There also were 40 pneumoconiosis deaths. Using the whole cohort as the referent population, an excess of respiratory cancer was observed only after cumulative exposures of 300 mppcf-years (relative risk = 1.39). However, only 15 of the 40 pneumoconiosis deaths occurred with exposures greater than 300 mppcf-years. When available smoking data were taken into account, lung cancer SMRs of 48 and 46 were calculated for non-smokers and ex-smokers, increasing to 206 for heavy smokers. There were seven mesothelioma deaths among the cohort.

The Liddell et al. study suffers in that an "unexposed" group is not used for dose-response analyses of lung cancer; thus, risk at low doses could not be estimated. Secondly, smoking-specific death rates were not used for calculation of expected lung cancer deaths, thus underestimating risks among non-smokers.

There is little or no evidence that cigarette smoking is related to increased risk of pleural or peritoneal mesothelioma (Hammond et al., 1972, 1979).

Data from two studies suggest that cigarette smoking may contribute to the risk of asbestosis. Hammond et al. (1979) reported that the asbestosis death rate of asbestos workers who smoked was 2.8 times as high as that of non-smoking

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asbestos workers. Weiss (1971) reported a prevalence of pulmonary fibrosis of 40% (30/75) among asbestos workers who smoked in contrast to a prevalence of 24% (6/25) among non-smoking asbestos workers.

A small experimental study indicated that the particle clearance in the smokers was considerably slower than in the non-smokers. Cohen et al. (1979) reported that after a year 50 percent of magnetic dust (Fe_3O_4) originally deposited remained in the lungs of the smokers while only 10 percent remained in the lungs of the non-smokers. The authors suggested that smoking may impair the clearance of other dusts, including those that are toxic. This may help to explain the higher incidence of lung disease in smokers.

In summary, both asbestos and smoking are independently capable of increasing the risk of lung cancer mortality. When exposure to both occurs, the combined effect with respect to lung cancer appears to be multiplicative rather than additive. From the evidence presented, we may conclude that asbestos is a carcinogen capable of causing, independent of smoking, lung cancer and mesothelioma.

VI. EXPOSURE TO ASBESTIFORM MINERALS OTHER THAN COMMERCIALLY MINED ASBESTOS

Gillam et al. (1976) reported a threefold excess risk of mortality from respiratory cancer and a twofold excess of non-malignant respiratory disease (excluding influenza and pneumonia) among miners exposed to amphibole fibers in the cummingtonite-grunerite ore series at concentrations less than 2.0 fibers/cm^3. A large majority of the airborne fibers was shorter than 5 μm in length. McDonald et al. (1978), in a subsequent study of the same mine, examined the mortality experience of persons with at least 21 years of employment at the mine and mill. This study showed significant excesses of pneumoconiosis (mainly silicosis), tuberculosis, and heart disease. No overall excess of malignant diseases was found. However, when the population was broken down by estimated exposure, respiratory cancer was in excess in the highest exposure group. The findings of McDonald et al. do not negate those reported by Gillam et al., but, rather, tend to strengthen them in that McDonald et al. used a rigid survival criteria (inclusion only of

those employed 21 or more years), and further diluted the underground exposed effect by including persons never exposed underground.

Commercial talc deposits are sometimes found to contain serpentines (chrysotile, antigorite, and lizardite) and fibrous and non-fibrous amphiboles. One important deposit studied has been mined in the Gouveneur Talc District of upper New York State. Talcs in this area contained less than 1-2% silica, but have been shown to contain tremolite and anthophyllite, resulting in elevated miner and miller exposures to these fibers (Dement and Zumwalde, 1979).

Kleinfeld et al. (1967, 1974) demonstrated elevated proportionate mortality due to lung cancer and respiratory disease among talc miners and millers in New York State. Brown et al. (1979) conducted a retrospective cohort mortality study among workers of one company in this area. The study cohort consisted of all white males initially employed sometime between January 1, 1947 and December 31, 1959, with followup through June 30, 1975. Expected cause-specific deaths were calculated using age, calendar time, and cause-specific mortality rates of the U.S. Among this cohort, 10 respiratory cancers were observed, whereas only 3.5 were expected. Excess mortality was also observed for non-malignant respiratory diseases. One case of mesothelioma was observed; however, this worker was known to have had prior employment with unknown exposures in the construction industry.

Gamble et al. (1979) studied respiratory disease morbidity among a cohort employed at the same mine and mill studied by Brown et al. (1979). A total of 121 currently employed workers were given a respiratory questionnaire, PA and lateral chest films, and spirometry tests. Talc workers with greater than 15 years employment were found to have an increased prevalence of pleural abnormalities compared to coal miners, potash miners, and chrysotile asbestos workers. FEV_1 and FVC reductions demonstrated significant association with particulate and fiber exposure.

Mesothelioma of the pleura and peritoneum have been detected in two villages in Turkey: Tuzkoy and Karain (Artvinli and Baris, 1979 and Baris et al., 1978). Mineralogical analysis of samples from ore and water has revealed the asbestiform mineral zeolite but no asbestos. These fibers were usually 1-2 μm in diameter and 30-40 μm in length. Annual rates of

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malignant pleural mesothelioma in Tuzkoy were found to be 22 cases per 10,000 people, and 182 cases per 10,000 in Karain, while studies in Pennsylvania (Lieben and Pistawka, 1967), Finland (Nurminen, 1975), and England, Wales, and Scotland (Greenberg and Davies, 1974) reported annual incidences of 1 to 2.3 cases per 1,000,000 persons.

VII. NON-OCCUPATIONAL EXPOSURE TO COMMERCIAL SOURCES OF ASBESTOS

Anderson et al. (1979) reported on the occurrence of X-ray abnormalities among household contacts of workers in an amosite asbestos factory. The study cohort consisted of 679 household contacts who had lived in the household of an actively employed amosite asbestos factory worker and who themselves had not had occupational exposure to asbestos or other fibrogenic dust. These individuals were given a PA chest film which was read by five readers according to the ILO/UC Classification of 1971. For comparison, 325 controls living in the same community as the study subjects, matched by age and sex, were examined.

Among the study population, there was a 17% prevalence of small opacities, versus 3% for the controls. Pleural calcifications were present in 8% of the household contacts and were seen in none of the controls. There were 35% with one or more radiological abnormalities among household contacts in contrast to 5% among controls. An increasing prevalence of all abnormalities with duration of exposure was observed.

Churg et al. (1978) reported a case of mesothelioma of the pericardium in a man treated 15 years earlier for angina pectoris by dusting of the pericardial cavity with a mixture of fibrous dusts including anthophyllite asbestos, tremolite asbestos, and fibrous glass.

VIII. DOSE-RESPONSE RELATIONSHIPS

Evidence available to date indicates that a large dose of asbestos will produce a bigger health hazard than a small dose. Seidman et al. (1979), using the length of time worked in an amosite asbestos factory as a measure of the dosage of asbestos, reported an increased risk of dying from lung cancer with increasing duration of employment. Henderson and Enterline (1979), using cumulative dust exposure as an estimate of dose,

reported that the dose-response relationship for lung cancer is more likely linear. They predicted the relationship to be SMR=100+0.658 times cumulative dust exposure (mppcf-years). Liddell et al. (1977) also reported a similar relationship, i.e., a tendency for the mortality for lung cancer to increase with the dose.

Berry et al. (1979) reported that the occurrence of crepitations, possible asbestosis, and certified asbestosis was related to the cumulative dose.

Newhouse and Berry (1973) suggested that the risk of dying from mesothelioma increases with increasing dose. Jones et al. (1979) reported a linear relationship between the mesothelioma rate and length of exposure. In a study of the women workers in a wartime gas mask factory, they found that women having a long employment period had a higher proportion of death due to mesothelioma than those who had a short period of employment.

Although there appears to be little dispute that a larger dose of asbestos will pose a greater health risk, the exact nature of the dose-response relationships may be subject to considerable debate. This is so primarily because of problems of exposure estimation. Methods of measuring dust levels have changed over time with respect to sampling instrument (thermal precipitation vs. midget impinger vs. membrane filter), location of sampling (personal vs. area), and dust counting (particles vs. actual fibers) and/or evaluation techniques (whole fields vs. eyepiece graticule). As a result, conversion of dust levels obtained by one method to levels comparable to another method is far from simple, and is subject to considerable error. Another factor which may lead to differences of opinion on the exact shape of the dose-response curve is the measure of the dose. The commonly used measures of exposure are the cumulative dose and the duration of employment. Since using cumulative dose as a measure of exposure gives equal weight to the concentrations of dust experienced in each year of exposure, exposure of many years ago is considered as important as recent exposure. This practice is unrealistic for the chronic diseases having a long latency period. Duration of employment has also been used as a measure of exposure under the assumption that increasing the work time approximates increasing the dose. This procedure has the same problem as using the cumulative dose. Fur-

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thermore, in the absence of reliable past exposure data, the duration of employment may not equal the total dose of asbestos.

With regard to the linear hypothesis, the British Advisory Committee on Asbestos stated the following in 1979:

> Our reasons for preferring a linear hypothesis are:
> (1) It fits the data for occupational exposures;
> (2) it is the simplest hypothesis and the one most readily used for extrapolation to the probable effects of low doses; (3) it is likely to lead to an overestimate rather than underestimate of risks at very low doses. (Final Report, Vol. 2, p. 14).

Data available to date provide no evidence for the existence of a threshold level. Virtually all levels of asbestos exposure studied to date demonstrated an excess of asbestos-related disease.

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Testimony of

Kathleen M. Rest, Ph.D., M.P.A.

Acting Director, National Institute for Occupational Safety and Health

Centers for Disease Control and Prevention

on

Workplace Exposure to Asbestos

Before the

Committee on Health, Education, Labor and Pensions

United States Senate

July 31, 2001

Mr. Chairman and members of the Committee, on behalf of the National Institute for

Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention, I am pleased to provide this testimony addressing the current scientific knowledge about health risks to workers from exposure to airborne asbestos.

Background

Asbestos is a term that is generally used in referring to a group of fibrous minerals with exceptional resistance to degradation by heat, acids, bases, or solvents. The minerals are not combustible and have a high melting point and low thermal and electrical conductivity. These and other useful properties had resulted in the development of thousands of commercial uses for asbestos-containing materials by the early 1970s. However, as the use of asbestos dramatically increased, the lethal effects of airborne asbestos became clear. Regulatory action and liability concerns related to the now well-established connection between inhalation of asbestos fibers and a variety of serious and often fatal diseases have reduced or eliminated the use of asbestos in many commercial products. However, asbestos and asbestos-containing materials are still found in many residential and commercial settings and pose a risk of exposure to workers and others.

Asbestos is defined in Federal regulations as the minerals chrysotile, crocidolite, amosite, tremolite asbestos, actinolite asbestos, and anthophyllite asbestos. These six minerals are regulated by the Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA) and the Environmental Protection Agency (EPA). Five of the six asbestos minerals were used commercially (actinolite asbestos was not) and, as a consequence, it has been possible to observe and characterize their adverse health effects on humans.

Asbestos-Related Diseases

Exposure to asbestos significantly increases the risk of contracting several diseases. These include: 1) **asbestosis**—a disease characterized by scarring of the alveolar regions of the lungs; 2) **lung cancer**—for which asbestos is one of the leading causes among nonsmokers, and which occurs at dramatically high rates among asbestos-exposed smokers; 3) **malignant mesothelioma**—a cancer of the tissue lining the chest or abdomen for which asbestos and similar fibers are the only known cause; and 4) **nonmalignant pleural disease**—which can appear as a painful accumulation of bloody fluid surrounding the lungs, but which more commonly is seen as thick and sometimes constricting scarring of the tissue surrounding the lungs. In addition, asbestos exposure is associated with excess mortality due to cancer of the larynx and cancer of the gastrointestinal tract. The malignant diseases—the cancers including mesothelioma—are often fatal within a year or a few years of initial diagnosis. In contrast, asbestosis deaths typically occur only after many years of suffering from impaired breathing.

It is not known exactly how asbestos fibers cause disease. What is known is that the fibers, too fine to be seen by the human eye, can become airborne during various industrial processes or from handling asbestos-containing materials. These microscopic fibers can be inhaled and/or swallowed. As much as 50 percent or more of inhaled asbestos fibers remain lodged in the lungs, where it is almost impossible for the body to dispose of them. Asbestos fibers are extremely resistant to destruction in body fluids, and many of these fibers are too long to be engulfed and removed by the cells that normally scavenge and remove particles that happen to deposit in the

lungs. Generally, as the burden of retained fibers increases in the body, so does the likelihood of the diseases mentioned previously. Most asbestos-related diseases, particularly the malignant ones, have long latency periods often extending 10-40 years from initial exposure to onset of illness. While asbestos-related lung cancer and mesothelioma are frequently not curable, they and other asbestos-related diseases are clearly preventable by eliminating or limiting exposures to asbestos. The amount and duration of exposure are factors which can determine the risk of adverse health effects.

Exposure to Asbestos in the Workplace

Workplace exposure to asbestos remains a serious occupational health problem in the United States, with both vast numbers of workers at risk due to past occupational exposures and many other workers experiencing ongoing occupational exposures. Since the beginning of World War II, as many as eight million workers have been exposed to asbestos. Although the number of newly exposed workers has declined sharply since the development of regulatory standards in the 1970s, there are still substantial numbers of workers with continuing exposure. In 1991, NIOSH estimated that nearly 700,000 workers in general industry remained potentially exposed to asbestos, but that estimate did not include mining, railroad work, agriculture, and several other industry sectors.

The U.S. Geological Survey reports that asbestos continues to be imported for use in friction products (e.g., brakes and clutches), roofing products, gaskets, and thermal insulation. Construction workers involved in the renovation or demolition of buildings that

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contain asbestos are at particular risk of asbestos exposure. Many workers in the relatively new

asbestos removal industry are potentially exposed, relying on personal protective equipment and

other methods for limiting inhalation of asbestos fibers. Industrial maintenance personnel are

also at risk when they repair equipment, sometimes in enclosed spaces, that is insulated with

asbestos-containing material, as are automotive service personnel involved in brake and

clutch repair work.

In addition, "take-home" exposures—involving family members of workers who bring asbestos

home on their hair, clothing, or shoes—is also a well-recognized hazard and was addressed in a

1995 NIOSH report to Congress.

Because of the hazardous nature of asbestos, approaches to consider for control of

exposure include the substitution of less hazardous materials and the labeling of all

asbestos-containing materials so that required exposure controls can be implemented.

Ongoing Research Into Asbestos Exposure

NIOSH currently is assessing workers' asbestos fiber exposure at selected horticultural

operations that are using vermiculite, and at operations that expand vermiculite ore. Most of the

vermiculite now being produced for domestic use is obtained from one of four mines, three of

them domestic and one located in South Africa. NIOSH will complete asbestos exposure

assessments at two expansion plants for each ore supplier, along with a number of horticultural

sites. We expect the field study to conclude by the end of calendar year 2001. At present, field

sampling has been completed at four expansion plants and three horticultural operations.

Options under consideration for future research activities include identifying and characterizing other downstream uses of fiber-contaminated vermiculite that have not been previously recognized.

