UNION CARBIDE CORPORATION
ETHYLENE OXIDE/GLYCOL DIVISION
P.O. BOX 8361, SOUTH CHARLESTON, WEST VIRGINIA 25303

IT'S A SNAP WITH SEAT BELTS.

PLAINTIFF'S EXHIBIT
UC-2636

June 14, 1983

TO: Dr. G. N. Guzzardo
Dr. R. G. Rowe
Dr. M. A. Tulla

COPY: Mr. Frank Garcia-Sharp
Mr. Omar Muniz-Diaz
Mr. R. E. Peele
Mr. R. L. Powell
Mr. Steve Robinson
Mr. Claude Sam
Mr. D. R. Shearer
Mr. W. R. van der Hoeven

FROM: V. H. Johnkoski

Attached is material from Dr. Lewinsohn relating primarily to asbestosis that may be of some interest.

Vinie Johnkoski/jgh
V. H. Johnkoski

VHJ/jgh

Attachment

UNION CARBIDE HEALTH SAFETY AND ENVIRONMENTAL AFFAIRS

HILTON C. LEWINSOHN, MB.BCH., F.C.C.P.
Assistant Corporate Medical Director
P2590
(203) 794-5214

June 7, 1983

TO: Dr. S. Austin
Dr. B. Ballantyne
Mr. J. Cornell
Dr. T. G. Fortney
Dr. W. F. Gorham
Mr. V. H. Johnkoski
Dr. A. A. Lang
Dr. T. A. Lincoln

The attached "abstracts" are from papers presented May 27-29, 1983 at the Thirteenth Annual Symposium on Chest Disease of the The Fleischner Society.

They may be of interest to you.

Hilton

OLD RIDGEBURY ROAD, DANBURY, CT 06817

ASBESTOS RELATED DISEASE:EPIDEMIOLOGIC & CLINICAL ASPECTS

Edward A. Gaensler

There are about 4 million persons alive today who have had heavy exposure to asbestos and an equal number with significant but lesser exposure (1). Among the several asbestos related disorders asbestosis, a term that should be reserved for pulmonary fibrosis (2), will remain an important but diminishing concern among the heavily exposed. The 3 pleural manifestations, hyaline plaques, benign asbestos effusion and mesothelioma, because of the lesser required exposure and long latent period, very likely will become increasing problems in all of the 8 million exposed persons. Concerning bronchogenic carcinoma, it is thought that 2 per cent of the 135,000 cases reported each year are related to asbestos exposure. Indeed, estimates of the percentage of all cancers caused by the single substance asbestos have varied from 1 to 18 per cent (1).

The radiologist's contribution in sorting out the asbestos related problems can be greatly enhanced by 1.) a strict adherence to accepted terminology and definitions, 2.) a working knowledge and use of the International Labor Organization Radiologic Classification of the Pneumoconioses, 3.)an effort to assemble old films for comparison, 4.) a detailed acquaintance with exposure history and with past history and 5.) an acquaintance with relevant epidemiology.

Asbestos: Fibrous hydrated silicates:Serpentine (chrysotile): white, curly, filamentous (90% of industrial use) and amphiboles, mainly Crocidolite (blue) and Amosite (brown). Others, including Anthophyllite and Tremolite mainly contaminants of talc.

Occupations at risk: (Incomplete list)

Process	Products (more than 3,000)	Occupations (Ex)
1. Production		
Mining, Milling	Asbestos Fiber	Mining,Crushing Transport, etc.
2. Primary use		
Spray Insulation	Fiber mixed with oil	Insulators, Construction
3. Manufacturing		
Textile	Cloth,Belts,Padding	Spinning,Card.
Cement Products	Roofing,Pipes,Gutters	Blending,cut.
"Paper" products	Felt,Electrical paper	Paper makers
Friction material	Gaskets,Clutch,Brake	Mixers,Blenders
Insulation	Pipe,Boilers,Bulkhead	Slurry,Chemical workers

Process	Products	Occupations
4. Application		
New Construction	Boards,Tile,Siding	Carpenters, Laggers,Heat.
Repair,Demolition		
Shipbuilding	Insulation:Pipes,hull	Laggers,Pipe-coverers
"Repair, Refits	"	Direct & In-direct (all)
Automotive	Undercoating,brake,etc.	Service,body shop

Epidemiology:

a.) Disease is dose-related. Exposure may have been brief and massive or lower dose for many years.
b.) "Twenty-year rule": Regardless of severity of exposure, signs and symptoms today are never seen until 10 or 15 years later and usually not until 20 years later.
c.) Asbestos manifestations correlate best with years since first exposure rather than number of years exposed. Manifestations progress despite removal from exposure.

I. Asbestosis:

This term should be reserved for a pneumoconiosis consisting of a diffuse chronic pulmonary interstitial pneumonia and fibrosis due to respirable asbestos fibers. The term should not be used for other asbestos-related manifestations or disease (2).

Asbestosis is demonstrably dose related, requires a considerable dose and therefore is not seen with out-of-plant neighborhood exposure or in relatives.

Cigarette-smoking is not a co-factor; and COPD occurs in asbestos workers with the same frequency and severity as in controls matched for age, sex and smoking history (3).

Clinical Diagnosis is based on history of exposure at least 15 and more usually 20 years earlier and at least 4 of the following 6 signs and symptoms:

1.) X-Ray: Linear-irregular markings (usually of lower lung fields) of ILO severity 1/1 or greater
2.) Dyspnea of Fletcher grade 2 or greater
3.) End inspiratory crackles (cellophane or velcro rales in 2 or more areas)
4.) Definite finger clubbing (usually late manifestation)
5.) Vital Capacity less than 80% of predicted
6.) Single breath diffusing capacity less than 80% of pred.

A clinical diagnosis is made when 4 of 6 of the above manifestations are present. "Permanent and total disability"

usually is associated with at least 2/2 radiographic profusion, an FVC of less than 50% and D_LCO of less than 40%. Lung biopsy should be required only in persons with a good exposure history but with atypical clinical or radiographic findings, or, on the contrary, when there are suggestive clinical findings but the exposure history is brief or unconvincing. The recently fashionable transbronchial biopsy may result in recovery of asbestos bodies but it is not a suitable technique for evaluating the presence or severity of interstitial pneumonia and fibrosis.

II. Parietal Pleural Hyaline Plaques:

The most recent I.L.O. classification distinguishes between diffuse pleural thickening and plaques or circumscribed pleural lesions (4). The latter, hyaline plaques, are the most common and also the most benign asbestos-related disorders.

Neither the early descriptions of the pathology of asbestosis nor the first clinical surveys in the 1930's called attention to parietal pleural lesions because at that time exposure was often severe and workers became disabled or died of asbestosis before plaques could form (5). Radiographic pleural calcifications of occupational origin were first noted in talc miners probably due to tremolite. Jacob and Bohlig (6) in their study of Dresden asbestos workers first mentioned calcifications as one of several roentgenographic features of asbestos exposure, and soon thereafter pleural plaques became established as markers of both occupational and non-occupational endemic asbestos exposure. More recent epidemiologic studies have led to the following generalizations concerning pleural plaques: (1) They are seen only following exposure to fibrous silicates. (2) Unlike asbestosis, they may result from casual, peripheral or neighborhood exposure. (3) They are rarely seen in less than 15 to 20 years after initial exposure. (4) Among asbestos workers first exposed 30 to 40 years ago, the prevalence may be as high as 35 to 60 per cent (5). (5) Only a small percentage of those present are seen radiographically. (6) They are an almost invariable finding at autopsy. (7) Plaques and calcifications occur on the parietal pleura and rarely cause pleural symphysis. The mechanism of their development is not known but probably they are due to mechanical rather than chemical irritation. (8) In the absence of asbestosis they are not harmful in that 1.) they are not associated with functional loss, 2.) they are not associated with symptoms and 3.) they do not predispose to other asbestos-related disease (CA, Fibrosis, Mesothelioma) compared to similarly exposed persons who do not have plaques. (9) Asbestos-related plaques and calcifications must be recognized and

propery labeled as such by radiologists. This usually requires an occupational history and review of earlier films. Proper recognition of such lesions will avoid much anxiety, unnecessary surgery and unwarranted litigation.

III. Benign Asbestos Pleural Effusion:

Benign asbestos effusion was not described as an entity until 1971 and the several series of cases reported since then have been summarized recently (7). Our definition is based on 4 criteria: 1) direct or indirect exposure to asbestos, 2) an effusion confirmed by a transient pleural change in serial chest films, by thoracentesis or surgery, 3) lack of evidence for any other disease related to pleural effusions, and 4) no malignant tumor detected within 3 years after the effusion.

Such effusions may result from slight or peripheral exposure much as all the other pleural manifestations. However, the 20-year-rule does not apply in that they may occur earlier than the other asbestos-related disorders. Indeed benign effusion is the most common asbestos-related manifestation during the first 20 years after initial exposure (7).

A recent epidemiologic study of 1,135 exposed workers followed for 3 to 40 years revealed 35 cases (5.2%) of otherwise unexplained effusions compared to none in an unexposed control group of 717 persons observed over a similar period (7). Effusions generally were small, one-fourth recurred and two-thirds were asymptomatic. Incidence was related to exposure: there were 9.2 effusions per 1,000 person-years for individuals working directly with asbestos, 3.9 effusions for those working in proximity to asbestos use by others, and 0.7 for administrative and office personnel who worked in shipyards or asbestos plants but probably had insignificant exposure.

IV. Mesothelioma:

Malignant mesothelial tumors have been described for 100 years and, notwithstanding recent interest, they have remained rare with incidences from 0.8 to 2.1 per million per year. Approximately 20 per cent are primarily abdominal. A relationship to asbestos exposure was first described by Wagner et al (8) in 1960 and this is now generally accepted. The actual percentage of the some 1,000 mesotheliomas reported in this country each year that result from asbestos exposure is not clear. Large cancer centers have reported infrequent asbestos exposure, 13 to 27%, but occupational histories before 1960 clearly were deficient. Other series reporting 100% exposure have come from near shipyards

or asbestos plants. Other types of exposure include long fiber Zeolites used for stucco and buildings. Sugar cane work, radiation and thorotrast cholangiography, as well as tuberculous empyema all have been associated with mesothelioma. McDonald and McDonald (9) have well summarized present knowledge by saying that the proportion of mesotheliomas due to occupational exposure is increasing but is certainly less than 100%, unlikely less than 50%, and probably accounts for two-thirds of all cases. They and others also have shown a gradient in mesothelioma-inducing potential from crocidolite down to chrysotile and anthophyllite.

Mesothelioma, much like the other pleural manifestations of asbestos exposure, may result from brief, slight or peripheral exposure - a finding of great concern. The latent period from initial exposure is usually very long, often 30 years or more and very rarely less than 20 years. Among asbestos workers the death rate from mesothelioma appears to be proportional to the third or fourth power of time from first exposure and is unrelated to smoking habits. The histologic diagnosis has remained difficult because the tumor arises from pleuripotential mesothelial cells and in consequence may present with widely varying histologic features. Three types are generally recognized: mesenchymal or sarcomatous, epithelial or tubolopapillary and mixed; additionally some tumors are poorly differentiated. Mesotheliomas are often diagnosed because of their typical gross appearance with spread along serosal surfaces, encasing of the lung by a continuous layer of tumor and failure to demonstrate a primary lesion in the lung. However, the same gross appearance may result from bronchogenic or metastatic tumors. These histologic problems explain why thoracenthesis or needle biopsy rarely proves diagnostic. In most of our cases a small open thoracotomy was required but thoracoscopy may be a less invasive alternative.

Mesotheliomas have not responded to any form of therapy. Pleuro-pneumonectomy or "debulking" entail high mortality and no improvement. Concerning recent chemotherapy, at Sloan-Kettering there were only 3 responses among 111 trials; and mean survival of treated and untreated cases has been the same: 9.1 vs. 9.6 months (10) and in our series it was 15.8 months for untreated vs. 12.4 months for chemotherapy.

V. Bronchogenic Carcinoma:

Case reports have accumulated since 1934 but it was not until 1955 that Doll (11) presented epidemiologic evidence

of an increased prevalence. Although acceptance came slowly it is now concluded beyond any reasonable doubt that commercial asbestos is a cause of human lung cancer, though other agents such as tobacco, may enhance its effect. The relative risk (RR), a number that represents the observed divided by the expected number od deaths from a given disease, tabulated by Backlake (2) and by McDonald (12) for 18 major cohort studies has varied from 1 (no increased risk) to 17, with the lowest values, 1 to 5, in miners and millers and the highest, 8 to 17, in pipecoverers and insulation workers. The interaction of smoking to asbestos exposure as risk factors is most important in clinical practice. Lung cancer develops only very rarely in nonsmoking asbestos workers whereas the risk from smoking and asbestos is more than additive, and more likely multiplicative. A relationship to intensity of exposure has been difficult to demonstrate because dust concentrations were rarely measured until 10 or 15 years ago. However the best available data suggest that the dose response relationship is essentially linear, but steeper for asbestos manufacture than for mining. The increased risk appears at about 20 years after first exposure and reaches a peak at 30 years, although obviously there is an interaction between age and lung cancer mortality.

The question of causal relationship or attributability is not a great problem with asbestosis or hyaline plaques which are specific for asbestos nor even for mesothelioma when there has been significant exposure. With bronchogenic carcinoma the situation is quite different in that only 1-2% of all cases can be related to asbestos exposure. The probability that a given case of lung cancer is due to asbestos exposure is based primarily on two factors: the intensity of exposure and the time since first exposure. For example, data of Enterline et al (13) indicate no increased risk (RR = 1.2) for asbestos workers who were exposed to less than 10 million particles per cubic foot (mppcf) and who were first exposed less than 20 years ago, whereas RR rose to 4.7 for those who were first exposed more than 30 years ago to more than 10 mppcf. The time since first exposure can be identified whereas in clinical practice the intensity of exposure almost invariably must be inferred from clinical and histolcgic evidence.

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E. NICHOLAS SARGENT, M.D.

THE ILO 1980 CLASSIFICATION SYSTEM (FACTS AND FALLACIES)

TERMINOLOGY: The definition of pneumoconiosis is clouded and its casual use has resulted in confusion. Under the ILO Classification System it is defined as the tissue reactions to dust inhalation and dust was meant to be an aerosol of solid inorganic particulates. (Coal is organic!!) The term "pneumoconiosis" often brings to mind aspects related to compensation and litigation. The term "occupational" also serves to remind physicians of the significance of the disease in question in a particular patient group. "Environmental" lung disease has also been suggested. The best method of defining and classifying pneumoconiosis for medical purposes should rest on morbid anatomical changes and thus it will embrace a variety of lung disorders. However, the term pneumoconiosis is so well entrenched in its usage for the past century, that its elimination is not realistic. Parkes suggests that pneumoconiosis should be defined as a non-neoplastic reaction of the lungs to inhaled mineral or organic dusts and the resultant alteration in their structure (excluding asthma, bronchitis, and emphysema).

ILO 1980 CLASSIFICATION SYSTEM: In the clinical practice it is customary for physicians to describe the radiographic findings associated with the pneumoconioses in a non-quantitative narrative form. However, when the information is to be used epidemiologically (or to evaluate pulmonary disability) the reporting must be more quantitative. The 1980 classification system is the latest in a series of classifications with numerous modifications since 1930. It is designed to permit codification of all types of pneumoconioses including coal workers pneumoconiosis, silicosis and asbestosis. A codification of the technical quality of the film is also now part of the system. To enhance consistency in the application of the classification of the system the use of standard radiographs for comparison is required. These films as well as a detailed description of the classification system may be obtained from the American College of Radiology, 6900 Wisconsin Ave., Chevy Chase, Maryland, USA, 20015 or by writing to the International Labor Office in Washington, D. C., USA or Geneva, Switzerland.

SMALL OPACITIES: With respect to the pulmonary findings, the system divides the opacities into two categories: small and large with each defined in specific quantitative terms. An opacity, of any size or shape which is larger than 10 mm in diameter, must be classified as a "large" opacity and not as a small opacity. With respect to small opacities, two shapes are recognized (small rounded or small irregular). For each shape the opacity is graded into three categories depending on their diameter and width. In the new scheme two letters must be used to denote the predominant size and shape.

The size and shape of small rounded and small irregular opacities have epidemiologic and clinical significance. Small irregular opacities occur following asbestos dust exposure, and usually begin at the lung bases. Small rounded opacities following coal and/or silica dust exposure are found radiographically in the upper and middle zones of the lung before they are observed in the bases. (Small irregular opacities may occur with coal and/or silica dust exposure but they are relatively

uncommon and are usually associated in conjuction with more rounded opacities.) Small rounded opacities by themselves are not seen with asbestos dust exposure.

For coal workers the dust content of the lung correlates well with the number of small rounded opacities of the p and q variety but not well with the small rounded opacities of the r variety. The p opacities tend to have pulmonary function abnormalities related to lower gas transfer of carbon monoxide, i.e. a decrement in gas transfer or alveolar capillary diffusion abnormalities. The irregular opacities of asbestos dust exposure do not correlate well with the quantity of dust found in the lung. However, abnormal pulmonary functions are more closely related to irregular opacities than they are to rounded opacities. The u opacities that occur with asbestosis have a much worse prognosis and have the most abnormal types of pulmonary function.

PROFUSION: This term refers to the concentration or number of small opacities per unit area observed within the lung fields. Twelve categories of profusion are recognized. The quanity of dust in the lungs (incinerated) correlates well with coal and silica in relation to the profusion but the quantity of asbestos dust in the lungs or asbestos fibers does not correlate with the profusion of irregular opacities. However, of all the characteristics of small opacities requiring codification, profusion is the most important for it is the best indicator of the seriousness of any disease that may be present.