Tracking of Work-Related Asbestosis Deaths
NIOSH, using data from death certificates, has been tracking asbestosis mortality in the United States. Deaths associated with asbestosis increased from fewer than 100 annually in 1968 to more than 1200 per year in 1998, the most recent year for which final national data are available. In approximately one-third of these deaths, asbestosis was reported as the underlying, or main, cause of death, a proportion that has not changed appreciably over time. In the other two thirds of deaths, asbestosis was reported to have contributed but not caused the death. Death certificate data indicate that workers in the "ship and boat building and repairing" industry and "insulation workers" appear to have experienced the greatest risk of asbestosis. It also shows, however, that elevated asbestosis mortality is associated with a wide-ranging variety of other occupations and industry sectors.

Among the occupations with significantly elevated asbestosis mortality are: insulation workers; plumbers; sheet metal workers; plasterers; heating/air-conditioning/refrigeration mechanics; electricians; welders; chemical technicians; mechanics and repairers; stevedores; masons; furnace and kiln operators; painters; construction workers; and janitors and cleaners. Please note that the

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fact that an occupation (or industry sector) has "significantly elevated asbestosis mortality" does not mean that all workers in the occupation or industry sector are exposed to asbestos.

The other industry sectors with significantly elevated asbestosis mortality include, but are not limited to: nonmetallic mineral products; construction materials and industrial chemicals; petroleum refining; tires and other rubber products; aluminum production, hardware, plumbing, and heating supplies; construction; electric power generation; railroads; glass products; building material retailing; paper manufacturing; and steelmaking.

Asbestosis mortality is a delayed phenomenon which reflects exposures that typically occurred decades earlier. To better describe more recent exposures, NIOSH recently prepared and published a summary of data describing the results of asbestos samples collected and reported by OSHA and MSHA inspectors in their agencies' centralized data systems. Over the decade-long period from 1987 to 1996, Federal occupational safety and health inspectors reported an average of about 600 air samples for asbestos each year, although the annual number of reported samples declined by about 50% for each agency during that decade. (Not all collected samples are reported into the centralized data systems.) In the construction industry, nearly 7% of the samples indicated asbestos fiber concentrations exceeding the applicable OSHA or MSHA permissible exposure limit (PEL), and the average asbestos fiber concentration of all samples was about one-half the PEL. In the industry classified as "miscellaneous nonmetallic mineral and stone products," (which includes sites regulated by OSHA and MSHA) over 30% of asbestos samples exceeded the exposure limit (either OSHA's or MSHA's, as applicable) and the asbestos

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fiber concentrations averaged nearly twice the relevant PEL. In the "motor vehicles and motor vehicle equipment" industry, 10% of asbestos fiber samples exceeded the PEL and the asbestos fiber concentrations averaged more than twice the PEL. While asbestos exposure concentrations generally decreased in the more recent years of that ten-year period, and although fewer samples were being collected, samples continued to exceed the PEL in all three of those industry sectors. Federal inspectors detected asbestos in other settings, as well, ranging from textile operations to schools.

The Definition of Asbestos

In 1990 testimony before OSHA, NIOSH broadened its science-based definition of "asbestos" as a result of concerns about the microscopic identification of the six regulated asbestos minerals. The six minerals can also occur in a non-fibrous (so-called "massive") form. The non-fibrous mineral forms of the six asbestos minerals can be found geologically in the same ore deposits in which the fibrous asbestos minerals occur or in deposits where other commercially exploited minerals are mined (e.g., industrial grade talc). "Cleavage fragments" can be generated from the non-fibrous forms of the asbestos minerals during their handling, crushing, or processing, and these "cleavage fragments" are often microscopically indistinguishable from typical asbestos fibers of the (fibrous) minerals.

The elemental composition of the six asbestos minerals can vary slightly as a result of geological conditions such as pressure, temperature, or proximity of other minerals. Recognizing these variations in elemental composition, NIOSH believes that the six asbestos minerals can be

defined by their "solid-solution" mineral series. For example, the mineral series tremolite-ferroactinolite contains the asbestos mineral actinolite. These mineral series are considered solid-solutions in which cations (i.e., sodium, calcium, magnesium, iron, etc.) are replaced by other cations which can affect the elemental composition of the mineral without significantly altering the structure.

NIOSH bases this expanded "asbestos" definition—encompassing the entire solid-solution mineral series for each of the six currently regulated asbestos minerals and including cleavage fragments from the non-fibrous forms of these minerals—on scientific evidence from cellular and animal studies suggesting that dimension, specifically length and diameter, as well as durability, may be more critical factors in causing disease than chemical or elemental composition.

Challenges to Preventing Asbestos Exposure: Areas of Possible Additional Research

There are other fibrous minerals that technically do not fall within either the current regulatory or the NIOSH definition of asbestos, even though fiber shape, size, and durability indicate their potential to induce health effects similar to those of the six regulated asbestos minerals. The inclusion of only six specified fibers within the asbestos regulations may create a false sense of security that those mineral fibers that are not included are without risk. Clearly, other fibers may act in the same way as the regulated fibers and pose significant health risk, and mixtures of fibers may be lethal as well.

Based on epidemiological studies, it is clear that occupational exposure to mineral fibers that contaminate vermiculite from Libby, Montana, caused high rates of asbestos-related diseases

among exposed workers. The fibers that contaminate vermiculite from Libby include tremolite, one of the minerals within the definition of asbestos as currently regulated. Some evidence indicates that only 10 to 20% of the fibrous mineral content of the Libby vermiculite was tremolite. A much higher proportion—80 to 90%—of the fiber contaminant in this vermiculite has been characterized as several other similar fibers that are not currently regulated as asbestos, such as richterite and winchite.

Another example of a mineral that can produce asbestos-related diseases but is neither regulated as asbestos nor classified as asbestos under NIOSH's current scientific definition, is erionite. Erionite is a known human carcinogen, and environmental exposures outside the U.S. have been associated with an increased risk of malignant mesothelioma and lung cancer. (We are unaware of any occupational exposure to erionite in the U.S.)

Additional research possibilities which may be considered include efforts to better determine physical and/or chemical characteristics affecting toxicity of these naturally occurring mineral fibers as well as durable manufactured fibers. Direct evidence by which to attribute particular health effects to each possible fiber type is not currently available; obtaining such evidence is another area under consideration for future research. Epidemiological studies of people exposed to naturally occurring or manufactured fibers would provide important new information and are also under consideration for future research, along with animal toxicologic studies to help supply needed information if epidemiologic studies are not feasible.

In addition, further research is under consideration in the areas of exposure measurement and analysis of fibers. Although asbestos is comprised of fibers of many diameters and lengths, risk assessments and exposure assessments are based on air concentrations of fibers detectable by a technique called phase contrast microscopy. This method leaves an undetermined number of asbestos fibers in each sample uncounted because they are too thin for detection. Because of this measurement bias, asbestos exposure risks are currently based only on fibers large enough to be detected. More sensitive methods are currently available, but these methods could benefit from better standardization. Additional work to improve and standardize the methods for asbestos fiber measurement is being considered because it would help advance prevention and control efforts to protect exposed workers.

Conclusion

In summary, we know much about the adverse health effects caused by the inhalation of asbestos fibers. Many exposures or potential exposures have been identified, and appropriate precautions are used when workers are handling or working around these materials. Increased understanding of the health effects of fibrous minerals that fall just outside the existing definitions of asbestos will help us find ways to provide appropriate protection for workers exposed to those materials. Further identification and tracking of potential exposures to fiber-contaminated vermiculite and other contaminated materials that may be identified will help us assure that no one is unknowingly exposed to these materials. While information is being gathered, public health prudence guides us to reduce known exposures to these potentially hazardous fibrous minerals.

Workplace Exposure to Asbestos

Statement of

Gregory R. Wagner, M.D.

Director, Division of Respiratory Disease Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention,
U.S. Department of Health and Human Services

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Mr. Chairman and members of the Subcommittee, I am Dr. Gregory Wagner, an occupational health expert at the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC). I am pleased to appear before you today to provide this testimony on behalf of NIOSH.

NIOSH is a research institute within CDC, a part of the Department of Health and Human Services. CDC, through NIOSH, is the federal agency responsible for conducting research and making recommendations to identify and prevent work-related illness and injury.

My testimony today will address the current scientific knowledge about health risks to workers from exposure to airborne asbestos. I also will discuss NIOSH's past findings and current research related to asbestos contamination in Libby, Montana.

Background

Asbestos is a term that is generally used to refer to a group of fibrous minerals with exceptional resistance to degradation by heat, acids, bases, or solvents. The minerals are not combustible and have a high melting point and low thermal and electrical conductivity. These and other useful properties had resulted in the development of thousands of commercial uses for asbestos-containing materials by the early 1970s. However, as the use of asbestos dramatically increased, the lethal effects of airborne asbestos became clear. Regulatory action and liability concerns related to the now

well-established connection between inhalation of asbestos fibers and a variety of serious and often fatal diseases have reduced or eliminated the use of asbestos in many commercial products. However, asbestos and asbestos-containing materials are still found in many residential and commercial settings and pose a risk of exposure to workers and others.

Asbestos is defined in Federal regulations as the minerals chrysotile, crocidolite, amosite, tremolite, actinolite, and anthophyllite. The Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA) and the Environmental Protection Agency (EPA) regulate these six minerals. All of the minerals, except for actinolite, have been used commercially. The results from epidemiologic studies of workers exposed to these minerals provide the scientific evidence of a causal relationship between exposure and adverse health effects in humans.

Asbestos-Related Diseases

Exposure to asbestos significantly increases the risk of contracting several diseases. These include:

1.) **Asbestosis**—a disease characterized by scarring of the air-exchange regions of the lungs;

2.)   **Lung cancer**—for which asbestos is one of the leading causes among

nonsmokers, and which occurs at dramatically high rates among

asbestos-exposed smokers;

3.)   **Malignant mesothelioma**—an almost invariably fatal cancer of the tissue

lining the chest or abdomen for which asbestos and similar fibers are the

only known cause; and

4.)   **Nonmalignant pleural disease**—which can appear as a painful

accumulation of bloody fluid surrounding the lungs, but which more

commonly is seen as thick and sometimes constricting scarring of the

tissue surrounding the lungs.

In addition, asbestos exposure is associated with excess mortality due to cancer of the

larynx and cancer of the gastrointestinal tract. The malignant diseases—the cancers

including mesothelioma—are often fatal within a year or a few years of initial diagnosis.

In contrast, asbestosis deaths typically occur only after many years of suffering from

impaired breathing.

We do not know exactly how asbestos fibers cause disease. We do know that

microscopic fibers can become airborne during various industrial processes or from

handling of asbestos-containing materials and can then be inhaled and/or swallowed.

As much as 50 percent or more of inhaled asbestos fibers can remain lodged in the lungs, where it is almost impossible for the body to eliminate them. Asbestos fibers are extremely resistant to destruction in body fluids, and many of these fibers are too long to be engulfed and removed by the cells that normally scavenge and remove particles that happen to deposit in the lungs. Generally, as the burden of retained fibers increases in the body, so does the likelihood of disease. Most asbestos-related diseases, particularly the malignant ones, have long latency periods often extending 10-40 years from initial exposure to onset of illness. While asbestos-related lung cancer and mesothelioma are frequently not curable, they and other asbestos-related diseases are clearly preventable by eliminating or limiting exposures to asbestos. The amount and duration of exposure are factors that can determine the risk of adverse health effects.

The Definition of Asbestos

In 1990 testimony before OSHA, NIOSH broadened its science-based definition of "asbestos" as a result of concerns about the microscopic identification of the six regulated asbestos minerals. The six minerals can also occur in a non-fibrous (so-called "massive") form. The non-fibrous mineral forms of the six asbestos minerals can be found geologically in the same ore deposits in which the fibrous asbestos minerals occur or in deposits where other commercially exploited minerals are mined (e.g., industrial grade talc). "Cleavage fragments" can be generated from the non-fibrous forms of the asbestos minerals during their handling, crushing, or processing, and

these "cleavage fragments" are often microscopically indistinguishable from typical asbestos fibers of the (fibrous) minerals.

The elemental composition of the six asbestos minerals can vary slightly as a result of geological conditions such as pressure, temperature, or proximity of other minerals. Recognizing these variations in elemental composition, NIOSH believes that the six asbestos minerals can be defined by their "solid-solution" mineral series. For example, the mineral series tremolite-ferroactinolite contains the asbestos mineral actinolite. These mineral series are considered solid-solutions in which cations (i.e., sodium, calcium, magnesium, iron, etc.) are replaced by other cations which can affect the elemental composition of the mineral without significantly altering the structure.

NIOSH bases this expanded "asbestos" definition—encompassing the entire solid-solution mineral series for each of the six currently regulated asbestos minerals and including cleavage fragments from the non-fibrous forms of these minerals—on scientific evidence from cellular and animal studies suggesting that dimension, specifically length and diameter, as well as durability, may be more critical factors in causing disease than chemical or elemental composition.

NIOSH Studies of Vermiculite Workers in Libby, Montana

In June 1980, OSHA asked NIOSH to provide technical assistance to investigate lung problems in workers at a plant using vermiculite that had been mined in Libby. Shortly thereafter, MSHA also requested technical assistance from NIOSH to investigate the

magnitude of health hazards in vermiculite mines. MSHA was particularly concerned

about two reported cases of "dust-related lung disease" in workers at the Libby mine.

In response to these requests, NIOSH initiated epidemiological studies in Libby,

Montana. The epidemiological studies carried out by NIOSH between 1980 and 1985

showed that occupational exposure to mineral fibers that contaminate Libby vermiculite

caused high rates of asbestos-related diseases among exposed workers at the Libby

mine complex. The fibers these workers were exposed to included tremolite, one of the

minerals within the definition of asbestos as currently regulated. Some recent evidence

indicates that only 10 to 20% of the fibrous mineral content of the Libby vermiculite was

tremolite. A much higher proportion—80 to 90%—of the fiber contaminant in this

vermiculite has been characterized as several other similar fibers that are not currently

regulated as asbestos, such as richterite and winchite. Richterite and winchite are

fibrous minerals that are not classified as asbestos by mineralogists.

NIOSH played a pivotal role in documenting the health hazard associated with

occupational exposure to asbestos-contaminated vermiculite at the mine in Libby,

Montana. NIOSH made its findings available beginning in 1985 through meetings in

Libby with workers and their representatives, employer representatives, and members

of the community. NIOSH also published its findings in several scientific papers to alert

the occupational health community about the identified problem. It is clear in hindsight

that further work remained to be done, in particular, with respect to further studies of

downstream users of Libby vermiculite products. NIOSH is applying what we learned from our Libby investigations to our current and future activities both in Libby and throughout our program.

Current NIOSH Studies

At present, NIOSH is following up on potential exposures of workers who use or process vermiculite from other sources. Since closure of the Libby mine in 1990, most of the vermiculite now being produced for domestic use is obtained from one of four mines, three of them domestic and one located in South Africa. The degree to which the vermiculite from these other sources is contaminated with asbestos is not clear. At OSHA's request, NIOSH is conducting environmental sampling at expansion plants and horticultural operations where vermiculite is used. NIOSH will complete asbestos exposure assessments at two expansion plants for each vermiculite ore supplier, along with a number of horticultural sites. We expect the field data collection to be completed by the end of 2002. At present, field sampling has been completed at four expansion plants and three horticultural operations. From these studies we expect to learn the degree to which an asbestos exposure hazard exists in vermiculite from sources other than Libby, Montana. Once these studies are completed, we plan to produce and disseminate a technical report that describes the extent to which newly mined or imported vermiculite presents an asbestos risk to current vermiculite worker. Based on the findings, we may issue further guidance for protective measures to be taken.