In advanced cases of pneumoconiosis there is usually no question radiographically regarding the diagnosis of the disease. However, when only small opacities are present which are few in number (i.e. low profusion) interpretation can be quite difficult. This is because small opacities can occur in a wide variety of situations both normal and abnormal, as well as in pneumoconiosis. For example, as individuals become older, periodic respiratory infections often result in pulmonary fibrotic changes that appear radiographically as small irregular opacities. These changes are particularly prevalent in cigarette smokers. Individuals who suffer from chronic congestive heart disease, in time develop fibrotic findings in the lung that may be confused with the early stages of pneumoconiosis. Many pathological conditions quite unrelated to dust (e.g. other interstitial diseases) at various times in there courses, manifest themselves radiographically by the appearance of small opacities. Thus it is evident that the radiographic findings in early pneumoconiosis are not so characteristic that their interpretation can be counted on to be unequivocal.

Although this twelve point scale of profusion implies a high degree of quantification for the recording of profusion levels, it must be pointed out that the definition of major profusion categories on which the scale is based, is rather non-specific. Hence, when the profusion levels of series of radiographs are evaluated by a group of physicians, substantial differences of opinion can be expressed. (Physicians generally have the greatest difficulty in separating a series of radiographs into normals and abnormals when profusion levels are nearer the divisions of 0/1 and 1/0.) A given physician will therefore exhibit some inconsistency in his or her codification of profusion. Because of the difficulties that exist in the interpretation of chest radiographs, it is perhaps not surprising that

inconsistencies arise when a number of physicians independtly evaluate a series of radiographs or when the same individual physician evaluates the series a number of times. However, it should be pointed out that such inconsistencies are unavoidable and indeed characteristic not only of radiographic procedures but all clinical testing (including history taking, physical examinations and physiological tests) due to uncertainties inherent in all methodologies in which human judgement is a factor.

COMPENSATION: For coal workers using the ILO Classification System the Department of Labor, Employment Standards Administration uses a profusion of 1/0 to indicate disability and casusality with ten or more years of coal mining. Thus with ten years or more of coal mining a 1/0 or better gives a miner a continuing disablity pension plus the survivors benefits even though he may or may not have been disabled. Great difficulities arise in the low levels of profusion (where one reader might call it a 1/0 and another reader might call it 0/1 for awarding compensation.

An additional characteristic of small opacities that must be codified in the ILO 1980 Classification System is the extent of the pulmonary disease. To record this parameter, the lung fields are divided into six zones, three on each side corresponding to the upper, middle and lower thirds of the lung fields. The new classification system combines roundness and irregularity of opacities but does not differentiate as to their individual location. No distinction is made between rounded or irregular opacities or the location of the opacities relative to compensation or eligibility. A miner with asbestosis dust exposure with small irregular opacities at the bases, could qualify for benefits if this person worked in a coal mine (in spite of the fact that he may have no rounded opacities due to coal or silica in the upper lung zones).

LARGE OPACITIES: The large opacities which represent a lesion greater than 1 cm are divided into three categories depending on their greatest diameter or length. The finding portends a much more serious prognosis and is usually associated with abnormal pulmonary functions. Many of these patients will progress with abnormalities resulting in progressive massive fibrosis, marked emphysema, distortion and destruction of the lung with eventual death from cor pulmonale. Contrary to the ILO Classification, by definition according to the American Society of Pathologists, the lesion must be at least 2 cm in diameter to classify as progressive massive fibrosis. Difficulties arise in the classification system in that other disease processes (e.g. neoplasm, tuberculosis, etc.) may appear as "large opacities" on the x-ray. Without the clinical, the laboratory, and without previous films, large opacities of disease processes not due to pneumoconiosis in some cases may be classified erroneously.

PLEURAL ABNORMALITIES: The 1980 Classification System goes into great detail in reference to pleural thickening. Particularly it is known that asbestos dust inhalation (unlike coal and silica) results in abnormal pleural thickening with abnormal pleural shadows which are quite characteristic in many instances (i.e. plaques). Thus, the system requires that the site (chest wall, diaphragm and costophrenic angle) and the extent of the thickening be recorded separately. It is recognized that

this thickening can be observed either in profile (edge on) or en face (face on). However, for pleural thickening observed face on, its presence can be recorded but its thickness cannot be measured. When the pleural thickening is observed in profile its width can be measured and the ILO System recognizes three grades of width. Measurements are quite difficult in many instances because the same plaques are frequently seen with both a profile and en face image. Thus greater numbers of plaques may be recorded erroneously. The measurements are at best a very rough approximation of the width and extent of the actual plaque.

While circumscribed localized pleural thickening in the form of a plaque is quite characteristic, the ILO System also recognizes that "diffuse" pleural thickening does occur with asbestos dust exposure. Although it is non-specific, the length and width of the diffuse pleural thickening is also graded using the same measurements that one uses for circumscribed pleural plaques.

Standard films provided for the classification of the pleural changes need to be revised. The standard films are quite inadequate in that they do not differentiate between diffuse pleural thickening or pleural plaques in a clear definitive manner. Pleural plaques are more characteristic than diffuse pleural thickening but there is an in between "gray area" where one cannot be certain that we are dealing with confluent plaque formation rather than diffuse pleural thickening. Pathologically diffuse pleural thickening of asbestos dust exposure generally is quite extensive and involves the costophrenic angle. The characteristics of "diffuse" pleural thickening following asbestos dust exposure have not been clearly defined radiographically. One questions if it should be called "diffuse" (on some of the standard films) when its extent is only a few interspaces. Arbitrarily, I would not call it "diffuse" unless it also obliterates the costophrenic angle (plaques generally do not obliterate the costophrenic angle). A revision of the Standard Films (increasing the numbers) to run the whole range of pleural abnormalities is required. Indeed fat and muscle shadows are quite troublesome and examples of these shadows should be included in standard films.

It is also recognized that radiographically only 15% of the pleural plaques associated with asbestos dust exposure show recognizable calcification, (approximately 85% will show calcification pathologically). Calcification when it occurs on the diaphragm, the chest wall, the mediastinum and the pericardium is recorded separately. A localized calcification which is seen due to asbestos dust exposure should be classified as a plaque, even, if the surrounding soft tissue component is not seen on the single PA view. This needs further clarification in the 1980 Classification System.

While it is emphasized that the simple PA chest radiograph is the keystone of all radiographic examinations of the chest, there are occasions when a more extensive examination is necessary. For example, pleural thickening can be more confidently detected and diagnosed most easily when it is seen in profile. Therefore, when localized thickening exists, as it frequently occurs in the case of asbestosis, it is desirable to take oblique views and lateral views of the chest in an effort to bring the lesions into profile for more accurate measurements, (and to exclude other "simulating" lesions). Computed tomography is particularly valuable: in differentiating ill defined pleural shadows and demonstrating additional plaques and

calcifications, demonstrating the extent of circumferential diffuse pleural thickening, demonstrating emphysema, in substantiating interstitial disease and even honeycombing, and demonstrating the extent of suspected mesothelioma.

PULMONARY FUNCTION: The radiograph is currently the best available clinical method of diagnosing pneumoconiosis and it is the simplest and relatively accurate method of assessing the degree of involvement of the lung for coal workers pneumoconiosis and silicosis. However, its limitations may result in false negative findings early in the disease, and in some discrepancy in the degree of involvement. Good film technique with experienced readers are essential to keep the discrepancy to a minimum.

Radiographic methods primarily record anatomical structure and with very limited exceptions they do not record function. The information provided by the chest radiograph on the structures of the lung and on the pathological changes that may exist within them, is much greater than information on how the lungs may actually be functioning. The chest radiograph is better in evaluating pathological characteristics of a disease and it must be used with caution in assessing any disability that may have resulted from the disease. These limitations of the chest radiograph in the evaluation of pulmonary impairment are not difficult to understand. In pneumoconiosis, the disease particularly in its early stages, frequently is confined to small portions of the lungs (e.g. the upper lobes) and in such instances large segments are relatively unaffected. The unaffected regions are likely to function reasonably well and therefore, regardless of how extensive the involvement may be in the diseased zones, pulmonary function may not be significantly impaired. On the other hand, there are times when the disease from the beginning involves much of the lung parenchyma, with fibrotic changes that may not be impressive radiographically, but because they are so widespread they may impair function and cause disability relatively early.

In coal workers pneumoconiosis, the presence of small opacities correlates better with the amount of dust retained in the lungs than it does with lung function. In both simple coal workers pneumoconiosis and silicosis there is little in the way of a relationship between the radiographic features and impaired lung function. Only in Stages B and C conglomerate silicosis and coal workers pneumoconiosis does radiographic category relate to lung function. Pathological correlation is good and in most cases the roentgenographic characteristics are such that the findings are essentially diagnostic.

Relative to asbestosis the greater the past cumulative dust exposure, the higher the probability of progressive pulmonary fibrosis. The progression of small, irregular opacities depends upon average and cumulative asbestos dust exposure. Thus the patient should be advised that based on this possibility, even small increments in cumulative dust exposure will increase the risk for future progression of pulmonary fibrosis. The progression of abnormalities, (i.e. small irregular opacities) correlates impressively with progressive pulmonary function decline.