Future Research Activities

Additional research possibilities that NIOSH is considering include efforts to better determine physical and/or chemical characteristics affecting toxicity of fibers including those occurring naturally and those manufactured. Direct evidence by which to attribute particular health effects to each possible fiber type is not currently available. Epidemiological studies of people exposed to naturally occurring or manufactured fibers would provide important new information, and studies conducted with animals could provide mechanistic and other toxicologic data.

Asbestos fibers have many different lengths and diameters. Additional work to improve and standardize the methods for asbestos fiber measurement is being considered because it would help advance prevention and control efforts to protect exposed workers. Human assessment of risk and occupational exposure limits is based on airborne fiber concentrations determined by the use of phase contrast microscopy (PCM). This analytical method leaves an undetermined number of asbestos fibers collected on each sample uncounted because many fibers are too small in diameter to be detected and because the standard procedure for counting fibers using PCM takes into account only fibers longer than 5 micrometers in length. Current asbestos exposure risk assessment is based only on a subset of fibers that can be detected using PCM techniques. More sensitive analytical methods are currently available, but these methods could benefit from better standardization.

Conclusion

In summary, we know much about the adverse health effects caused by the inhalation of asbestos fibers. Increased understanding of the health effects of fibrous minerals that fall outside the existing definitions of asbestos will help us find ways to provide appropriate protection for workers exposed to those materials. Further identification of workplace sources of vermiculite exposure and the tracking of persons potentially exposed to fiber-contaminated vermiculite and other contaminated materials will help us develop appropriate public health strategies for preventing exposure to these materials. While information continues to be gathered, public health prudence requires that vermiculite from the Libby mine or products containing vermiculite originating in Libby be considered potentially dangerous and that proper precautions be taken to minimize the generation and inhalation of any dust during the handling of these materials until analysis of the particular vermiculite or vermiculite-containing product shows that it does not produce an asbestos hazard.

Radiographic Abnormalities and Exposure to Asbestos-Contaminated Vermiculite in the Community of Libby, Montana, USA

Lucy A. Peipins,[1,] Michael Lewin,[1] Sharon Campolucci,[1] Jeffrey A. Lybarger,[1] Aubrey Miller,[2] Dan Middleton,[1] Christopher Weis,[2] Michael Spence,[3] Brad Black,[4] and Vikas Kapil[1]*

[1]Agency for Toxic Substances and Disease Registry, Atlanta, Georgia, USA; [2]U.S. Environmental Protection Agency, Denver, Colorado, USA; [3]Montana Department of Health and Human Services, Helena, Montana, USA; [4]Lincoln County Department of Environmental Health, Libby, Montana, USA

Mining, handling, processing, and personal or commercial use of asbestos-contaminated vermiculite have led to widespread contamination of the Libby, Montana, area. We initiated a medical testing program in response to reports of respiratory illness in the community. The purpose of this analysis was to identify and quantify asbestos-related radiographic abnormalities among persons exposed to vermiculite in Libby and to examine associations between these outcomes and participants' self-reported exposures. A cross-sectional interview and medical testing were conducted in Libby from July through November 2000 and from July through September 2001. A total of 7,307 persons who had lived, worked, or played in Libby for at least 6 months before 31 December 1990 completed the interview. Of those, 6,668 participants ≥ 18 years of age received chest radiographs to assess the prevalence of pleural and interstitial abnormalities. We observed pleural abnormalities in 17.8% of participants and interstitial abnormalities in < 1% of participants undergoing chest radiography. We examined 29 occupational, recreational, household, and other exposure pathways in the analysis. The prevalence of pleural abnormalities increased with increasing number of exposure pathways, ranging from 6.7% for those who reported no apparent exposures to 34.6% for those who reported ≥ 12 pathways. The factors most strongly associated with pleural abnormalities were being a former W.R. Grace worker, being older, having been a household contact of a W.R. Grace worker, and being a male. In addition to being a former W.R. Grace worker, environmental exposures and other nonoccupational risk factors were also important predictors of asbestos-related radiographic abnormalities. *Key words:* asbestos-related disease, medical screening, pleural plaques, radiographic opacities, radiography, tremolite-actinolite, vermiculite. *Environ Health Perspect* 111:1753–1759 (2003). doi:10.1289/ehp.6346 available via *http://dx.doi.org/* [Online 2 July 2003]

Mining and processing of vermiculite from the world's largest deposit near Libby, Montana, began in the early 1920s and continued for 70 years. In 1963, W.R. Grace acquired the mine from Zonolite Company and operated it until it was closed in 1990. These operations included open-pit mining and on-site milling of the mineral; transporting the raw material by truck and rail to two processing plants in Libby and to plants throughout the United States and Canada, where it was heated and expanded (exfoliated); and finally, shipping the finished product by truck and rail to distribution centers nationally (Myers 1960). Vermiculite is a silicate mineral with the unique property of expanding 8- to 12-fold in volume upon heating (Meisinger 1980; Myers 1960; Otis 1960). Because of its fire-resistant and absorptive properties, vermiculite is used commercially in the construction industry as insulation and filler material, and in agriculture as a soil additive and carrier agent for fertilizers and other chemicals (Lockey 1981; Meisinger 1980). Vermiculite from Montana has been shown to be contaminated with tremolite, actinolite, and other forms of the amphibole series of asbestos, ranging from 2 to 26% in the raw form (Amandus et al. 1987b; Atkinson et al. 1982; Bank 1980; Dixon et al. 1985; Moatmed et al. 1986).

Thus, mining, handling, processing, and personal or commercial use of vermiculite have led to widespread contamination of the Libby area with asbestos-contaminated vermiculite (Dixon et al. 1985).

Although no serious health effects from vermiculite alone have been reported to date (Addison 1995), health effects such as pleural thickening, pleural calcifications, pleural effusions, asbestosis, mesothelioma, and lung cancer from occupational exposure to asbestos have been well documented. Early evidence of pulmonary fibrosis among Libby mine and mill employees was described in an X-ray survey of miners in 1959 (McDonald et al. 1986a). Additional evidence came from a report of 12 cases of pleural effusions over a 12-year period among employees of an Ohio fertilizer plant that processed vermiculite from Libby, followed by a cross-sectional study of workers in the plant that demonstrated a relationship between cumulative fiber exposure and radiographic changes and pleuritic chest pain (Lockey et al. 1984). Two separate but parallel cohort studies of workers at the vermiculite mine in Libby showed excess mortality from lung cancer, malignant mesothelioma, and nonmalignant respiratory disease (Amandus and Wheeler 1987; McDonald et al. 1986a). These same investigators also

conducted radiographic studies of then-current workers and found that the prevalence of pleural thickening and small opacities increased with increasing levels of cumulative fiber exposure (Amandus et al. 1987a; McDonald et al. 1986b). Together, these findings provide substantial evidence that exposure to the amphibole type of asbestos from the Libby vermiculite mine results in adverse respiratory health effects similar to those seen with exposure to other forms of asbestos.

Reported cases of mesothelioma among household contacts of asbestos workers led to a growing concern that asbestos exposure and the risk of later disease could spread beyond the workplace to the home and community (Anderson et al. 1976; Berry 1997; Hansen et al. 1993, 1998; Magnani et al. 2000, 2001; Newhouse and Thomson 1965; Wagner et al. 1960). Several studies have reported an increased prevalence of pleural thickening, pleural plaques, and calcifications as well as parenchymal opacities among household members of asbestos workers (Anderson et al. 1976, 1979; Kilburn et al. 1985). Libby area physicians have reported cases of asbestos-related pulmonary disease among household contacts of former mine workers and other residents of the community who were not directly associated with the mining or processing operations (Whitehouse 2000).

Although household contacts may have been exposed by workers taking home asbestos on their clothes, shoes, and hair, numerous

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other sources of environmental asbestos exposure exist for Libby community members. Air sampling in downtown Libby in 1975 and at several points in the 1980s detected levels of asbestos well above the Occupational Safety and Health Administration's occupational limit of 0.1 fiber/cm^3 over 8 hr of exposure (Atkinson et al. 1982; Dixon et al. 1985; U.S. Department of Labor 1994). Residents could have also been exposed to asbestos through the use of vermiculite in gardening activities, in home insulation, as aggregate in driveways, or through other uses around the home. Additionally, Libby residents have described other activities that involved close contact with vermiculite, such as playing in piles of vermiculite at the processing facilities, expanding or "popping" vermiculite at home by heating pieces of the ore over the stove, playing at the baseball field located adjacent to the vermiculite expansion plant, and playing along Rainey Creek Road that leads from town to the vermiculite mine.

A community-based medical testing program was initiated in response to reports of illness among people exposed to asbestos-contaminated vermiculite in Libby. In this article we outline the results from radiographic testing and self-reported exposure pathways for 7,307 persons who participated in this program. The main objectives were to *a*) identify and quantify possible asbestos-related pleural and interstitial abnormalities among participants and *b*) examine associations between these outcomes and the participants' exposure histories.

Materials and Methods

Participants and data collection. People were eligible for participation in the medical testing program if they had resided, worked, attended school, or participated in other activities in the Libby, Montana, area for ≥ 6 months before 31 December 1990. We identified participants from local telephone directories and through paid newspaper, radio, and television advertisements placed locally and throughout the northwest region of the United States, and in the major newspapers in Chicago, Illinois; Boston, Massachusetts; New York, New York; and Dallas, Texas. The highest readership days of each newspaper were targeted. In addition, word of mouth and medical referrals brought participants to the testing program. A toll-free telephone line was established for interested persons to obtain information about the program and to determine eligibility for screening participants. Telephone screening to determine eligibility began in April 2000 and continued through September 2001. Eligible persons living outside of Libby had to provide their own transportation to Libby for medical evaluation. In-person interviews and medical testing were conducted in Libby in two waves:

from July through November 2000 and from July through September 2001. After informed consent was obtained, trained interviewers administered a computer-assisted questionnaire to obtain demographic characteristics, residential history, occupational history, household contact history, recreational activities and other potential pathways for vermiculite exposures, cigarette smoking status, medical history, and self-reported symptoms and illnesses. The medical screening consisted of spirometric testing and chest radiographs. In this article we report on the radiographic findings of this program. Spirometric results will be reported separately.

Medical evaluation and classification of outcomes. Chest radiographs were offered to participants ≥ 18 years of age and included posterior–anterior (P-A), right anterior-oblique, and left anterior-oblique views. Women of child-bearing age were informed that they should postpone their chest radiograph if they were pregnant. The physician on site assessed the consistency and quality of each chest radiograph taken and provided a routine radiologic interpretation, which included recording asbestos-related changes on a summary report form. If findings on a chest radiograph suggested the need for urgent medical attention, the physician completed a referral form, and the participant was counseled and directed to an appropriate source of medical care.

After initial evaluation and interpretation by the on-site physician, the participants' chest radiographs were read and classified independently by three B-readers certified by the National Institute for Occupational Safety and Health, without knowledge of the subject's age, smoking history, or exposure category, according to guidelines developed by the International Labor Organization (ILO 1980). Although the P-A view is recommended by the ILO's guidelines for the classification of radiographs (ILO 1980), we used the lateral right and left oblique views as well as the P-A view for evaluating abnormalities. The addition of right and left oblique views increases the precision and the sensitivity and specificity of chest radiographs in finding pleural abnormalities not evident on the P-A view alone (Lawson et al. 2001; Levin et al. 2000).

A subject was classified as having a pleural abnormality if two out of three B-readers indicated *a*) any unilateral or bilateral pleural calcification on the diaphragm, chest wall, or other site or *b*) any unilateral or bilateral pleural thickening or plaque on the chest wall, diaphragm, or costophrenic angle site, consistent with asbestos-related pleural disease, using the P-A view, the oblique views, or a combination of those views. A subject was classified as having an interstitial abnormality if two out of three B-readers indicated the

presence of opacities, applying ILO guidelines, with a profusion of 1/0 or greater using the P-A view only.

Exposure characterization. To describe potential exposures to asbestos or vermiculite, participants were asked if they had ever worked for W.R. Grace or Zonolite (WRG) or as a contractor for WRG; if they had ever been exposed to dust at non-WRG jobs; if they had ever mixed, cut, or sprayed asbestos; if they had ever had other occupational exposure to asbestos; or if they had exposure to asbestos in military service. In addition, participants where asked if they had ever had a job as a pipe or steam fitter, plumber, brake repair person, insulator, dry wall finisher, carpenter, roofer, electrician, or welder. Some questions sought information about potential exposures in daily life, including having been a household contact of a WRG worker (during the time the worker was at WRG), length of residence in the Libby area (categorized by quartiles for analysis: 6 months through 14 years, 15–22 years, 23–34 years, and > 34 years), and having asbestos products in the home or using vermiculite in gardening or insulation (yes or no). There were questions about recreational activities such as playing in vermiculite piles, popping vermiculite, and playing on the baseball field near the expansion plant, or playing along the Rainey Creek Road—the road to the mine (never, sometimes, or frequently). Participants were also asked if they had any other contact with vermiculite (never, sometimes, or frequently).

Covariates. Age, sex, cigarette smoking status, a history of chest injury or chest surgery, tuberculosis, pneumonia, scleroderma, lupus, rheumatoid arthritis, congestive heart failure, cancer, or pulmonary disease were ascertained

Table 1. Distribution and characteristics of participants in the Libby medical screening program.

Variable	No. (%)
Age	
10–17	600 (8.2)
18–44	2,519 (34.5)
45–64	3,031 (41.5)
≥ 65	1,157 (15.8)
Sex	
Male	3,601 (49.3)
Female	3,706 (50.7)
Smoking history	
Never	3,711 (50.8)
Ex-smoker	2,156 (29.5)
Current	1,438 (19.7)
Years lived in Libby	
0.5–13	1,864 (25.7)
14–21	1,892 (26.1)
22–33	1,761 (24.2)
≥ 34	1,747 (24.1)
BMI	
0–18	234 (3.2)
19–24	2,185 (30.2)
25–29	2,529 (34.9)
≥ 30	2,292 (31.7)

from the examiner-administered questionnaire. Participants were also asked if they were *a*) not at all, *b*) a little, or *c*) very concerned that something in the neighborhood environment may be harmful. Body mass index (BMI) was calculated from height and weight measurements obtained during the medical examination and classified into standard categories (< 18, 19–24, 25–29, and ≥ 30) for descriptive purposes and into quartiles (< 24, 24–27, 28–31, ≥ 32) on the basis of its distribution in the participants for statistical modeling. Age was modeled as a continuous variable, and cigarette smoking status was classified as never smoked or ever having smoked (ex-smoker and current smoker).

Statistical analysis. We used unconditional logistic regression modeling to estimate, by use of the odds ratio (OR) and 95% confidence intervals (CI), the risk of respiratory abnormalities for each of the exposure pathways while controlling for all other exposure pathways and other established and suggested risk factors for respiratory illness. Models were estimated separately for the outcomes of pleural abnormalities and interstitial abnormalities.