On the other hand, progression of pleural abnormalities is primarily dependent on time, and is not likely to be influenced by modest additional average or cumulative exposure. Unlike the lung changes, progression of

pleural thickening and pleural plaques is related to length of exposure and time since first exposure, but not to average or cumulative dust dose. Thus, the findings are consistent with the common clinical and radiologic observations of long latency of pleural effects (particularly calcification), the frequent finding of extensive pleural abnormalities in the absence of parenchymal disease, and the correlation of progressive parenchymal fibrosis (asbestosis) with heavy dust exposure. Diffuse pleural thickening is more likely to cause abnormal pulmonary function. Pleural plaques unless very extensive do not cause pulmonary function decrements. The patient might still be advised to continue in his occupation without any change if no other jobs were available.

The physiological limitations of the chest radiograph should in no way cause a lowering in one's mind of its value (either from a clinical or public health standpoint), in the evaluation of persons suffering from pneumoconiosis. Its objectivity in reliably assessing the pathological anatomy, short of a tissue specimen is unequalled.

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ASBESTOS RELATED DISEASE - PLEURAL ABNORMALITIES

E. Nicholas Sargent, M.D.

The pleural abnormalities following asbestos dust exposure include: (1) plaques (circumscribed or localized). (2) diffuse pleural thickening (circumferential or interlobar), (3) effusion, (4) mesothelioma. Pleural changes are more frequently found without associated pulmonary parenchymal abnormalities.

The normal pleural shadow (e.g. pleural stripe, accompanying shadow) has often been called pleural thickening. It consists mainly of internal intercostal muscle bundles and some fat. The parietal pleura is only 10 to 60 micra in thickness, as is the visceral pleura, and thus the normal pleura contributes very little to the shadow. Normally the shadow tapers from the apex and disappears usually below the fourth or fifth rib. Diffuse pleural thickening often follows a gravitational event in the pleural space (e.g. infection or trauma)and usually obliterates the costophrenic angle(casting a shadow which is wider inferiorly and tapers towards the apex).

The characteristic pleural plaque following asbestos dust exposure does not involve the pleural space or the mesothelial layer of the pleura and is subjacent to the parietal pleura. On the PA projection it is found along the costal reflection of the pleura, along the mid third of the thoracic wall. It does not involve the apical regions or the costophrenic angles until it becomes very extensive. Plaques also occur in the areas of reflection of the diaphragmatic parietal pleura (and the mediastinal pleura as well). Parietal pleural plaques occur over bony prominences and tendonous surfaces (thus involving primarily the pleura overlying the central tendon of the diaphragm). Pathologically plaques show great variation in size and shape. They are rarely thicker than 1 centimeter in cross section, until they are very far advanced.

Radiographically in the PA projection the plaques are described as shadows which are seen in "profile" with a sharply defined edge; or en face with ill defined margins. Frequently many of the plaques are projected partially in profile and partially en face. Thus the x-ray images are the result of the size, shape, and location of the plaque, but particularly the shadow will vary with the direction of the x-ray beam and the thickness of the tissue. The use of oblique projections is particularly important not only to confirm suspected questionable shadows on a PA projection but to discover additional areas of plaque formation that are not obvious on the PA projection. By rotating the patient in the oblique projection, plaques which are seen en face can be brought out in profile, and the true cross-sectional width more accurately measured.

Frequently difficulties arise as to whether certain shadows seen on the radiograph may be due to causes other than plaques. On the average it takes 20 or more years for a plaque to form and be radiographically identifiable. It usually takes three to five years for a plaque to change its size or shape. The use of comparison films for progression is helpful in the differential diagnosis. Furthermore, one must be familiar with shadows that simulate plaques.

Interdigitations of the external abdominal oblique and serratus anterior muscle slips cause shadows overlying the ribs. When they are bilateral, symmetrical and equal they are readily identifiable. They tend to disappear on the oblique view. Not infrequently, single muscle slips can cause difficulties. Comparison with old films or future films for

progress is of value as one cannot always be certain that an early plaque is beginning in the area of a suspected muscle shadow. Subpleural fat casts problematical shadows. Computed tomography is helpful. Rib injuries with overlying pleural thickening, iatrogenic and postoperative pleural changes can cause localized pleural thickening. Subpleural metastatic disease, (e.g. myeloma, breast metastases, thymomas, and melanomas) is a consideration; as well as uncommonly metastatic Hodgkin's histiocytic lymphoma and other lymphomas causing localized pleural thickening (can be differentiated clinically).

Characteristically calcifications in pleural plaques occur in the center of the plaque. However, calcification is seen only in 15% of asbestos related plaques radiographically, whereas it is found in 85% of the cases pathologically. Calcifications secondary to tuberculosis empyema, hemothorax, and other etiologies which are events that occur in the pleural space, resulting in calcifications which are more medially disposed and are further away from the internal surfaces of the ribs. Tuberculosis tends to be unilateral but can be bilateral. Finding other evidence of old Tbc is helpful. With rib injuries present on the film this leads one more towards the diagnosis of the calcification being due to trauma, particularly if it is unilateral. Other rare causes of calcifications which may simulate plaques are irradiation, mineral oil aspiration, pulmonary infarction adjacent to the pleura, and even calcification of the pleura secondary to scleroderma has been described. Although calcifications in plaques are more commonly bilateral they can be unilateral and a careful history as well as seeking evidence of other disease processes helps in the differential diagnosis.

The calcifications that are seen en face radiographically are varied and can be nodular, linear, circumferential, irregular, pseudovascular, and amorphous. Occasionally when they are very extensive they appear to have a "holly leaf" or "candle wax" appearance. The use of oblique views for defining their extent and width is of great value (also in differentiating calcifications in cartilages and in granulomas). On the PA projection calcifications occur not only in the region of the leaves of the diaphragm and along the thoracic wall, but they can occasionally be found in the mediastinum and even in the pericardium. Oblique views help to show the extent of the calcification along the mediastinal area and the pericardial region. Computed tomography is a much more sensitive method of picking up plaques and calcifications in all involved areas.

The most common finding in surveys of large numbers of patients exposed to asbestos dust is a noncalcified parietal pleural plaque located along the costopleural margin or on the surface of the diaphragm. This does not mean that less frequently one can see associated diffuse pleural thickening with or without plaques; interstitial disease with or without plaques; or pleural effusions with or without plaques. Any of these events can overlap with one another. All findings appear to be dose and time related. Generally, a light exposure results in an asymptomatic patient showing isolated plaques after a long latent period. With a heavy exposure one tends to find more interstitial disease in a shorter time frame. Occasionally, however, with very heavy exposure one can find extensive diffuse plaques with calcification, with a short latent period.

Diffuse pleural thickening is non-specific but when it occurs following asbestos dust exposure, it tends to involve more of the visceral pleura rather than the parietal pleura. Radiographically one cannot differentiate

visceral or parietal pleural thickening except when one finds thickening in the interlobar fissues. Diffuse pleural thickening usually obliterates the costophrenic angle. Computed tomography is particularly helpful in outlining circumferential pleural thickening of the diffuse type which might not be recognized on the plain film. Interlobar visceral pleural thickening does occur less commonly and even interlobar calcified plaque formation can occur.

A rare type of "hyalinosis progressiva maligna" or "hyalinosis complicata" has been described. This may or may not be accompanied by pleural effusions. Diffuse pleural thickening usually occurs unilaterally, but spreads contralaterally over a short period of time. Pathologically, both visceral and parietal pleura are thickened. There is a diffuse exudative pleural "rind" and these patients have been operated on with no evidence of mesothelioma formation. They have a very poor prognosis and tend to die of infections and respiratory failure.

Benign pleural effusions are now recognized with increasing frequency (occurring from 8 to 10 years on the average after the initial exposure). They may be clear or bloody and can be unilateral or bilateral occurring with or without plaque formation. More frequently they result in diffuse pleural thickening but often they disappear with no evidence of any residual pleural changes. However, one must exclude a malignant mesothelioma by careful clinical evaluation and follow-up of the patients. Pericardial effusions and pericardial calcifications have been described.

Any patient with a history of asbestos dust exposure pleural effusion should be considered as having a mesothelioma until proven otherwise. Characteristically the pleural effusions usually do not cause a shift of the heart or mediastinum. This is usually due to the encompassing pleural tissue "rind". Computed tomography is helpful in outlining the extent of the mesothelioma particularly when used for prognosis during therapy. The incidence of mesothelioma is not related to cigarette smoking as is bronchogenic carcinoma. Mesotheliomas do metastasize both ipsilaterally and contralaterally (usually before the patient dies there are distant metastases). Clubbing is more common with mesotheliomas but mesotheliomas are much more infrequent tumors than are bronchogenic carcinomas.