Table 2. Number (percent) of participants reporting each exposure pathway.[a]

Exposure pathway	No. (%)
Ever work for WRG	370 (5.1)
Secondary contractor work	465 (6.4)
Dust exposure at non-WRG jobs	2,396 (32.8)
Vermiculite exposure at non-WRG jobs	1,103 (15.2)
Worked non-WRG job	
As a pipe fitter or steam fitter	164 (2.2)
As a plumber	168 (2.3)
As a brake repair person	249 (3.4)
As an insulator	240 (3.3)
As a dry wall finisher	221 (3.0)
As a carpenter	568 (7.8)
As a roofer	362 (5.0)
As an electrician	187 (2.6)
As a welder	467 (6.4)
Mixing, cutting, or spraying asbestos	144 (2.0)
In a shipyard or performed ship construction or repair	129 (1.8)
Exposed to asbestos	851 (11.8)
Worked around anyone performing non-WRG jobs (listed above)	804 (11.0)
Asbestos exposure in the military	182 (2.7)
Lived with WRG workers	1,418 (19.5)
Vermiculite insulation in Lincoln County homes	3,017 (45.8)
Asbestos products in Lincoln County homes	1,155 (17.4)
Used vermiculite for gardening	3,702 (51.9)
Used vermiculite around the home	638 (8.8)
Handled vermiculite insulation	3,635 (50.5)
Recreational activities along Rainey Creek Road	4,898 (67.4)
Played at ball field near expansion plant	4,772 (65.5)
Played in vermiculite piles	2,442 (33.7)
Popped vermiculite	2,797 (38.4)
Other contact with vermiculite	2,232 (31.0)

[a]Participants may have answered "yes" to more than one category.

We first tabulated the frequencies of demographic and other participant characteristics to obtain a descriptive profile of the participants. We then tabulated prevalence of pleural abnormalities and interstitial abnormalities for each of the occupational, recreational, and household exposure pathways and for each of the covariates, as well as for the increasing number of exposure pathways. Crude ORs and 95% CIs for pleural abnormalities and interstitial abnormalities were calculated for each of these pathways and covariates. We began an unconditional logistic regression multivariate model with all potential exposure pathways and covariates. The presence of effect modification was evaluated in this model by use of interaction terms between the exposure variables and demographic characteristics. We modeled age as a continuous variable and, when appropriate, included linear and nonlinear terms in the model. Criteria for inclusion in the final model included statistical significance of the explanatory variables ($p < 0.10$), stability of the estimate, effect on other variables in the model (confounding), biologic plausibility of the interaction, and fit of the model. We used a logistic regression model to describe an exposure–response relationship with the number of exposure pathways while controlling for covariates. A chi-square test and pairwise contrasts between pathway levels were used to assess the statistical significance of this trend. We used Procedures in SAS, release 8.01 (SAS Institute 2001) to perform all statistical analyses.

Results

Description of the participants. Of 12,829 persons screened by telephone, 3,527 did not meet the criteria for eligibility and 66 had unknown eligibility status. Of those eligible, 1,689 either did not schedule an appointment or did not report for medical testing, 231 refused medical testing, 4 had died before they were tested, and 5 were physically unable to come in for testing. The remaining 7,307 current and former residents of Libby and the surrounding area participated in the medical testing program (6,149 in the first wave and 1,158 in the second wave, resulting in a 78.6% participation rate). Among those who participated, 81% stated that they currently lived in Montana, and of those, 80% currently resided in the Libby, Troy, or Eureka areas. Most of the participants outside of Montana came from Idaho, Oregon, and Washington. Because participants in the first and second years of medical testing were similar in demographic characteristics, exposure pathways, concern about neighborhood contamination, and prevalence of outcomes, the data from both years were combined.

Of the 7,307 participants, 6,668 (91.2%) were ≥ 18 years of age and therefore were eligible for and received chest radiographs. During

the two waves of medical testing, the physician on site determined that 525 radiographs could not be read because of poor quality, and these were later repeated.

Characteristics of the participants are presented in Table 1. The participants were almost evenly divided by sex with 49% male and 51% female. The majority of participants were 18–64 years of age (76.0%). Almost half of the participants were former or current smokers. Roughly 74% of participants had lived in the Libby area for ≥ 14 years. Many of the participants were overweight. A BMI of 25–29.9 is considered overweight, and a BMI of ≥ 30 is considered obese; 67% of participants had a BMI of ≥ 25, with almost 32% of all participants in the obese category.

The 29 exposure pathways used in the analyses and the number of participants reporting each pathway are presented in Table 2. These include occupational, recreational, household, and other potential exposures. Participants may have reported one, several, or none of these exposures. The most common pathways were recreational activities along Rainey Creek Road (4,898, or 67.4%), playing in the baseball fields near the expansion plant (4,772 participants, or 65.5%) and playing in the vermiculite piles (2,442, or 33.7%). The most common occupational exposure was dust exposure at non-WRG jobs (2,396, or 32.8%), and the least common occupational exposure was working in a shipyard or ship construction or repair (129, or 1.8%).

Males were much more likely than females to have reported occupational exposures. Among those who reported having worked at WRG, 341 (92.2%) were male and 29 (7.8%) were female. Males also were more likely than females to have been exposed to asbestos or vermiculite during nonoccupational activities, although differences were less pronounced when compared with the occupational exposures. For instance, among the exposure pathways, males were more likely than females to report dust exposures at work (76.8% vs. 23.2%), working at any job with exposure to asbestos (71.2% vs. 28.8%), vermiculite exposure at other jobs (77.2% vs. 22.8%), frequently playing in vermiculite piles (61.1% vs. 38.9%), or frequently popping vermiculite (54.4% vs. 45.6%). The only notable exception was that females were more likely than males to have been a household contact of a WRG worker (60.0% of household contacts were female).

Pleural and interstitial abnormalities. Table 3 presents the crude prevalence rates of pleural and interstitial abnormalities by exposure pathways for 6,668 participants, ≥ 18 years of age, who underwent chest radiography. The pathways presented here are not mutually exclusive; for example, a participant who reported having been a WRG worker, playing

on the baseball field, and using vermiculite for gardening would be represented in all three categories. The overall prevalence of pleural abnormalities was considerably greater than the prevalence of interstitial abnormalities. Almost 18% of participants who underwent chest radiography had a pleural abnormality, compared with only 1% of participants having an interstitial abnormality. The exposure pathway with the highest unadjusted rate for pleural abnormalities was being a former WRG worker, with 186 (51.0%) having pleural abnormalities. WRG workers also had the highest rate of interstitial abnormalities (3.8%). Other pathways associated with high rates of pleural abnormalities included history of asbestos exposure in the military (42.9%), working in a shipyard or performing shipyard construction or repair (34.9%), and being a secondary contract worker for WRG (34.8%). The lowest prevalence of pleural abnormalities (14.4%) was seen for the "sometimes" exposure category of playing at the baseball field near the expansion plant.

The rate of pleural abnormalities increased from 5.1% in younger adults 18–44 years of age, to 20.0% for participants 44–65 years of age, to 39.7% for participants ≥ 65 years of age. Males had a significantly higher rate of pleural abnormalities (26.6%) compared with female participants (9.1%). The crude OR for pleural abnormalities among males compared with females was 3.61 (95% CI, 3.14–4.15). Current and former smokers (ever smokers) were twice as likely to have findings of pleural abnormalities than those who never smoked (crude OR, 2.18; 95% CI, 1.91–2.49). Participants with a high BMI were more likely to have a finding of pleural abnormalities than were those with a lower BMI. This risk increased with increasing quartiles of BMI. Compared with the first quartile, the crude ORs for pleural abnormalities were 1.80 (95% CI, 1.44–2.24) for the second quartile, 2.80 (95% CI, 2.253–3.49) for the third quartile, and 3.71 (95% CI, 2.99–4.60) for the highest quartile. Increasing length of residence in the Libby area was also associated with increasing risk of pleural findings. Compared with participants residing in the Libby area for < 14 years, crude ORs ranged from 0.91 (95% CI, 0.73–1.13) for a residential duration of 14–21 years to 3.62 (95% CI, 3.00–4.36) for residential duration of > 34 years.

Table 4 presents the final unconditional logistic regression model in which all exposure pathways, as well as other risk factors and interaction terms, were assessed for their contribution to the risk of pleural abnormalities. The model shows that the following factors were associated with pleural abnormalities: having been a WRG worker, having been a household contact of a WRG worker, having

been exposed to asbestos in the military, having played in vermiculite piles, being male, being older, having lived in the Libby area for a longer period of time, having smoked cigarettes, and having a high BMI.

We found significant interaction terms between age and being a former WRG worker and between sex and being a household contact of a WRG worker. Although the odds of finding a pleural abnormality is higher for former WRG workers than for nonworkers, the magnitude of the OR decreases with increasing age. Table 5 shows that estimated odds of finding a pleural abnormality ranges from 4.18 for a 30-year-old former WRG worker compared with a nonworker, to 1.14 for a 90-year-old former worker compared with a non-WRG worker, after adjusting for all other variables in the model. The model also shows that the estimated odds of finding a pleural abnormality is almost five times greater for males than for females (among nonhousehold contacts) after adjusting for other variables in the model (OR,

4.84; 95% CI, 3.83–6.11). The estimated odds of finding a pleural abnormality is 3.62 (95% CI, 2.70–4.83) times greater for females who were household contacts of former WRG workers when compared with females who were not. The corresponding increased odds of pleural abnormalities among male household contacts is 1.71 (95% CI, 1.32–2.22).

As age increases, the odds of finding a pleural abnormality increase, although the rate of that increase slows. For example, among non-WRG workers, the estimated odds of finding a pleural abnormality for a 40-year-old was three times greater than for a 30-year-old (OR, 3.04; 95% CI, 2.69–3.43). However, the odds reduce to 2.02 (95% CI, 1.87–2.18) when comparing a 60-year-old with a 50-year-old. This effect is slightly attenuated for age contrasts involving former WRG workers (OR = 2.45 for a 40-year-old vs. a 30-year-old; OR = 1.63 for a 60-year-old vs. a 50-year-old). Among the recreational exposure pathways, those who played in the

Table 3. Number (percent) of pleural and interstitial abnormalities by exposure pathways.

Exposure pathway	Pleural, all views	Interstitial, P-A view
All participants ≥ 18 years of age (n = 6,668)	1,186 (17.8)	54 (0.8)
Ever worked for WRG (n = 365)	186 (51.0)	14 (3.8)
Secondary contractor work (n = 463)	161 (34.8)	8 (1.7)
Dust exposure at non-WRG jobs (n = 2,390)	527 (22.1)	21 (0.9)
Vermiculite exposure at non-WRG jobs (n = 1,100)	254 (23.1)	8 (0.7)
Worked non-WRG job		
As a pipe or steam fitter (n = 164)	54 (32.9)	2 (1.2)
As a plumber (n = 168)	50 (29.8)	3 (1.8)
As a brake repair person (n = 247)	68 (27.5)	2 (0.8)
As an insulator (n = 240)	44 (18.3)	1 (0.4)
As a dry wall finisher (n = 221)	41 (18.6)	0 (0.0)
As a carpenter (n = 566)	129 (22.8)	2 (0.4)
As a roofer (n = 361)	79 (21.9)	2 (0.6)
As an electrician (n = 187)	48 (25.7)	3 (1.6)
As a welder (n = 465)	122 (26.2)	5 (1.1)
Mixing, cutting, or spraying asbestos (n = 143)	47 (32.9)	2 (1.4)
In a shipyard or performed ship construction or repair (n = 129)	45 (34.9)	4 (3.1)
Exposed to asbestos (n = 849)	208 (24.5)	7 (0.8)
Worked around anyone performing previous 12 jobs (n = 801)	184 (23.0)	6 (0.8)
Asbestos exposure in the military (n = 182)	78 (42.9)	2 (1.1)
Lived with WRG workers (n = 1,376)	358 (26.0)	17 (1.2)
Vermiculite insulation in homes (n = 2,819)	600 (21.3)	27 (1.0)
Asbestos products in homes (n = 1,071)	222 (20.7)	9 (0.8)
Used vermiculite for gardening (n = 3,469)	702 (20.2)	29 (0.8)
Used vermiculite around the home (n = 586)	120 (20.5)	1 (0.2)
Handled vermiculite insulation		
Sometimes (n = 2,739)	572 (20.9)	25 (0.9)
Frequently (n = 732)	191 (26.1)	9 (1.2)
Recreational activities along Rainey Creek		
Sometimes (n = 3,134)	546 (17.4)	21 (0.7)
Frequently (n = 1,433)	307 (21.4)	15 (1.1)
Played at ball field near expansion plant		
Sometimes (n = 2,034)	293 (14.4)	10 (0.5)
Frequently (n = 2,290)	432 (18.9)	16 (0.7)
Played in vermiculite piles		
Sometimes (n = 1,430)	269 (18.8)	8 (0.6)
Frequently (n = 875)	220 (25.1)	5 (0.6)
Popped vermiculite		
Sometimes (n = 2,140)	460 (21.5)	13 (0.6)
Frequently (n = 538)	138 (25.7)	9 (1.7)
Other contact with vermiculite		
Sometimes (n = 1,759)	340 (19.3)	14 (0.8)
Frequently (n = 323)	73 (22.6)	5 (1.6)

vermiculite piles frequently had twice the risk of pleural abnormalities compared with those who never played in the piles (OR, 2.02; 95% CI, 1.59–2.57).

The rate of interstitial abnormalities increased from 0.04% in younger adults 18–44 years of age, to 0.5% for participants 44–65 years of age, to 3.2% for participants ≥ 65 years of age. Males had a higher rate of interstitial abnormalities (1.2%) compared with female participants (0.4%). The crude OR for interstitial abnormalities among males compared with females was 2.68 (95% CI, 1.47–4.86). Current and former smokers (ever smokers) were twice as likely to have findings of interstitial abnormalities than were those who never smoked (crude OR, 2.18; 95% CI, 1.91–2.49). BMI was not associated with interstitial abnormalities. Participants residing in the Libby area for > 34 years had a 4-fold increased risk of interstitial abnormalities (crude OR, 4.38; 95% CI, 1.82–10.54).

We assessed the independent contributions of the exposure pathways and covariates to the risk of interstitial abnormalities using multivariate logistic regression. The strongest predictors of interstitial abnormalities were having been a former WRG worker (OR, 2.71; 95% CI, 1.26–5.87) and being male (OR, 2.48; 95% CI, 1.08–5.68). Increasing age, having worked on a ship or done ship repair, and having a history of pneumonia were also significantly associated with interstitial abnormalities.

The models above demonstrate the relative importance of various exposure pathways and covariates in predicting pleural and interstitial abnormalities. However, the majority of participants reported multiple pathways rather than a single exposure pathway. Only 2% of the participants reported "no" to all exposure pathways, whereas 48.1% of the participants

reported six or more exposure pathways. The prevalence rates for pleural and interstitial abnormalities among participants with multiple exposures compared with those with no apparent exposures is displayed in Figure 1. An exposure–response relationship is apparent between the number of exposure pathways and the prevalence of pleural abnormalities. Among those who reported "no" to all exposure pathways, 6.7% had pleural abnormalities, compared with an almost 35% prevalence among those reporting ≥ 12 pathways. An exposure–response relationship is not seen for interstitial abnormalities, which had a prevalence of about 1% regardless of the number of pathways reported. This trend in increasing pleural abnormalities with increasing number of pathways could not be solely attributed to former WRG workers. This relationship was apparent, although slightly attenuated, even after we removed the workers from the analysis (30.1% prevalence of pleural abnormalities among those reporting ≥ 12 pathways). Table 6 presents the results from an unconditional logistic regression model of this relationship controlling for age, sex, BMI, smoking, and residential duration. There was a statistically significant trend of increased pleural abnormalities with increasing number of pathways, with ORs ranging from 1.40 for one pathway to 3.75 for ≥ 12 pathways.

Discussion

In this analysis we sought to identify radiographic abnormalities and significant exposure pathways among participants in a community-based medical testing program in Libby, Montana. Almost 18% of the participants undergoing radiography had pleural abnormalities identified by at least two of three certified B-readers. Interstitial abnormalities

were identified in 1% of participants. These findings are consistent with clinical reports by Libby area physicians that patients more commonly have pleural abnormalities and that interstitial disease is generally diagnosed at a later stage (Whitehouse 2000). Pathologic effects of asbestos and of asbestos-contaminated vermiculite have been established for both the pleura and parenchyma (Amandus et al. 1987a; Becklake 1976; Lockey et al. 1984; McDonald et al. 1986b), and the severity of these effects has been associated with latency, duration, and intensity of exposures among workers. Our findings of predominantly pleural effects suggests less prolonged or intense exposures and/or shorter latency periods. Alternatively, the cross-sectional study design may have removed a disproportionate number of people suffering or dying from more severe disease. Furthermore, differential respiratory health effects observed in a number of asbestos-exposed populations also may be due to differences in the physical and chemical properties of the mineral fiber exposures (ATSDR 2001).

Our analyses further demonstrated a statistically significant increase in the prevalence of pleural abnormalities with an increasing number of exposure pathways. Participants reporting more pathways might be expected to have more cumulative exposure than would those reporting fewer pathways. Those who reported ≥ 12 exposure pathways had a prevalence rate of almost 35% for pleural abnormalities, compared with a prevalence of 6.7% for those who reported no exposure pathways. No directly comparable Montana or U.S. population studies are available to estimate the rate of pleural abnormalities among those in Libby with no work-related exposures. Studies of differing groups within the United States believed to have no substantive work-related asbestos exposures have found prevalence of pleural abnormalities ranging from 0.2% among blue-collar workers in North Carolina (Castellan et al. 1985), to 2.3% among patients at Veterans Administration hospitals in New Jersey (Miller and Zurlo 1996), to 4.6% among urban New Jersey residents (Anderson et al. 1979). Subjects in our category of "no apparent exposure" had a greater rate of pleural abnormalities (6.7%) than did those in the

Table 4. Risk of pleural abnormalities by exposure pathways and covariates.[a]

Variable	Level	Beta	Adjusted OR (95% CI)
Intercept		−19.46	
Workwr	Yes	2.08	—[b]
HHWR	Yes	1.29	—
Vermplay	Sometimes	0.60	1.82 (1.48–2.25)
	Frequently	0.70	2.02 (1.59–2.57)
Sex	Male	1.58	—
Resdur (years)	14–21	0.25	1.29 (0.97–1.71)
	22–33	0.22	1.25 (0.96–1.62)
	≥ 34	0.75	2.12 (1.66–2.70)
ln(Age)		3.86	—
BMI	2nd quartile (24–27)	0.18	1.20 (0.91–1.60)
	3rd quartile (28–31)	0.56	1.75 (1.32–2.32)
	4th quartile (≥ 32)	1.14	3.12 (2.37–4.12)
Smoke	Ever	0.30	1.35 (1.14–1.59)
Age × Workwr	Yes	−0.02	—
HHWR × sex	Yes × male	−0.75	—
Milexp	Yes	0.47	1.61 (1.10–2.35)
Age × ln(Age)		−0.05	—

Abbreviations: HHWR, household contact with WRG worker; Milexp, asbestos exposure in the military; Resdur, duration of residence in Libby area; Vermplay, played in vermiculite piles; Workwr, ever worked for WRG.
[a]Twenty-nine exposure pathways and all covariates were assessed for their contribution to the risk of pleural abnormalities; final model fit: Hosmer-Lemeshow goodness-of-fit test, $\chi^2 = 2.47$, degrees of freedom = 8, $p = 0.96$. [b]A single value cannot be presented for adjusted ORs involving interaction terms.

Table 5. Risk of pleural abnormalities for former WRG workers compared with non-WRG workers at different ages.

Age (years)	OR (95% CI)
30	4.18 (2.20–7.94)
40	3.37 (2.14–5.29)
50	2.71 (2.00–3.67)
60	2.18 (1.66–2.86)
70	1.76 (1.19–2.58)
80	1.41 (0.80–2.48)
90	1.14 (0.53–2.44)

control groups or general populations found in other studies. Given the ubiquitous nature of vermiculite contamination in Libby, along with historical evidence of elevated asbestos concentrations in the air, it would be difficult to find participants who could be characterized as unexposed. Our unexposed category was based on negative responses to specific pathway questions and is likely to have missed some potential exposure pathways.

Not unexpectedly, being a former WRG worker was a significant risk factor for each of the outcomes examined in these analyses. With respect to pleural abnormalities, we found a significant interaction between age and being a former WRG worker, in which the magnitude of the OR among former WRG workers compared with nonworkers decreases with increasing age. This may be due to nonworkers having had the opportunity for accumulating multiple, nonoccupational exposures with increasing age, thus making them more similar to former WRG workers. This result may also be attributed to a survivor effect. If workers are at a higher risk of fatal respiratory disease than nonworkers, and that risk of dying increases with age, a cross-sectional design might show older surviving workers to be more similar to older nonworkers in terms of pleural outcome. A study that linked death certificate data with employment information from a Libby mining and milling facility found that, between 1979 and 1998, 11 of 12 asbestosis decedents, 21 of 124 lung cancer decedents, and 2 of 3 mesothelioma decedents were former workers (ATSDR 2002). Given the relatively small proportion of former WRG workers in this study, differential mortality of workers may explain this interaction.

In addition to being a former WRG worker, results from our multivariate logistic regression models indicate the other factors most strongly related to having pleural abnormalities were being older, being a household contact of a WRG worker, and being male. Women household contacts of former WRG workers compared with noncontacts were at a greater risk of pleural abnormalities than were male contacts versus noncontacts. This may be due to gender differences in responsibilities for laundry and cleaning that may lead to greater

exposure to "take-home" dust. Additionally, women workers, who traditionally are more likely to be found in administrative or office occupations within industries, may have been exposed to less vermiculite on the job site than were male workers and thus brought less vermiculite home. Men had almost five times the risk of pleural abnormalities compared with women. Although men and women may have engaged in similar occupational and recreational activities, gender differences in intensity or duration of activities may explain this excess risk among men. Other pathways of exposure associated with pleural abnormalities included playing in vermiculite piles and having been exposed to asbestos in the military.

BMI was also associated with pleural abnormalities in these analyses. Although there is no known biologic or pathologic relationship between body mass and the development of pleural abnormalities, a heavier BMI can make it more difficult to distinguish between pleural abnormalities and subpleural or extrapleural fat (Proto 1992; Sargent et al. 1984). Nevertheless, even after controlling for BMI, we were able to demonstrate a significant trend in increasing pleural abnormalities with increasing number of exposure pathways. Current and former smokers were also more likely to have findings of pleural abnormalities than were those who never smoked. Smoking was not associated with pleural changes in previous studies of Libby vermiculite workers, although the authors suggest that the small number of nonsmokers may have limited its assessment (Amandus et al. 1987a; McDonald et al. 1986b). Our finding of a smoking effect on the prevalence of pleural abnormalities may indicate an independent effect, or it may have resulted from an association between cigarette smoking and one or more exposure risk factors or with unmeasured exposures. Although we found that current and former smokers were twice as likely to have interstitial abnormalities (crude OR, 2.2; 95% CI, 1.9–2.5), this association was no longer statistically significant in the full model. The exposures and covariates most strongly associated with interstitial abnormalities were increasing age, having been a former WRG worker, having worked a job in a shipyard, and having a history of pneumonia.

The association with shipyard work would not be unexpected given the probable higher levels of exposure.

The principal limitations of these analyses are the cross-sectional design of the testing program and self-selection of participants, rather than random selection. Studies involving volunteers are subject to selection bias that can occur in a number of ways. It is possible that those who volunteered for the program were more likely to have been previously diagnosed with an illness or were more likely to have experienced symptoms compared with a randomly selected population. Also more likely to participate may have been the "worried well" or very concerned healthy persons. Alternatively, persons who believed they had little or no exposure may have chosen not to participate, or those already diagnosed with disease may have felt they had little to gain from participation. The requirement for travel to Libby also may have contributed to selection bias. In addition, cross-sectional studies are limited in assessing in- or out-migration that may have important effects on the population. Nevertheless, the medical testing program screened 7,307 people in Libby and the surrounding area. Of those, 5,846 were from the Libby area. This represents a substantial proportion (61%) of the 9,521 persons in central Lincoln County—a population that has been relatively stable for the past 30 years (U.S. Bureau of the Census 2002). Before the start of the medical testing program, there had been national-level press coverage of the asbestos-contaminated vermiculite in Libby that may have resulted in a high level of community awareness. This, along with an intensive community outreach campaign, resulted in high participation rates.

Another potential limitation in this analysis was that the B-readers knew that the radiographs were from the Libby medical screening program and control films were not included among the Libby series of radiographs. Readers were, however, blinded to the exposure pathways and other characteristics reported by these participants. Additionally, observer bias was limited by following established standards for interpretation of chest radiographs that require
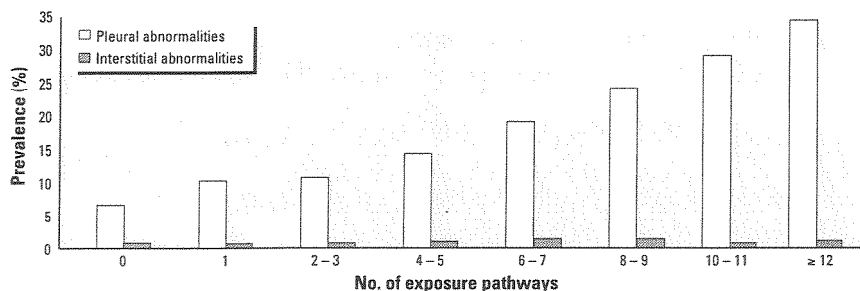

Figure 1. Prevalence of abnormalities by number of exposure pathways.

Table 6. Risk of pleural abnormalities by number of exposure pathways (baseline: no apparent exposure) controlling for age, sex, BMI, residential duration, and smoking.

No. of exposure pathways	OR (95% CI)
1	1.40 (0.60–3.26)
2–3	1.36 (0.62–2.97)
4–5	1.80 (0.83–3.90)
6–7	2.41 (1.11–5.23)
8–9	3.12 (1.43–6.83)
10–11	3.48 (1.56–7.77)
≥ 12	3.75 (1.65–8.50)

Final model fit: Hosmer-Lemeshow goodness-of-fit test, χ^2 = 5.45, degrees of freedom = 8, p = 0.71.

the use of B-readers trained in detection of occupational disease, and agreement in two of three B-readers. Nevertheless, differences in interpretation of radiographs remains a source of variation (Bourbeau and Ernst 1988). All films were taken in one location, and those judged to be of poor quality or unreadable were repeated, thereby limiting variability in radiographic technique and quality.

The Libby community medical testing program was designed primarily to identify illnesses experienced by participants exposed to asbestos to better inform local health care providers and to characterize pathways of exposure. However, these results may have broader implications because vermiculite from the Libby mine was shipped to and processed at facilities throughout the country. For example, a recent case report describes a 65-year-old accountant who presented with extensive pleural plaques and end-stage pulmonary fibrosis (Wright et al. 2002). This patient progressed rapidly to respiratory failure and death. His only exposure to asbestos was during a summer job in a vermiculite expansion plant 50 years before his death. The asbestiform fibers found in his lungs were very similar to those contaminating the vermiculite mined near Libby, Montana. In addition to occupational exposures at the many vermiculite expansion plants, asbestos-contaminated vermiculite was placed in millions of homes and businesses across the country as insulation. The U.S. Environmental Protection Agency recently decided to warn consumers that disturbing this insulation can release asbestos fibers, resulting in hazardous respiratory exposures (Schneider 2003).

The magnitude of the public health problem nationally is not yet clear, but this analysis provided important information on the prevalence and degree of asbestos-related abnormalities among current and former Libby residents. As such, it forms a foundation for further analyses of exposure pathways in Libby and other sites where vermiculite was shipped, handled, and processed. The results of this analysis will inform those planning intervention services and those future health investigators of the natural history of respiratory illnesses among people exposed to asbestos-contaminated vermiculite.

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OCCUPATIONAL DISORDERS OF THE LUNG:
Recognition, Management, And Prevention

Edited by

David J. Hendrick, MSC, MD, FRCP, FFOM
Professor of Occupational Respiratory Medicine, University of Newcastle upon Tyne,
Department of Respiratory Medicine, Royal Victoria Infirmary,
Newcastle upon Tyne, UK

P. Sherwood Burge, MSC, MD, FRCP, FFOM, DIH
Director, Occupational Lung Disease Unit,
Birmingham Heartlands Hospital,
Birmingham, UK

William S. Beckett, MD, MPH
Professor, Enviromental Medicine and Medicine,
University of Rochester School of Medicine and Dentistry,
Rochester, NY, USA

Andrew Churg, MD
Professor, Department of Pathology,
University of British Columbia,
Vancouver, BC, Canada

BENIGN PLEURAL DISEASE

Robin Rudd

Contents

INTRODUCTION

Pleural disease of occupational origin is almost exclusively a result of asbestos exposure, although other naturally occurring silicates are occasionally responsible, and there is a possible link between pleural plaques and ceramic fibers. Pleural thickening may accompany silicosis but the intrapulmonary changes dominate the picture. Rarely, pleural disease is a consequence of occupational injury or the occupational contraction of tuberculosis. Asbestos causes both benign and malignant pleural disease. The benign disorders are considered in this chapter; the malignant disease of mesothelioma is dealt with in Chapter 22.

Asbestos exposure causes several different types of benign pleural disease:

- plaque
- pleurisy without effusion
- pleurisy with effusion
- diffuse thickening
- entrapped 'folded (or enfolded) lung'.

Folded lung is also known as rounded atelectasis or Blesovsky's syndrome after the surgeon who first described it; it is closely associated with overlying diffuse pleural thickening. Although most cases of benign pleural disease are recognized from plain chest radiographs, there is greater diagnostic sensitivity from computed tomographic (CT) scans, and a few cases are identified initially at thoracotomy or

autopsy. The frequency of each type of disease increases with increasing cumulative dose of asbestos inhaled. All types of asbestos may cause each type of disease, but there are some differences between fiber types in their propensity to cause different types of pleural disease. For example, in the anthophyllite exposed population of Northern Karelia in Finland, plaques are very common but pleurisy, diffuse pleural thickening, and mesothelioma are uncommon. By contrast, in areas of Turkey where there is exposure to erionite, pleurisy and diffuse thickening are relatively more common and the incidence of mesothelioma is extremely high [1].