Pleural plaques do not degenerate into mesotheliomas. A pleural plaque merely means that the patient has been exposed to asbestos dust and is a "marker" for asbestos dust exposure. Bronchogenic carcinomas must always be looked for on the radiograph for any patient in which plaques are found (since the plaques mean asbestos dust exposure). Cigarette smoking and asbestos dust exposure are synergistic in causing bronchogenic carcinoma.

A change which is being recognized with increasing frequency is infolding of the lung associated with plaque formation or other pleural thickening. Infolding of the lung near areas of abnormal pleura is associated with segmental and subsegmental atelectasis resulting in "pseudotumor" formation (which must be differentiated from bronchogenic carcinoma). Characteristically, a relatively wide line extending towards the costopleural margin from the shadow of the "pseudotumor" should make one suspect a possible non-neoplastic situation. Computed tomography, needle aspiration biopsy and comparison with previous films are helpful

in the differential diagnosis. The finding is non-specific. It has also been found following pneumothorax, pleural fluid with tuberculosis, and hemorrhage secondary to trauma. It should be considered in patients known to have been exposed to asbestos dust and careful study to prevent an unnecessary thoracotomy is required.

Family exposure does occur and the finding of plaques in a young adult particularly when calcified, should alert one to the fact that the occupational history should include not only the immediate family, but other relatives and also all areas in which the patient has lived. It should be emphasized that it does not take a heavy expsure to cause a pleural plaque. Exposures of only a few months have been described resulting in plaques after a very long latent period (as much as 25-30 years after a light exposure).

Bilateral pleural plaques will be discovered with increasing frequency when they are particularly looked for on every radiograph. They merely mean that the patient has had asbestos dust exposure and should be correlated particularly with a lifetime occupational and family history. The patients are usually asymptomatic and must be cautioned not to smoke. Lifetime radiographic surveillance for any progressive changes as well as the possibility of a future occurrence of a pleural or parenchymal neoplasm, is indicated.

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MEDICAL PROGRESS

THE PATHOGENESIS OF ASBESTOS-ASSOCIATED DISEASES

JOHN E. CRAIGHEAD, M.D., AND BROOKE T. MOSSMAN, PH.D.

ASBESTOS is one of our most useful minerals. Over 3000 manufactured products of contemporary importance contain it. Asbestos is employed in construction materials because it is resistant to thermal and corrosive destruction and increases the tensile strength of the product. These properties are also the basis for the use of the mineral in friction equipment and in a wide variety of consumer items requiring a relatively inexpensive insulation material that is light and subject to molding. Since the turn of the century, about 3×10^7 tons of asbestos have been used in construction and in the fabrication of manufactured goods in the United States. At present, several million Americans are employed in industries that use asbestos products, and countless millions of American citizens are exposed to asbestos cryptically in the course of their daily lives.

Public concern over the effects of asbestos on health is mounting. Although a total ban on its use in this country has been proposed, most would agree that asbestos cannot be replaced expeditiously in many products. Litigation based on personal injury consequent to pulmonary fibrosis and cancer is an increasing problem for companies involved in the manufacture, use, and distribution of asbestos. About 12,000 suits have been brought against 260 companies by workers, their families, and members of the general public.[1,2] The spectrum of liability has now widened to involve the federal government for alleged negligence in establishing adequate environmental standards.

This review summarizes our current knowledge of the adverse effects of asbestos on health and provides a perspective on the pathogenetic mechanisms of the diseases associated with exposure. Since there are several different mineralogic types of asbestos, we will attempt to assess the extent to which findings with one type can be applied to another. Detailed analyses of the issues addressed in this paper have been published elsewhere.[3-6]

MINERALOGY

Asbestos is not one mineral but a family of fibrous hydrated silicates that are divided on the basis of mineralogic features into two groups: the serpentines and

From the Department of Pathology, University of Vermont College of Medicine, Burlington, VT 05405, where reprint requests should be addressed to Dr Craighead.

the amphiboles (Fig. 1). The term "asbestos" refers to the commercial product after mining and processing and is not a mineralogic designation. Although the length:width ratio of the mineral fiber known as asbestos is by definition ≥3:1, the individual fibers making up the materials used in commerce vary substantially in width and length (Fig. 2).

Chrysotile is the only serpentine of commercial importance. It is composed of pliable, curly fibers made up of fibrillar subunits. These fibrils are arranged in pseudohexagonal arrays composed of silicon oxide sheets formed into scroll-like structures. The magnesium ion, which imparts a strongly positive charge to the fiber, is an integral component of the lattice.

The amphiboles are straight, rodlike fibers consisting of double chains of tetrahedral groups having a basic silicon oxide composition and linked by one or more cations. The amphiboles differ from chrysotile in both physical and chemical makeup. There are several types of amphibole, but crocidolite and amosite are the two minerals of major importance.

Although an asbestos type is classified on the basis of its mineralogic characteristics, the products of different mines are not necessarily the same. Moreover, a commercial type of asbestos is not always mineralogically pure. For example, Canadian chrysotile contains small amounts of an amphibole fiber, tremolite. In addition, industrial grades of asbestos are contaminated with extraneous inorganic and organic substances that are acquired either naturally or during processing.

Deposits of serpentine and amphibole are ubiquitous in the crust of the earth. Outcrops are found in many geologic formations and probably account for the mineral fibers commonly found in surface water. Asbestos is also found with other minerals of commercial importance, such as the iron ore taconite and industrial-grade talc. Canada and South Africa are the major suppliers in the western world, although mines of limited commercial importance are found in many countries. In the United States serpentine and amphibole minerals are distributed widely in geologic strata, but only two relatively small mines in Vermont and

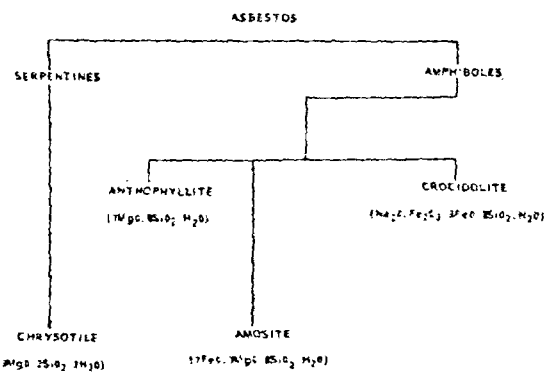

Figure 1. Types of Asbestos of Commercial and Medical Importance and Their Chemical Compositions

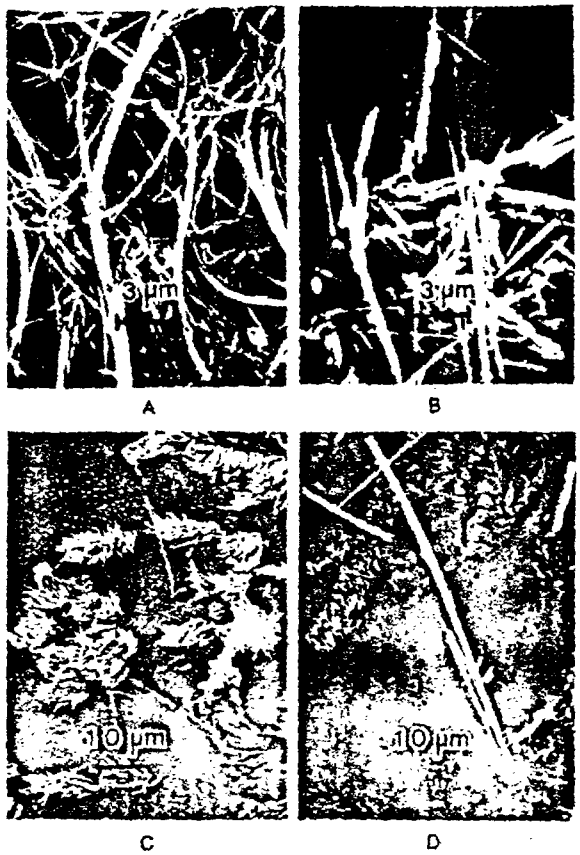

Figure 2. Differing Structural Features of Serpentine (Chrysotile) and Amphibole (Crocidolite) Asbestos.

These scanning electron micrographs of International Union against Cancer reference samples of chrysotile (Panel A) and crocidolite (Panel B) asbestos illustrate the heterogeneity of fibers in both length and diameter. Micrographs of the hamster tracheal epithelium after exposure in vitro to asbestos illustrate the curly, pliable nature of chrysotile (Panel C) and the straight, rod-like form of crocidolite (Panel D). Note the dimensions of the fibers in comparison to the cilia. Photomicrographs were furnished by Mr. Craig Woodworth, Department of Pathology, University of Vermont College of Medicine.

California are active. The amount of asbestos produced in the Soviet Union and the People's Republic of China far exceeds that extracted in the West.

Chrysotile currently accounts for over 90 per cent of the total asbestos marketed in this country and abroad. Crocidolite is the most widely used amphibole, but for reasons considered below, its commercial importance has decreased over the past several decades (Table 1).