PLEURAL PLAQUES

Background

Plaques are circumscribed areas of thickening of the parietal pleura of the chest wall and diaphragm. Occasionally they affect the visceral pleura, including that in the fissures.

Causes and epidemiology

Pleural plaques occur in members of the general population without identified exposure to asbestos, but they occur more frequently in subjects with known exposure [2] and are by far the most common respiratory effect of asbestos inhalation. Autopsy studies show a higher prevalence of

plaques than do radiographic surveys, primarily because direct observation is diagnostically more sensitive than plain radiographs, but partly because a population studied at autopsy is generally older and more likely to have sustained occupational exposure than one undergoing chest radiography in life. For example, in a Swedish study, plaques were found in 6.8% of autopsies of which only 12.5% were detected by radiography [3]. In a UK study of a general urban population, plaques were reported from 4.2% of routine autopsies but this figure rose to 11.2% when a specific search for plaques was made in a subsequent series [4]. Plaques may occur after occupational exposure at a lower level than is required to cause asbestosis and are found in household contacts of asbestos workers and in persons exposed to environmental contamination with asbestos [2].

In certain areas, such as parts of Finland, Turkey, and Greece, plaques occur with much increased frequency. This has been attributed to the presence of asbestos in the soil and outcropping rocks [2]. In general, however, plaques are more common in urban than in rural dwellers [5]. Among an urban population, the frequency and extent of plaques at autopsy increases in relation to lung asbestos fiber content [6]. Similarly, among occupationally exposed persons, the prevalence of plaques increases in relation to the degree of asbestos exposure and in relation to the time elapsed since first exposure [7].

Pleural plaques are seldom apparent on plain chest radiographs less than 20 years after first exposure; calcified plaques are rarely seen in this period. In a group of 624 asbestos workers from various industries, plaques were seen in none within 10 years, in 10% by 19 years, in 29% by 29 years, in 32% by 39 years and in 58% by 49 years [8]. In a study of 1117 insulation workers, pleural calcification was found in none of 346 men less than 10 years after first exposure, in only 1.1% of 379 men less than 20 years, in 10.4% up to 30 years, in 34.5% up to 40 years, and in 57.9% more than 40 years after first exposure. The extent of calcification also increased with time [9]. This pattern is probably largely a consequence of long latency and slow progression, though a contributory factor may be that the subjects with the longest periods since first exposure will tend to be the older subjects who were exposed historically to higher doses. There is conflicting evidence concerning the role of smoking. In a study of workers in an asbestos manufacturing plant, the prevalence of plaques was greater in smokers [10] but this relationship was not apparent among insulation workers [11].

Pleural plaques also occur in kaolin workers and talc workers, but in the latter the plaques are proba-

bly caused by contamination of commercial talc [asbestos since asbestos fibers can be identified in bro choalveolar lavage samples from affected subjec [12,13]. There is some evidence that pleural plaqu may be also caused by exposure to refractory ceram fibers, which are amorphous silicates belonging the man-made vitreous fibers group. They are used industrial processes requiring high-temperature ins lation. A retrospective cohort and nested case-contr study of 652 workers involved in the manufacture these fibers identified 19 (3.1%) with plaques, ar one with diffuse pleural thickening [14]. Plaques wei more common more than 20 years after first exposu and increased in frequency in relation to the cumul tive level of exposure. This provides biologic plausib ity of a causal relationship. A nested case-contr study showed that asbestos exposure did not accoui for the observed association between ceramic fib exposure and plaques.

Prognosis

Plaques may become more extensive and they m become more dense through increasing calcification although they may be present for many years witho calcifying. In a few patients, plaques may becom confluent over large areas and lead to a restricti ventilatory defect.

Pleural plaques are not thought to lead directly any of the other benign varieties of asbestos-induce pleural disease, nor to pose any risk of malignan change leading to mesothelioma. Their presenc may indicate, nevertheless, a cumulative level asbestos exposure at which there is an increased ri of mesothelioma or other asbestos-related disorder On average, in the absence of any other eviden about exposure, it is reasonable to assume that su jects with plaques will have had higher exposure asbestos than subjects without plaques. The fr quency of development of other complications asbestos exposure in persons with plaques is no function of the presence of the plaques but of t asbestos exposure that caused the plaques. Sinc plaques may occur after a wide range of differe exposures, the risks of other asbestos-related cond tions may differ widely between different populatio and individuals with plaques.

Persons with plaques' may develop other benig asbestos-induced conditions. A survey of 175 na dockyard workers found that of 143 men who initial had plaques, 33 (23%) had diffuse pleural thickenir at follow-up 10 years later or before death if th occurred within 10 years [15]. Among 155 livir men with benign pleural lesions, mostly plaques, wl were reexamined 10 years later, 16 (10.3%) had sm opacities of category 1/1 pneumoconiosis or high on the scale of the International Labor Office (ILC

presenting radiologic evidence suggestive of asbesto-sis. In addition, 4.5% also had bilateral inspiratory basal crackles and impairment of the gas transfer factor below 75% of predicted, representing clinical evidence of asbestosis [15]. Comparable data were not provided for men who had no pleural abnormalities at the initial survey.

The presence of pleural plaques has been shown to be a risk factor for the development of malignancy. In a Swedish study of 1596 men with plaques followed for 16 369 person-years, there were nine mesotheliomas compared with 0.8 expected [16]. A necropsy-based Italian study found a higher frequency of plaques in subjects with mesothelioma than in other subjects and the odds ratio for mesothelioma increased with the size of the plaques, suggesting that larger plaques were associated with higher doses of asbestos [17].

The Swedish follow-up study of 1596 men found 40 bronchial carcinomas compared with 32.1 expected after correcting for smoking habits, indicating a 1.4-fold risk factor [16]. However, there have been conflicting reports as to whether or not patients with plaques are at increased risk of lung cancer. One review suggested that those studies that have supported an increased risk of lung cancer in subjects with plaques were the most subject to selection bias [18]. Each of the studies reviewed was unsatisfactory in one or more ways: they concerned populations with unknown or low level asbestos exposure, control for the effect of smoking was unsatisfactory, latency was ignored, follow-up was incomplete, and statistical power to detect small increases in risk was not estimated. The extent to which persons with plaques are at risk of cancer will depend upon the exposure experienced rather than the presence of the plaques and, therefore, the risk will vary between different populations with plaques. Unrealistically large population studies would be needed to demonstrate small increases in risk (e.g. of the order of 1.1) resulting from relatively low levels of environmental asbestos exposure, whereas studies of heavily exposed persons with plaques have demonstrated significantly increased risks factors of up to two- to threefold [19,20].

Recognition

Clinical features

Plaques are usually an incidental finding on a chest radiograph. They are not usually responsible for any symptoms, although rarely patients may be aware of an uncomfortable grating sensation associated with calcified plaques and ventilatory movement. Breathlessness is usually caused by a coexisting condition. Clinical examination reveals no abnormalities.

Investigation

Chest radiology

The diagnosis is usually obvious from the chest radiograph, which shows discrete areas of pleural thickening that may contain calcification. The plaques have well-circumscribed edges, which distinguish them from diffuse pleural thickening [21]. Calcification is not a reliable distinguishing feature as this may occur in areas of diffuse pleural thickening as well as in plaques, perhaps because the diffuse pleural thickening has developed in visceral pleura that has then fused with adjacent calcified parietal plaque. Plaques often follow the line of the ribs and may be elongated. Diaphragmatic plaques, by contrast, are more often symmetrical. The plaques usually have an irregular outline, and descriptive terms that have been applied include 'candle wax' and 'holly leaf' appearances.

If plaques are not apparent on a posteroanterior (PA) or lateral view and are being specifically sought, right and left 45 degree anterior oblique films increase diagnostic sensitivity since they occasionally reveal plaques that are not evident (or are partially obscured) on the conventional views, or which appear only as ill-defined hazy densities that are hard to discern and evaluate (Fig. 21.1) [22]. However, the incremental detection rate is low. In one study, 2.5% of 326 workers with normal PA films and 13% of 46 subjects with parenchymal but not pleural shadows on PA films had pleural abnormalities detectable only on oblique films [20]. Plaques are usually bilateral but unilateral plaques are not uncommon, particularly when few in number, constituting 19.3% of definite and 33.9% of probable plaques in one particular study [24]. Among subjects with unilateral plaques there is an unexplained left-sided predominance [24,25].

A high-resolution CT scan has slightly greater sensitivity for the detection of plaques than plain radiography and also assists in distinguishing between diffuse pleural thickening and multiple plaques. The latter on a plain chest radiograph may appear to overlap and hence mimic diffuse pleural thickening [26]. The plaques are then said to be confluent. However, CT is less useful than a plain chest radiograph in demonstrating diaphragmatic plaques since image and thin plaque are in the same plane [22].

Lung function

Surveys of groups of workers with plaques have shown that they are associated with small mean decrements in ventilatory capacity and total lung capacity (TLC) [27–30]. Elastic recoil pressure is increased and lung compliance is reduced in comparison with controls [31]. These alterations in lung function are probably a result of associated early

Fig. 21.1 Posteroanterior (a) and oblique (b,c) chest radiographs showing pleural plaques.

pathology in the underlying lung rather than the presence of the plaques themselves. Plaques are also associated with evidence of small airways dysfunction, which may be caused by an accompanying peribronchial reaction to asbestos fibers [32].

For an individual with plaques, lung function test results are usually within the normal range and breathlessness is usually absent; if it is present it is usually owing to coexisting respiratory or cardiac disease. Exceptionally extensive plaques that are fused (confluent) over a large area may be associated with sufficient restrictive impairment of ventilatory function to cause breathlessness, particularly if there is coexisting respiratory impairment from other causes, which produces an interactive adverse effect.

Further investigation is rarely required but occasionally the configuration of a plaque is atypical, leading to the suspicion of a malignant process. A pleural biopsy is then appropriate, either by means of a percutaneous cutting needle if the pleura is thick enough for this to be feasible, or by an open or thoracoscopic surgical procedure.

Pathology

Plaques may be situated within the parietal pleural overlying the chest wall, diaphragm, mediastinum, and pericardium. They rarely occur in the visceral pleura or in the peritoneum. They are smooth or coarsely nodular. Histology shows relatively acellular, avascular, hyalinized, collagenous bundles apparently arranged parallel to the surface in a 'basket weave' pattern, and a surface covering of mesothelial cells (Fig. 21.2). In nodular plaques the collagen bundles have a whorled arrangement [2]. Calcification may be evident.

There may be asbestosis of adjacent lung tissue but the frequency will depend upon the degree of exposure experienced. In a series of 56 cases selected on the basis that pleural plaques were identified at autopsy, there had been clinical evidence of asbestosis in 16 (29%). Histologic evidence of asbestosis was found in a further 8 (14%) [4]. Asbestos bodies are not found in plaques although they are commonly present in lung tissue. Subjects found to have plaques at autopsy have higher numbers of asbestos bodies in lung tissue than those without plaques, as might be expected since plaques are more likely to identify subjects with excessive exposure, and there is an excess of long amphibole fibers of commercial origin, but not of chrysotile [33]. Small numbers of asbestos fibers can be found by electron microscopy in plaques, but chrysotile is the predominant fiber type even if amphiboles predominate in lung tissue [34]. The reason for this is not known and many uncertainties remain concerning the pathogenesis of plaques [35]. The route by which asbestos fibers reach the parietal

Fig. 21.2 Histologic appearances of pleural plaque.

pleura has not been fully elucidated. Alternative suggestions are via retrograde flow in the lymphatic system and direct penetration from the lung across the pleura. The distribution of asbestos fibers in the parietal pleura itself is heterogeneous. It has been recognized that anthracotic pigment, found in high concentrations in coal miners, accumulates preferentially in 'black spots' located near lymphatic vessels on the parietal pleura. Thoracoscopic biopsies of such areas, identified visually, contained higher concentrations of amphibole fibers than other areas of the parietal pleura, and in these areas chrysotile fibers were few or absent [36]. There was concordance between the amphibole content of the black spots and that of the lung tissue. The authors postulated that the black spots correspond to normal lymphatic stomata known as 'milky spots' and that amphibole fibers that have migrated directly through the visceral pleura are reabsorbed into the parietal pleura through the 'black spots'. The accumulation of amphiboles in such areas may explain the susceptibility of the parietal pleura to plaque formation and mesothelioma.
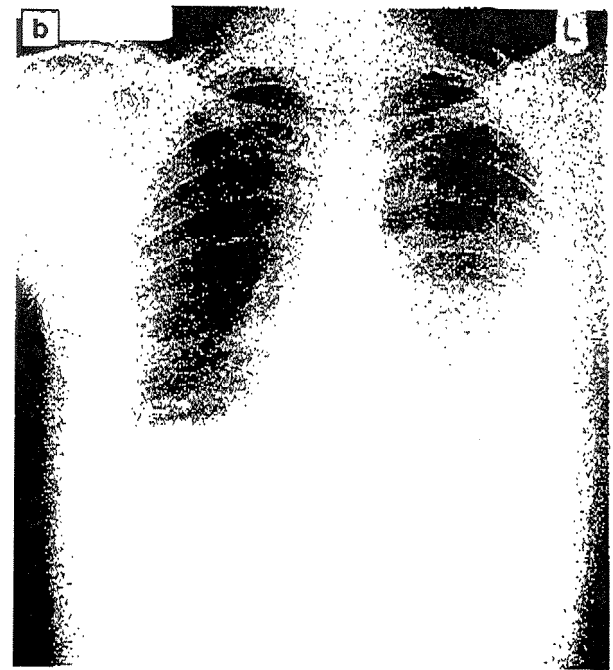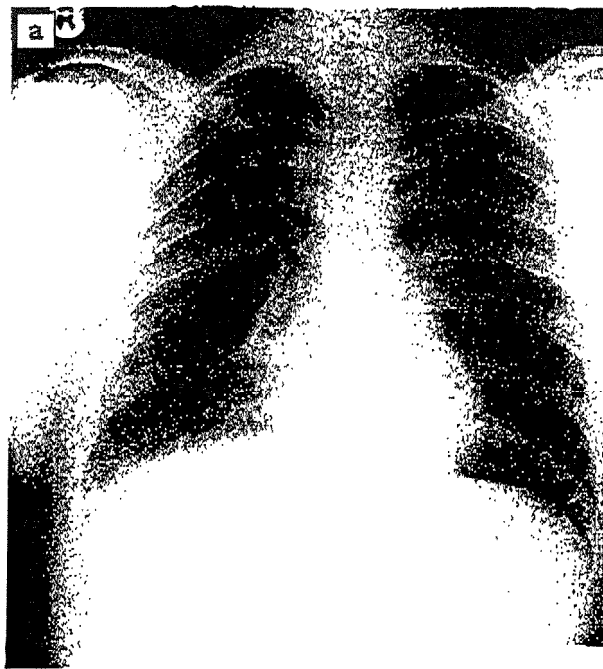
Management of the individual

The patient with plaques should be reassured that the condition itself is of no serious consequence and that the plaques are not likely to progress to cause symptoms in the future.

PLEURISY AND PLEURAL EFFUSION

Background

Asbestos may cause acute pleurisy, which is commonly but not invariably associated with an effusion. Pleural effusion is consequently the hallmark of asbestos-induced pleurisy. Although first described in

1962 [37], the condition did not become a widely recognized consequence of asbestos exposure until much later [38]. A causal relation was supported by a case-control study in which asbestos exposure was identified more frequently in persons with 'idiopathic' pleural effusion than in controls [39].

Epidemiology

Pleural effusion as a consequence of asbestos may develop earlier after first exposure than pleural plaque or asbestosis. It is the most common asbestos-related condition to occur during the immediately following 20 years, although in an exposed population effusions have been noted to appear up to 40 years after first exposure [8]. In a series of 20 insulation workers, the effusion occurred a mean of 26 years after first exposure, but in four it occurred within 10 years [40]. In a further series of 60 patients, the first effusion occurred a mean of 30 years after first exposure, with a range of 1 to 58 years [41]. The risk of benign effusion increases with the dose of asbestos [8].

Prognosis

The effusion commonly resolves to leave behind diffuse pleural thickening, which characteristically involves the costophrenic angle [40]. In some patients, however, there is complete reabsorption without sequelae. The effusion may recur on the same side, or more commonly on the contralateral side, after an interval of months or years (Fig. 21.3) [40,41]. In one series after a mean follow-up of 9.7 years, recurrent effusions occurred in 28.6% [8]. Ipsilateral recurrence is less common, probably because the pleural layers are frequently left fused together by diffuse pleural thickening. The risks of other asbestos-related conditions are related to the underlying level of exposure, the development of pleurisy with or without effusion providing clinical evidence of such exposure.

Recognition

Clinical features

The patient usually presents with pleuritic chest pain, though on occasions there are no symptoms and the condition is recognized only if there is a chance chest radiograph. There may also be breathlessness, depending on the quantity of associated pleural fluid. Mild fever and systemic disturbance are common, but not invariable, giving rise to the suspicion of infection. This is the initial diagnosis in many patients with asbestos pleurisy. Failure to identify any infective organism and lack of response to antibiotics point to the correct diagnosis. However, malignancy cannot be excluded without further investigation.

Fig. 21.3 Sequence of chest radiographs from an insulation worker showing asbestos-induced pleural effusions resolving to leave bilateral diffuse pleural thickening. The first shows a small right pleural effusion blunting the costophrenic angle. The second, 10 months later, shows a larger right pleural effusion and an even larger left pleural effusion. The third, after a further 7 months, shows bilateral diffuse pleural thickening.

Investigation

The chest radiograph and CT scan commonly show only a pleural effusion, but there may be coexisting pleural plaques. The effusion should be aspirated. The fluid is an inflammatory exudate, which may show neutrophils, mononuclear cells, and eosinophils [42]. Asbestos bodies are not seen. The effusion is commonly serosanguinous and may be frankly bloody. In the presence of fever, the alternative possibility of empyema or tuberculosis should be considered, and pleural fluid cultures are needed. The erythrocyte sedimentation rate (ESR) is usually elevated [43].

Pleural biopsies should be obtained in addition to fluid aspiration in order to exclude the possibility of malignancy. Negative results from blind biopsies, such as are obtained by Abrams needle, and cytologic examination of aspirated fluid do not provide adequate reassurance that malignancy is not present since the diagnostic sensitivity of these procedures is low [44,45]. Video-assisted thoracoscopic pleural biopsy gives the most satisfactory outcome, and if this proves negative for malignancy a diagnosis of benign asbestos pleurisy can generally be accepted [45].

Differential diagnosis

The presence of blood in the pleural fluid gives rise to the suspicion of malignancy, which is appropriate, since mesothelioma and metastatic carcinoma

re prominently among the differential diagnoses. Nevertheless, benign asbestos-induced effusions are commonly blood stained, and this sometimes leads to the suspicion of pulmonary embolism. When the effusion is not blood stained, a parapneumonic effusion becomes the most probable alternative diagnosis. Parapneumonic effusions without empyema, and effusions consequent upon pulmonary embolism, usually resolve without leaving pleural thickening [42].

Empyema should be confirmed by pleural fluid culture, and a tuberculous effusion by culture or the typical histologic findings on biopsy of granulomatous inflammation. If the effusion is eosinophilic, parasitic infection should be considered if geographically appropriate, but the eosinophils may simply indicate chronicity. Drug-induced effusions (e.g. from amiodarone) should also be considered, and current medication should always be clarified. This may provide a valuable clue to the existence of an undisclosed, but relevant, additional disease.

Rheumatoid pleural disease, comprising effusions and visceral pleural thickening, shows a striking male predominance and occurs usually in patients with moderate to severe joint disease. Occasionally, pleural disease appears before joint disease. Biopsy of the pleural lesions occasionally shows the characteristic features of rheumatoid nodules, and rheumatoid factor is commonly present in both serum and pleural fluid. The latter characteristically has a low glucose content, a low pH, and may show diagnostic 'rheumatoid cells' (scavenger mononuclear cells with ingested immune complexes involving rheumatoid factor) [42]. Pleuritis associated with systemic lupus may present with small effusions, which may be blood stained. Other pulmonary and systemic manifestations of lupus are commonly present, lupus erythematus cells are often present in pleural fluid, and immunologic tests give the diagnosis [42].

Pathology

The pleura shows the non-specific features of an organising effusion, including reactive mesothelial cells, proliferating fibroblasts and capillaries, and, often, chronic inflammatory cells. Distinction from desmoplastic mesothelioma may be difficult but in the latter condition invasion of chest wall or lung, bland necrosis, or sarcomatoid areas can usually be identified [46]. Granulomas are not present and asbestos bodies and fibers are seldom found [38].

Management of the individual

It is important to complete diagnostic procedures before draining all the fluid from the chest. If this is done too early, it may make later thoracoscopy difficult

or impossible. Any residual fluid can be drained at the time of thoracoscopy. The effusion commonly does not recur and so it is not necessary to attempt pleurodesis routinely. In fact, pleurodesis is better avoided until a histologic diagnosis is available because if mesothelioma of epithelioid variety at an early stage is confirmed, which is potentially suitable for extrapleural pneumonectomy, a pleurodesis may make subsequent surgery more difficult. Pleurodesis may become appropriate, however, if the effusion recurs and is large enough to cause breathlessness and require drainage.

If the effusion is repeatedly recurrent over short periods and accompanied by systemic markers of inflammation such as raised ESR, it is reasonable to attempt corticosteroid therapy. Anecdotally such treatment may be useful although there are no randomized trials demonstrating efficacy.

DIFFUSE PLEURAL THICKENING

Background

The term diffuse pleural thickening relates to thickening that does not have well-circumscribed margins [21]. It principally involves the visceral pleura (and so is sometimes called visceral pleural thickening) though this is often adherent to the parietal pleura. It is believed to represent the outcome when the resolution of benign pleural effusion involves fibroblast infiltration and a fibrotic healing response. Hence the width is variable depending on how much fibrous tissue is laid down, and the process effectively glues parietal to visceral pleura, as occurs with the resolution of other inflammatory effusions.

Epidemiology

A study of asbestos cement workers found that the incidence of diffuse pleural thickening increased with dose of asbestos sustained, although the relationship was less strong than for parenchymal fibrosis [47]. Another study of asbestos cement workers found that the prevalence of pleural thickening increased with duration of exposure but not estimated cumulative dose [48]. A study of amosite workers found the prevalence increased with intensity of exposure and time since first exposure [49].

As with plaques, there has been conflicting evidence as to whether smoking affects the development of diffuse pleural thickening. A study of naval dockyard workers reported an increased prevalence of pleural lesions, including diffuse pleural thickening, in smokers [50], as did a study of sheet metal

workers [51]; however a study of plumbers and pipefitters found no relation between smoking status and pleural thickening [52].

Prognosis

A study of asbestos cement workers found that 23% of subjects with diffuse pleural thickening showed radiologic progression over a 10-year period. The risk of progression was related to cumulative dust exposure [48]. An Australian study of Wittenoom crocidolite miners reported that the rate of radiologic progression of pleural thickening was greater in those with earlier onset of disease after first exposure to asbestos. The rate of progression decreased with time and there was no evidence of progression more than 15 years after first detection of pleural thickening [53]. A longitudinal study found no evidence that smoking affected progression [54]. Longitudinal lung function data over a mean period of 9 years in 36 subjects showed a significant decrement in forced expired volume in 1s (FEV_1) and forced vital capacity (FVC) in excess of that predicted from ageing alone [55]. Rarely diffuse pleural thickening may progress to the point of causing ventilatory failure and death [56].

The patient's risks of mesothelioma and other asbestos-related diseases are related to past asbestos exposure but are not additionally influenced directly by the presence or absence of diffuse pleural thickening [57]. As with the other manifestations of asbestos-induced benign pleural disease, however, the presence of diffuse pleural thickening provides crude surrogate evidence of such exposure.

Recognition

Clinical features

Diffuse pleural thickening of limited extent may be an asymptomatic incidental finding on a chest radiograph. More extensive disease commonly gives rise to symptoms. There is often a history of chest pain, which may have been pleuritic in nature. In a study of 64 affected patients, more than half reported chest pain of plausible relevance at some time [55]. A past history of diagnosed pleurisy is common, and the patient may be aware of an earlier pleural effusion for which no definite cause was identified. In a minority of cases there is persistent chest pain, which is commonly but not always of a pleuritic nature, and which may be quite disabling [58]. Breathlessness on exertion is the other principal symptom. Some patients, particularly in the early stages of the disorder when there is an active inflammatory process, have systemic symptoms such as mild fever, sweats, and malaise.

On physical examination chest expansion may be diminished, symmetrically if the condition is bilateral, but on one side only if it is predominantly uni-lateral. On auscultation there may be fine mid to late inspiratory and fine early to mid expiratory crackles [59]. Their timing suggests that they are caused by friction between the pleural layers, which is maximal in mid-inspiration and mid-expiration. Clubbing is not a feature.

Rarely the clinical features of pericardial constriction may occur because of accompanying asbestos-induced pericardial thickening, which may occur in association with pleural disease [60]. An association between retroperitoneal fibrosis and asbestos exposure has been reported [61] and this may give rise to hydronephrosis.

Investigation

Chest radiology

A PA chest radiograph usually demonstrates the extent of the disease but, as with plaques, this is occasionally demonstrated much better by oblique views. Commonly, strands of fibrosis appear to extend across the lung fields from the thickened pleura and this has been described as a 'crow's foot' appearance (Fig. 21.4) [62].

High-resolution CT scanning is more sensitive and accurate for the detection of pleural disease. This results in greater interobserver agreement as to the extent and type of pleural disease than is possible by plain chest radiography [26]. The CT scan well demonstrates 'crow's feet' and its constituent parenchymal bands extending from thickened pleura, appearances that indicate involvement of the visceral pleura rather than parietal plaque [63].

The CT scan may also disclose the nature of rounded (rolled) atelectasis, otherwise known as folded (or enfolded) lung or Blesovsky's syndrome [64]. This has a characteristic appearance of vessel and bronchi radiating towards the hilum from a solid looking shadow contiguous with the pleura (Fig. 21.5). On the plain chest radiograph such lesion often suggest tumor, but if the characteristic features are present from CT scanning a confident diagnosis can be made and an unnecessary biopsy avoided.

In most cases, diffuse pleural thickening in asbestos exposed workers involves the lower zones and middle zones, but in one series a minority showed pleural thickening that affected the apices – either predominantly or exclusively. Upper zone disease was observed in 40 of 1600 (2.5%) patients in one series [65]. Such appearances, sometimes associated with upper lobe parenchymal fibrosis, can be difficult to distinguish from those of tuberculosis [65,66] or other fibrosing diseases (for example that associated with ankylosing spondylitis and the HLA B27 genotype), and it is not universally accepted that such upper zone involvement is a consequence of asbestos exposure.
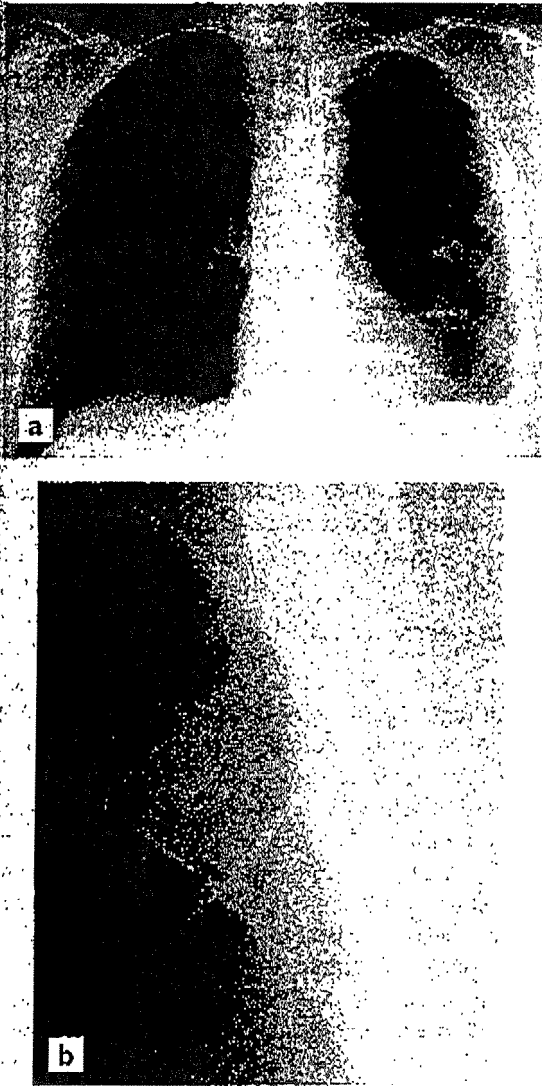
Fig. 21.4 Chest radiograph showing diffuse thickening (a) with 'crow's foot' (b).
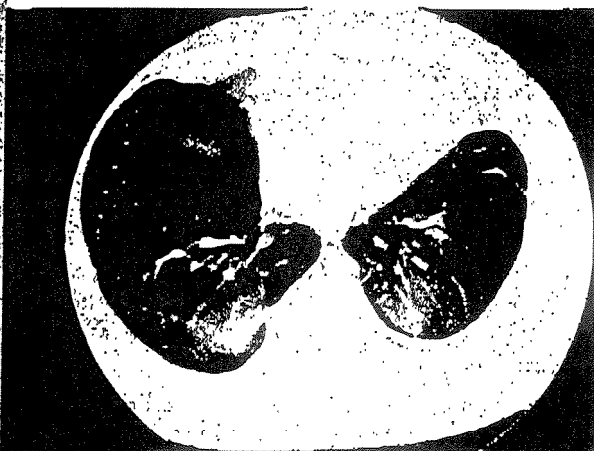

Fig. 21.5 High-resolution CT scan showing folded lung (rounded atelectasis).