Uses of Asbestos

The unique physical properties of asbestos dictate its continued use by industry, despite contemporary concerns about its effects on health. Although various man-made and naturally occurring substances have been developed as substitutes for asbestos, none

Table 1. Consumption of Different Types of Asbestos in the United States in 1978.*

Use	Type of Asbestos			Total Asbestos
	Chrysotile	Crocidolite	Amosite	
	metric tons			
Asbestos cement pipes	119,700	24,100	200	144,000
Asbestos cement sheeting	7,900	—	—	7,900
Flooring products	90,000	—	200	90,200
Roofing products	26,500	—	—	26,500
Packing and gaskets	12,200	100	—	12,300
Insulation, thermal	6,000	—	—	6,000
Insulation, electrical	2,900	—	—	2,900
Friction products	43,700	—	—	43,700
Coatings and compounds	10,900	—	—	10,900
Plastics	1,200	100	—	1,300
Textiles	1,900	—	—	1,900
Paper	400	100	—	500
Other	9,000	—	1300	10,600
Total	332,300	24,400	1700	358,700

*Modified from the data of Fagan.[7]

matches asbestos in providing tensile strength and moldability as well as resistance to fire, heat, and corrosion. In addition, many of the manufactured substitutes are comparatively expensive.[8]

About 25 per cent of the asbestos consumed in the United States is incorporated into cement piping for water mains and sewage lines. Over 320,000 km of pipe, containing about 10 to 20 per cent asbestos, is believed to be in use in this country. Asbestos-containing cement is employed widely in corrugated and flat sheeting, panels, tiles, and moldings for the construction industry. The mineral is used extensively in roofing and paneling and as a filler in architectural dead spaces. In the past, suspensions of asbestos were sprayed onto the structural steel of buildings to provide insulation and fire protection.

Because of its thermal stability, asbestos is well suited for use in friction material and is applied to molded brake linings. Although substitutes are being increasingly employed in disk brakes, as in the aircraft industry, a drum-brake lining for passenger cars that does not contain asbestos is not available commercially.

Textiles and plastics of a variety of types and applications contain asbestos in various concentrations, since it imparts resistance to fire and corrosion as well as tensile strength without inordinately altering the properties of the product or increasing its weight.

The countless additional industrial uses of asbestos are of concern because they can be overlooked by the manufacturer and unrecognized by the consumer. Although asbestos was known to industry before the turn of the century, its use in the United States increased dramatically during the mobilization that accompanied World War II. Asbestos was employed liberally in the construction and reconditioning of ships and in such diverse war industries as the manufacture of aircraft engines, combat vehicles, and gas masks. Although worldwide production has continued to increase since the war, consumption in this country has dropped substantially during the past decade. This trend can be expected to continue. Since the latency period for the diseases associated with asbestos is usually 20 years or longer, most patients seen today were initially exposed in the 1940s and 1950s, when control measures were often not rigorous.

Diseases of the Respiratory Tract and Thorax

The major pathologic effects of asbestos result from the inhalation of fibers suspended in the ambient air. The occurrence of disease is influenced by the type of mineral and the dimensions of the fibers that constitute it, as well as by the concentration of fibers and the duration of exposure.

Deposition and Transport in the Lungs

Timbrell et al.[9] studied the deposition of fibers of asbestos in the respiratory tract, using a cast of the porcine tracheobronchial tree. The diameter of the individual fibers proved important; length was a less important determinant.[10,11] Fibers with a relatively broad diameter are deposited in the upper respiratory tract, whereas thin fibers are carried peripherally into the parenchyma of the lung, where they lodge in the terminal airways. Bifurcations are common sites for fiber impaction, since patterns of air flow are altered at these sites.

The shape of the fibers also has a role in transport. Aerodynamically, chrysotile has a relatively large theoretical cross-sectional diameter because of its curled configuration. Thus, fibers of this type tend to be deposited more proximally than the needle-like amphiboles, which are transported more readily to the periphery of the lung. These theoretical and experimental considerations have been verified by analyses of the lungs of rodents experimentally exposed to asbestos of different types.[12]

Three biologic mechanisms participate in the clearance of fibers from the lower respiratory tract. By far, the bulk of the dust is removed by the mucociliary escalator of the tracheal bronchial tree, and the material is either expectorated or swallowed.[13-15] In the peripheral airways, short fibers are ingested by macrophages, and at least some of these cells probably migrate across the wall of the bronchioles and acini.[15-18] Asbestos fibers are also taken up by the epithelial cells lining the airways and appear to move between cells of the mucosa.[18,20] This material accumulates in the interstitium and is carried to regional lymph nodes.[17] In general, short fibers are cleared more readily than long fibers,[17] which tend to be retained in the lumens of the respiratory bronchioles and the alveolar ducts.

About a third of the inhaled particles initially lodge in the distal airways. However, only about a quarter of this burden is retained in the respiratory tract one month later.[13] There are two phases of clearance through the tracheobronchial tree. About half the asbestos is removed within a few days. Subsequently,

clearance continues for extended periods. The bulk of this material is excreted in the feces.[15]

A variety of extraneous influences such as cigarette smoke and air pollutants affect the clearance and intrapulmonary deposition of fibers. However, these factors are extraordinarily complex, in part because individuals appear to differ in their responses to inhaled dust.[21-29]

Asbestosis

Diffuse pulmonary fibrosis is the typical lesion associated with prolonged, heavy exposure to asbestos.[30] It develops slowly over a period of years and seems to progress in the absence of continued exposure to asbestos. Initially, fibrosis is found in and around the respiratory bronchioles and alveolar ducts, where relatively long fibers deposit. With time, the fibrotic lesion progresses in a seemingly centrifugal manner, so that increasing numbers of respiratory units are involved. Fibers of asbestos tend to accumulate preferentially in the lower lobes and adjacent to the visceral pleura. Fibrosis is usually prominent in these regions, and the pleural surfaces of these lobes are frequently thickened by a dense layer of fibrous tissue. In advanced asbestosis, the fibrotic pulmonary tissue contracts and is reorganized to form the new air space typical of the honeycomb lung.

Ferruginous bodies are the histologic hallmark of exposure to asbestos.[31-34] They consist of fibers coated by complexes of hemosiderin and glycoproteins and are believed to be formed by macrophages that have phagocytized the particles. Asbestosis can exist when ferruginous bodies are difficult to demonstrate in the lungs by light microscopy. On the other hand, ferruginous bodies can often be found in the absence of serious parenchymal disease.[35,36] Thus, their presence alone is probably not a stimulus for the proliferation of fibrous tissue. Although they have been shown to form from foreign inorganic and organic fibers of many different types,[37] ferruginous bodies in most human lungs have asbestos as a core.[36] For this reason, the structures are commonly known as asbestos bodies.

The number of uncoated fibers in the lung greatly exceeds the number of asbestos bodies in the tissue.[38,39] It is not known why some fibers are coated and form the typical asbestos bodies, whereas others are uncoated. Since uncoated fibers are usually difficult or impossible to demonstrate by light microscopy, lung tissue must be digested and the residue examined by either phase or electron microscopy in order to carry out qualitative and quantitative studies of the fibers. Whereas relatively long fibers (>5 μm) are found by light microscopical techniques, electron microscopy makes it possible to identify very small particles.[40,41] Thus far, attempts to correlate the extent of disease with either the number of asbestos bodies or the overall content of fibers in the lungs have been difficult, although fibrosis is usually evident when 10^6 fibers per gram of lung (wet weight) are present. Quantitative studies pose many problems and are only a crude measure of exposure, partly because many fibers are cleared from the lungs and others fragment to increasingly smaller particles with time.

Macrophages are a key element in the response of the host to asbestos. Whereas these cells phagocytize short fibers and remove them from the airways, they cannot encompass and transport the longer fibers. Although retention of these long fibers in the distal airways appears to be an important consideration in the causation of pulmonary fibrosis,[18,30] the pathogenesis of the lesion is not understood. Incomplete phagocytosis of asbestos fibers in the airways could result in spillage of lysosomal enzymes[42] and release of soluble fibrogenic factors from macrophages.[43] On the other hand, oxygen free radicals liberated by macrophages and other inflammatory cells might also injure lung tissue. This idea is supported by our observations that superoxide dismutase, an inhibitor of biologic oxidants, protects cultured respiratory epithelial cells from the cytotoxic effects of chrysotile (Mossman BT, Landesman JM: unpublished data). Chrysotile is cytotoxic in vitro presumably because the magnesium of the fibers interacts with the plasmalemma and damages it, along with lysosomal membranes of cells.[44,45] It is unclear whether this is an important mechanism of tissue injury, however, since pulmonary macrophages and epithelial cells in the lungs of animals exposed to aerosolized chrysotile fail to reveal ultrastructural evidence of injury.[18,19]

Other biologic phenomena may prove important in the causation of pulmonary fibrosis. Asbestos activates complement by the alternative pathway[46] — a reaction that may be expected to result in the accumulation of leukocytes in the tissue and the release of lysosomal enzymes. This observation is consistent with the finding of an acute inflammatory response in some early lesions.[30,47] Finally, consideration must be given to the possibility that asbestos stimulates the production of collagen by cells. When chrysotile is added to cultures of fibroblasts in vitro, the cells elaborate reticulin and collagen at an accelerated rate.[48,49]

Although the hypothetical mechanisms mentioned above could account for the deposition of fibrous tissue in the lungs, the pathogenesis of asbestosis in human beings remains to be established. The question may be moot, however, since modern environmental controls have dramatically reduced exposure in the work place. The dust concentrations permitted by current regulations will probably not induce substantial pulmonary fibrosis during the lifetime of an industrial worker.

Pleural Lesions

Plaques are curious lesions made up of hyalinized fibrous tissue located on the parietal pleura of the thorax, diaphragm, mediastinum, and pericardium.[50,51] They are usually but not invariably associated with exposure to asbestos.[38] Although the occurrence of plaques correlates with the duration and intensity of exposure, it is common to find lesions in the absence of

obvious disease of the pulmonary parenchyma. Thus, relatively small amounts of dust can induce the development of plaques. These benign lesions do not appear to develop into malignant mesotheliomas.

Characteristically, plaques are located in the intercostal spaces on the anterior and posterior lateral aspects of the thorax and on the dome of the diaphragm at sites where the visceral and parietal pleuras approximate during respiratory excursions. The configuration of the plaques is highly variable. For example, on the chest wall they usually follow the contour of the rib, whereas on the diaphragm they are customarily either disk-shaped or geometrically shaped and have a nodular surface. Over time the lesions become calcified, permitting easy recognition on x-ray films. Although most of the available epidemiologic information is based on radiologic surveys,[52-55] it is not always clear in published reports whether plaques were differentiated from the fibrous lesions of the visceral pleura that accompany pulmonary asbestosis.

Since plaques are found most often in persons exposed occupationally to asbestos for extended periods,[54-56] their overall prevalence in the United States is low.[57] In Eastern Europe and Asia Minor the lesions are frequently found in older members of the general population who lack documented exposure to asbestos. The presence of fibrous minerals in soil and in local construction materials may account for the common occurrence of pleural plaques in these regions.[58-61]

Malignant mesotheliomas of the pleural and peritoneal cavities are considered pathognomonic of exposure to asbestos, although in many patients a history of contact with the mineral cannot be elicited.[62-64] These rare tumors are of particular concern from a public-health standpoint because they are thought to occur in persons who have had either transient or indirect exposure to asbestos.[65-67] The development of mesotheliomas as a consequence of casual exposure, however, is an uncommon event. On the other hand, the prevalence of the tumor in workers who have had heavy exposure over extended periods is about 2 to 3 per cent and has been reported to approach 10 per cent.[68,69] It is difficult to determine how often mesotheliomas actually occur, because the latency period is usually 20 years or longer and can often be as long as 40 to 50 years. Some suggest that an epidemic of mesotheliomas will appear in the late decades of this century, consequent to the exposure of large numbers of workers during World War II.

The pathogenesis of the pleural lesions associated with exposure to asbestos is not known, but it is a topic of considerable contemporary interest. Fibrosis of the visceral pleura, plaques of the parietal pleura, and mesothelioma probably develop by different mechanisms, although a rigorous defense of this conclusion would be difficult. As mentioned above, asbestos is deposited preferentially in the periphery of the lung after inhalation. It penetrates the visceral pleura and is carried in the pulmonary lymphatics to the pleural surface. One is tempted to attribute the fibrous lesions on the visceral pleura to irritation by the physical presence of fibers on or near the surface. This mechanism might also explain the occurrence of plaques in the parietal pleura. Alternatively, the lesions may represent an organized fibrinous exudate resulting from the physical movement of the lungs against the pleural surface of the thorax.

However, these hypotheses are not fully consistent with the pathological observations. For example, plaques are often found without fibrosis of the visceral pleura or adhesions between the pleural surfaces. In addition, the lesions are localized and do not occur in the apexes or in the costophrenic angles. The pathogenesis of the lesions cannot be defined at present, in part because plaques occur only in human beings and experimental models have not been developed.

Experimental studies by Stanton et al.[70,71] provide an intriguing basis for speculation about the pathogenesis of mesothelioma. The dimensions of the fiber, but not the chemical composition, were found to be the critical determinant affecting the development of tumors in rats. Long, thin fibers of a variety of types proved carcinogenic when introduced into the pleural space, whereas short fibers and those with a relatively broad diameter failed to induce mesotheliomas. These findings are consistent with epidemiologic observations documenting the relatively common occurrence of tumors in populations exposed to grades of crocidolite consisting predominantly of long, thin fibers and the rarity of tumors in persons exposed to the comparatively blunt, shorter fibers of amosite and anthophyllite.[63,72-74] A fibrous zeolite, erionite, has recently been associated with the occurrence of pleural fibrosis and mesothelioma in a rural area of Turkey where commercial mining of asbestos does not occur.[61] Since the fibers of this mineral do not possess the chemical properties of asbestos but are morphologically similar to crocidolite fibers, the observation is consistent with the experimental findings of Stanton and his associates.[70,71]

The basis for the development of mesotheliomas in the peritoneum is uncertain. Presumably, fibers of asbestos in the lungs are transported in lymphatics to the abdomen, where they have been recovered from lymph nodes and other organs.[75,76] Asbestos is also transported across the mucosa of the gut after ingestion.[77,78] Whatever the mechanism for entry of asbestos into the abdomen, it is assumed that the pathogenesis of the tumors in the peritoneal and pleural cavities is similar. Peritoneal mesotheliomas occur only in persons exposed to amphibole asbestos. The gradual disintegration of chrysotile in tissue may account for the relatively uncommon occurrence of mesotheliomas of both the pleural and peritoneal cavities in persons exposed exclusively to chrysotile.[79]

The mechanism of malignant transformation of mesothelial tissues is obscure. Surprisingly little experimental information has accumulated, although there is reason to believe that the lesions may be com-

parable to the foreign-body sarcomas induced subcutaneously in animals by sheets of plastic, glass, and metal. The cell of origin is not certain, since some tumors are made up of malignant serosal cells, whereas others have the histologic features of fibrosarcoma. Mesothelial cells phagocytize asbestos[80] and proliferate when exposed to asbestos in vitro,[81] but malignant transformation has not been demonstrated after exposure of cultured mesothelial cells to asbestos. Cocarcinogenic substances and cigarette smoke do not appear to be pathogenetic factors in vivo.

Bronchogenic Carcinoma

Epidemiologic studies have documented an association between bronchogenic carcinoma and occupational exposure to asbestos.[82-87] The prevalence of tumors is higher in persons working with the finished products (such as insulators) than in miners and millers. The severity of the pulmonary parenchymal fibrosis correlates with an increase in the number of neoplasms.[88,89] However, the incidence of tumors is also increased in asbestos workers who lack radiologic evidence of asbestosis.

Some controversy exists over the most common histologic type of tumor, but among persons with asbestosis, adenocarcinomas predominate.[90-91] The lesions tend to occur more frequently in the lower lobes in conjunction with severe degrees of fibrosis.[30] Atypical hyperplasia of bronchiolar epithelium and multifocal adenocarcinomas are often found in these sites.

A linear dose-response relation between the cumulative dosage of asbestos and the development of bronchogenic carcinoma has been reported in miners and millers of chrysotile in Canada[85] and factory workers in the United Kingdom.[83] In the former study, those at greatest risk were exposed to concentrations of asbestos in the air that were higher than the current regulations of the United States Occupational Safety and Health Administration permit. A higher carcinogenic potential for crocidolite than for chrysotile has been suggested by studies of occupational groups exposed to either type of asbestos or to the two in combination.[92] Mortality among chrysotile workers is increased 2.4-fold, whereas it is five times higher than normal among miners of both chrysotile and crocidolite.

Surveys of the smoking habits of insulators,[93] factory workers,[94,95] and miners and millers[96] have consistently shown that bronchogenic carcinoma is uncommon in those who do not smoke. Whereas there is only a slight increase in the prevalence of lung cancer among nonsmokers, heavy users of cigarettes (those smoking more than 20 per day) have an 80-fold to 90-fold greater predisposition to cancer of the lung.[93,94] Thus, the combined effects of asbestos and smoking appear to be multiplicative rather than additive.[97]

What is the mechanism of asbestos-induced carcinogenesis in the respiratory tract? A consideration of contemporary concepts of neoplastic transformation is appropriate in developing an answer to this question. As initially recognized by Berenblum, carcinogenesis is a sequence of events that can be divided into steps of initiation and promotion.[98] An initiator interacts with the DNA of the target cell — an event that can result in malignant change. The carcinogen either acts directly with the DNA of the cell or requires metabolic activation by cellular enzymes. A promoter is generally neither mutagenic nor carcinogenic, although it is required if the neoplasm is to develop. For example, if the skin of a mouse is painted with a small amount of a chemical carcinogen, such as a polycyclic aromatic hydrocarbon, tumors fail to develop unless a phorbol ester is subsequently applied to the site. Promoting substances cause cellular division and proliferation as well as biochemical changes in the cell that appear to be essential for neoplastic transformation.[99]

Although epidemiologic data link exposure to asbestos with bronchogenic carcinoma in human beings, the precise role of the mineral in the process has yet to be defined. Since asbestos is not a potent mutagen[100] and inconsistently causes chromosomal aberrations in cells,[101-103] a mode of action comparable to that of a classic chemical carcinogen is unlikely. It therefore seems more plausible to suggest that asbestos increases the susceptibility of epithelial cells of the bronchi and their branches to transformation by carcinogens in the environment.