Lung function

Diffuse pleural thickening reduces pulmonary compliance [67] and causes a restrictive ventilatory defect with reduction in total lung capacity [51,68,69]. The radiographic extent of pleural disease, as assessed by chest radiographs or CT scan, correlates with reduction in FEV_1, FVC, residual volume (RV), and TLC [26,69,70]. The FEV_1/FVC ratio is either normal or increased, unless there is coexisting airflow obstruction, which may obscure the characteristic pattern. Restrictive pleural disease is also associated with reduction in gas transfer factor (diffusing capacity) [26,71] but the gas transfer coefficient (diffusion constant) is normal or increased, reflecting the relative lack of impairment of parenchymal function and the reduction in alveolar volume. This pattern of impairment is sometimes described as 'constrictive', distinguishing it from the restrictive pattern associated with intrapulmonary fibrosis. Impairment of lung function is particularly associated with radiologic evidence of obliteration of the costophrenic angles [72]. This may be because obliteration of the costophrenic angles implies that the parietal pleura over the lower chest wall is stuck to the parietal pleura over the periphery of the diaphragm, thereby interfering with the diaphragm's descent and preventing the lung from expanding into this potential space on full inspiration. This does not happen with plaques and is possibly an important mechanism by which diffuse pleural thickening usually impairs ventilatory function but plaques usually do not [73].

The presence of rounded atelectasis is not independently associated with loss of lung function in excess of that resulting from the associated diffuse pleural thickening [71]. Respiratory muscle function is not adversely affected by asbestos-related pleural disease [74].

It is important to appreciate that if both asbestosis of lung tissue and diffuse pleural thickening are present, the gas transfer factor may be reduced but the gas transfer coefficient may be normal or even increased, reflecting a greater effect of pleural thickening on lung volume than of parenchymal disease on gas transfer. In this situation a normal or increased gas transfer coefficient does not imply that parenchymal function is normal or that asbestosis is not contributing to impairment of lung function [75].

Occasionally diffuse pleural thickening is accompanied by pericardial thickening and consequently restricted cardiac motion/function. This possibility should be considered in patients where breathlessness appears disproportionate to the observed impairment of lung function and can best be investigated by magnetic resonance imaging [76].

Pathology

The macroscopic findings indicate diffuse visceral pleural thickening, which may be very extensive and suggestive of mesothelioma. Pericardial thickening with pathologic features similar to those in the pleura may also occur [77]. The pericardial thickening occurs in association with pleural thickening but does not just reflect involvement of adjacent pleura. Rounded atelectasis on radiography corresponds to extensive wrinkling and folding of the visceral pleura with deep invaginations into pulmonary tissue, which is compressed and in some cases shows interstitial fibrosis [78]. It has been suggested that rounded atelectasis occurs either when diffuse fibrotic changes in the pleura contract, forcing part of the adjacent lung to become atelectatic, or when a pleural effusion causes a segment of lung to become atelectatic, causing its components to become adherent to each other and remain so after the effusion has been reabsorbed [78,79].

The histologic findings are of paucicellular collagen deposition. A basket weave appearance as seen in plaques has been described [80] but other authors do not report this [81]. Lung tissue immediately beneath the thickened pleura usually shows interstitial fibrosis up to 1 cm in depth [80]. This differs from the appearances in classical asbestosis, where changes are more diffuse rather than being confined to areas beneath pleural thickening [81], and it is a matter of controversy as to whether the fibrosis occurring only beneath diffuse pleural thickening should be taken as histologic evidence of asbestosis. There may be reactive mesothelial hyperplasia, which may be difficult to distinguish from mesothelioma. Immunohistochemical stains may be helpful: epithelial membrane antigen (EMA) is generally positive in mesothelioma but negative in benign mesothelial hyperplasia. Amphibole counts are usually raised in lung tissue whereas relatively few fibers, mainly chrysotile, are found in the pleural tissue [77]. The range of amphibole counts is broadly comparable to the ranges found in patients with pleural plaque, mesothelioma, and mild asbestosis [77].

Differential diagnosis

Patients with diffuse pleural thickening may have a raised ESR and a few have weakly positive antinuclear factor and rheumatoid factor in serum, consistent with the presence of systemic disturbance [82]. In the presence of such features, consideration should be given to the possibility of connective tissue disorders such as rheumatoid disease, systemic lupus erythematosus, and ankylosing spondylitis as the cause of the pleural disease.

The differential diagnosis should also include druginduced pleural disease, and appropriate inquiries should be made concerning relevant agents. For example ergot drugs (known as ergolines; methysergide, bromocriptine, nicergoline, pergolide and dopergine), practolol, amiodarone, and nitrofurantoin. Useful distinguishing features of drug-induced pleural thickening are said to be more rapid development, absence of associated pleural calcification, and, most importantly, rapid diminution of chest discomfort and fall in ESR on drug withdrawal. Radiologic regression is, however, slower and incomplete [83].

Rounded atelectasis is usually caused by asbestos-induced diffuse pleural thickening, but it may occur with diffuse pleural thickening of other causes including chest traumal [79]. Cryptogenic fibrosing pleuritis is a label applied to bilateral diffuse pleural thickening in the absence of any identifiable extrinsic cause [84]. Like asbestos-induced disease, it may evolve by way of pleural effusions.

Management of the individual

Surgical resection of thickened visceral pleura (decortication) has been attempted in patients with folded lung but this more often leads to further decline in lung function than to an improvement [85]. Parietal pleurectomy has been performed in an attempt to alleviate persistent pain, with occasional benefit in patients whose pain was of a pleuritic rather than neuropathic type [86]. Surgery should be considered as a last resort for relief either severe ventilatory restriction, and ensuing breathlessness of disabling degree, or intractable pain. If there is clinical evidence of progressive pleural disease, often accompanied by systemic markers of inflammation such as raised ESR, it reasonable to attempt to suppress this with corticosteroid therapy. Anecdotally, such treatment may be useful, although there are no randomized trial demonstrating efficacy.

GENERAL MANAGEMENT

Of the individual

As indicated above, the patient with plaques should be reassured that the condition itself is of no serious consequence and that the plaques are not likely to progress to cause symptoms in the future. The patient with asbestos pleurisy, effusion, or diffuse pleural thickening should be given realistic information about the chances of future progression.

Patients with any type of asbestos-induced pleural disease should be advised that its presence indicates that a clinically significant quantity of asbestos has been inhaled and that there are, therefore, risks

other asbestos-related diseases in future. Patients who are smokers should be firmly advised to quit the habit, with explicit explanation of the synergistic interaction between tobacco and asbestos in causing lung cancer.

The patient should also be advised of the possibility of claiming compensation if eligible under local jurisdiction. In the UK, Industrial Injuries Disablement Benefit is not payable in respect of plaques or effusion but it is payable in respect of diffuse pleural thickening that meets the following criteria as to minimum extent: at least half the length of one chest wall (or this length cumulatively from both chest walls) with a maximum thickness of at least 5 mm. In the UK, a patient with any type of asbestos-related pleural disease can pursue a claim at common (i.e. civil) law for damages, either on a final award basis, which takes account of all possible eventualities, or a provisional basis, which provides a lower award of damages but allows a return to court in the event of serious deterioration in the future. This may involve the progression of existing pleural disease or the development of a new condition (i.e. asbestosis, mesothelioma, or asbestos-related lung cancer).

Of the workforce

The discovery of an asbestos-related condition in a member of a workforce may create anxieties in other workers, particularly those who have worked in conditions similar to those encountered by the affected individual. Appropriate reassurance should be offered, but if there are individuals with a history

of significant exposure during a period sufficiently distant to put them at risk of present disease, a screening program of exposed workers often helps to allay anxiety. There is increasing interest in the possibility that early detection of lung cancer by screening of high-risk subjects with helical CT may reduce mortality; asbestos-exposed smokers are an ideal group for study. The prospect of reducing mortality from mesothelioma by similar means appears more remote.

PREVENTION

Current legal requirements in the UK concerning exposure to airborne asbestos dust should, if properly enforced, prevent new cases of pleural disease. In some other parts of the world, protection remains inadequate. In the UK, control limits for exposure are as shown in Table 21.1. The full effects of current regulations are not likely to be seen for several decades in view of the long latencies involved.

Table 21.1 Control limits specified by the Control of Asbestos at Work Regulations (1987) in the UK

	Fibres per ml of air averaged over	
	4 h	10 min
Chrysotile	0.5	1.5
Crocidolite	0.2	0.6
Amosite	0.2	0.6

DIFFICULT CASE

History

A man born in the early 1930s worked as an electrician from leaving school for nearly 40 years. In the course of his work he sometimes used asbestos rings for electrical insulation. He did not cut them himself but simply put them in place. From time to time he also worked in the vicinity of other tradesmen who stripped asbestos lagging from pipes prior to repair work and who used asbestos materials to restore the lagging afterwards. In earlier years, he wore a simple dust mask, but in later years he was provided with a rubber mask with a filter. He smoked 10–15 cigarettes daily and was not known to have ever received medication for migraine.

In the course of a routine medical evaluation in the late 1980s, a chest radiograph showed slight diffuse pleural thickening in the left mid-zone, and further films 3 and 5 years later demonstrated mild progression. Thereafter the appearances were stable until a clinical evaluation in mid-1990s.

There was then a reduced FEV$_1$: FVC ratio, a reduction in TLC, a mild reduction in gas transfer factor, and an increased gas transfer coefficient; the picture overall suggested a mixed obstructive and restrictive impairment of ventilatory function of moderate degree.

About a year later, he developed abdominal pain and malaise, and was investigated. The ESR was 80. An ultrasound study of the abdomen showed left hydronephrosis, and a CT scan demonstrated a mass partially obstructing the left ureter. The appearances suggested retroperitoneal fibrosis. He was treated with corticosteroids and a left ureteric stent was inserted. The hydronephrosis resolved and his symptoms improved. The pleural disease persisted unchanged.

Issues

The chief issues of interest are whether the presumed retroperitoneal fibrosis and the unilateral diffuse pleural thickening shared the same cause or had different causes,

whether the occupational exposure to asbestos was relevant to either, and whether any additional investigation would be useful.

Comment

A clear majority of the book's contributors thought the pleural fibrosis was an effect of asbestos exposure but that the peritoneal fibrosis was not. A small minority considered that a common cause was likely, whether or not this was asbestos, and a modest minority favored additional investigation. CT of the chest was suggested to evaluate the pleural shadowing, and an abdominal biopsy was suggested to confirm the diagnosis of retroperitoneal fibrosis and exclude the possibility of peritoneal mesothelioma.

DIFFICULT CASE

History

A 48-year-old man underwent a statutory medical examination for the purpose of assessing fitness for work as an asbestos removal operative. These examinations are required at 2-yearly intervals in the UK under the Control of Asbestos at Work Regulations 1987. The assessment includes a history of occupational exposures and respiratory symptoms, clinical examination of the chest, chest radiograph, and spirometry. The examining physician must be approved by the Health and Safety Executive as suitably experienced but need not be a specialist respiratory physician. He/she is not required by statute to give the employer specific advice as to fitness for work but may give advice to the subject according to his/her own judgement. In practice, employers' liability insurance requires that employers do obtain such advice, whether from the physician carrying out the statutory examination (with the examinee's consent) or from another physician.

The subject was asymptomatic and no abnormalities were revealed except that the chest radiograph showed a few small calcified pleural plaques on the chest walls and diaphragms. The occupational history revealed that after leaving school at the age of 16 he had worked for 2 years in the insulation trade using asbestos materials in various forms. He had been heavily exposed to asbestos without any respiratory protection. After that he had worked in a variety of other jobs, none of which had involved exposure to asbestos. He had been entirely well and had not had any chest radiographs prior to the current film obtained in the course of the statutory examination soon after he had been offered employment in the insulation trade. In this job, he would have been using asbestos-free materials but from time to time he might have been required to assist in asbestos removal work under strictly controlled conditions using all recommended precautions to ensure that his exposure did not exceed currently permitted limits. The examining physician considered that as he had an asbestos-related disease he was not fit for asbestos removal work. This was communicated to the subject who informed his prospective employer of the advice. The job offer was consequently withdrawn with serious adverse economic consequences for the subject.

Issues

The issues are whether further exposure to asbestos within the limits permitted by current regulation is likely to make any difference to this man's existing pleural plaques or to his risks for the future development of other more serious asbestos-related disorders, and whether he should be regarded as unfit for asbestos removal work.

Comment

A small minority of the book's contributors considered that additional exposure, at what is likely to be a very low level (barring accidents), would materially increase the risk for asbestos-related malignancy, but a clear majority thought such exposure would have no meaningful effect. The latter view implies that there is no valid medical reason why he should not undertake asbestos removal work using all currently recommended precautions. However, this man had already sustained a heavy level of exposure, albeit briefly, some years earlier and so is at some risk of developing other asbestos-related disorders anyway. A new employer might reasonably be wary of offering employment in such circumstances because, in the unfortunate event that a further asbestos-related disorder does emerge, additional exposure during the period of employment (however trivial) might lead to the charge that it played a contributory role.

SUMMARY POINTS

Recognition

- Plain chest radiographs provide the means by which most cases of benign asbestos-induced pleural disease are recognized, oblique views enhancing the sensitivity of detection.
- CT scans have much greater sensitivity and diagnostic precision, and provide the best means of resolving doubt as to whether:
  - pleural shadowing is a consequence of plaque, diffuse pleural thickening, or both
  - pleural effusion is isolated or associated with probable mesothelioma
  - a pleural-based opacity is caused by folded lung or tumor.
- When circumscribed pleural shadows show calcification, they are almost pathognomonic of plaques caused by asbestos exposure.
- Blunting of the costophrenic angle favors a diagnosis of diffuse pleural thickening over one of plaque.
- Once parapneumonic effusion/empyema, tuberculosis, malignancy, and rheumatoid disease are excluded in a patient with an exudative pleural effusion, asbestos becomes the most likely cause if there has been regular occupational exposure – particularly if pleurisy has been recurrent.
- Bilateral diffuse pleural thickening is commonly a consequence of recurrent asbestos-induced pleurisy and seldom the result of other causes apart from bilateral parenchymal tuberculosis.
- Unilateral diffuse pleural thickening is more commonly a consequence of other causes but is nevertheless a common consequence of asbestos exposure.
- Folded lung is usually a consequence of asbestos exposure.

- Asbestos is the only common cause of a benign blood-stained pleural effusion apart from pulmonary embolism.
- A thoracoscopic pleural biopsy should be obtained to exclude mesothelioma or other malignancy before a diagnosis of benign pleurisy is accepted as the explanation for a blood-stained pleural effusion in an asbestos-exposed patient.

Management

- Inform the patient of the nature of the disease, including its cause, effects, and prognosis. Inform the patient of the possibility and methods of seeking compensation for occupational disease.
- Drug therapy is usually not indicated, but occasionally corticosteroid therapy may be employed for the treatment of active pleural inflammation.
- Routine follow-up is not currently of proven value but may provide psychologic support in selected individuals.
- Surveillance programs may prove to be of value in the future if emerging methods of early detection of lung cancer and mesothelioma lead to a reduction in mortality.

Prevention

- End use of asbestos.
- Identify asbestos already in place in buildings and elsewhere, assess its condition, and seal or remove where necessary.
- Ensure building maintenance personnel are aware of the presence and location of asbestos so they do not disturb it inadvertently.
- Enforce strict regulations to prevent dissemination and inhalation of dust during disturbance or removal of asbestos.

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