What biologic mechanisms account for the synergistic carcinogenic effects of asbestos and cigarette smoke in the respiratory tract? A plausible hypothetical construct should be consistent with the apparent lack of a threshold in human beings and the occurrence of neoplasms in the absence of appreciable degrees of pulmonary asbestosis.

Asbestos has many of the properties of classic tumor promoters, such as the phorbol esters.[104] Proliferation and squamous metaplasia are induced in the respiratory mucosa of rodents in vitro.[105] Asbestos interacts with the membranes of cells[106,107] and induces the synthesis of the polyamines that accompany cell division.[108] Since cigarette smoke also contains a host of substances with promoter effects, the inhalants may act in either an additive or a synergistic fashion to enhance the susceptibility of the respiratory mucosa to carcinogens.

However, alternative mechanisms are worthy of consideration. Asbestos can be phagocytized by the bronchial epithelium and can be transported intracellularly both free in the cytoplasm and in phagolysosomes.[20] These fibers may serve as a physical carrier of the carcinogens in cigarette smoke to the basal cell, the presumptive progenitor of the neoplasms. Transfer of polycyclic aromatic hydrocarbons to and through biologic membranes occurs promptly and efficiently when the hydrocarbon is adsorbed to asbestos.[109] Thereafter, the hydrocarbons are converted by microsomal mixed-function oxidases to biologically active epoxides and diolepoxides, which can interact with the DNA of basal cells.[110] Another (but less attractive) hypothesis involves the alveolar macrophage, which phagocytizes asbestos in the airways and possesses the

enzymatic capacity to convert polycyclic hydrocarbons to active metabolites.[111] At present, the mechanism of asbestos-associated carcinogenesis is unclear, although the mineral appears to act like a classic tumor promoter. The fibrous nature of asbestos is critical, since exposure to nonfibrous oxides of silicon (for example, quartz) and a variety of silicates is not associated with an increased risk of bronchogenic carcinoma in human beings.

Cancers of the Digestive System and Other Organs

Asbestos is implicated in the causation of cancer in the upper and lower gastrointestinal tract and the kidney.[112-115] Oropharyngeal and esophageal tumors occur more frequently in asbestos workers who smoke, whereas a direct relation between smoking and the development of carcinoma of the large intestine and the kidney has not been established.

Selikoff and Hammond[114] and Elmes and Simpson[112] have reported a statistically significant twofold to threefold increase in the prevalence of tumors of the digestive tract in insulators, factory workers, and shipyard employees. Other surveys have either demonstrated a smaller increase or failed to establish an association between exposure to asbestos and neoplasms in this system.[116] We believe that the evidence must be assessed cautiously because the associations thus far reported are relatively weak. Since death certificates are used to obtain data in most studies, it is possible that peritoneal mesotheliomas have been confused with metastatic carcinomas of gastrointestinal-tract origin.

The general population is exposed to small amounts of asbestos in drinking water, beverages, food, drugs, and agricultural products. Potable water often contains mineral fibers that are presumably derived from geologic deposits and refuse dumps. The finding of fibers of amphibole asbestos in the drinking water of Duluth, Minn., resulting from the disposal of taconite tailings into Lake Superior,[117] prompted investigations to determine the concentration and characteristics of mineral fibers in water supplies throughout the United States. Fibers with the properties of both serpentine and amphibole asbestos were found in over half the samples of water studied (Table 2). Thus, many Americans consume water containing asbestos-like minerals.

Table 2 Concentrations of Asbestos-Like Mineral Fibers in the Water Supplies of Selected but Representative Communities in the United States.*

City	Concentration
	no. of fibers >5 μm/liter
Atlanta	5.75
Boston	3.98
Duluth	1.72
Dallas	0
Kansas City, Mo.	0.07
New York	0
Philadelphia	16.95
San Francisco	0.60
Seattle	0.85

*Prepared from Table E-2 in Levine.

Mineral fibers have been detected in the urine of residents of Duluth in numbers corresponding to the concentration of asbestos in drinking water.[118] Interestingly enough, fibers have been found in the glomeruli and tubules of rats exposed in inhalation chambers to synthetic fibers.[119] These observations suggest that asbestos migrates to the kidney after clearance from both the gastrointestinal and respiratory tracts. Whether this has an influence on the occurrence of tumors in the gastrointestinal tract is unknown.

When fed to laboratory animals, asbestos interacts with the mucosa of the gut.[78] Fibers enter cells of the mucosa and prove cytotoxic.[120] The experimental evidence strongly suggests that ingested asbestos is disseminated to abdominal organs by the lymphatics and blood vessels. This conclusion is supported by postmortem studies of occupationally exposed persons; these studies have demonstrated asbestos bodies and uncoated fibers in most major organs.[76]

How does the ingestion of asbestos induce gastrointestinal carcinomas in human beings? In efforts to address this question, rodents were fed large amounts of asbestos over extended periods. With one exception,[121] these studies failed to demonstrate an increase in the prevalence of tumors in the gut.[122-124] The possible synergistic effects of asbestos on the induction of intestinal neoplasms by chemical carcinogens has also been examined.[125] Intragastric administration of asbestos failed to augment tumor development in rodents fed azoxymethane, a recognized intestinal carcinogen.

The carcinogenic potential of asbestos in the gastrointestinal tract appears to be low. The pathogenetic basis for the purported increase in the prevalence of carcinomas in certain occupational groups remains to be established.

Pathogenic Potential of Asbestos Types

As emphasized above, asbestos is not one but a family of fibrous minerals, each of which has distinctive physical and chemical characteristics. Minerals from various parts of the world and geologic formations often have dissimilar physical properties, even though they are classified under a specific mineralogic type. These differences are relevant to our understanding of the effects of asbestos on health, since the characteristics of the fiber have been fully defined in only a few epidemiologic and experimental studies. The problem of evaluating the effects of different types of asbestos on health is compounded by the common practice of custom blending of various minerals for specific industrial applications and the use of one type and then another, depending on availability and conditions of the market.

Since the serpentine chrysotile is used extensively in industry today, it is important to ask whether its pathogenic importance is comparable to that of the amphiboles crocidolite and amosite. These latter minerals are of historical importance, particularly since

they were used widely during and immediately after World War II and are probably responsible for a substantial proportion of the disease occurring today.

Much current debate centers around the question of whether all types of asbestos possess the capacity to induce mesothelioma. Experiments in animals yield an affirmative answer, but the results of this work may not be applicable to human beings, since pathogenic potential and intrapulmonary transport of fibers are independent considerations. Of all the types, crocidolite is clearly the most strongly associated with the occurrence of the tumor. But there are interesting differences in prevalence, related to the physical character of this fiber type. For example, in Northwest Cape, South Africa, and western Australia, mesotheliomas occur commonly in persons with occupational or casual exposure to crocidolite.[65] The mineral mined in these regions is composed of relatively long, thin fibers. In contrast, mesotheliomas are rare in the Transvaal of South Africa, where the crocidolite fibers are much coarser.

Another amphibole, amosite, is associated sporadically with mesothelioma, whereas the tumor rarely if ever occurs in workers exposed to anthophyllite. Both these latter types are made up of relatively short, blunt fibers. A number of studies have been conducted in miners and millers in Quebec and Italy, where the serpentine chrysotile is extracted.[74,126] Although the results are debated, the bulk of the evidence indicates that chrysotile is not an important cause of mesothelioma in these workers.

However, the data from certain occupational groups, such as workers in the textile industry and insulators who are exposed predominantly but not exclusively to chrysotile, are not as definitive. The risk appears to increase as the mineral is processed or when dust concentrations cannot be evaluated critically. Unfortunately, most epidemiologic studies concerned with this important question are clouded by uncertainty because of the prolonged latency period of mesotheliomas. Considerable effort has focused on determining whether the various types of asbestos differ in their capacity to induce bronchogenic carcinoma and fibrosis of the lung. Unfortunately, there is no good answer to these questions at present, since dose-related differences in the prevalence of disease have not been established.

Regulatory Considerations

No topic is more complex and subject to controversy than the establishment of criteria on which to base standards for air quality in the work place. Regulations are exceptionally difficult to develop, because it is necessary to use data on morbidity and mortality documenting disease retrospectively in members of occupational groups who have had heavy exposure either in the remote past or over a lifetime. The difficulties are compounded by the long latency period of asbestosis and the asbestos-associated cancers.

Although recommendations for levels of asbestos in the air of occupational settings in this country were formulated in the 1940s, it was not until 1970 that federal regulations were promulgated as a result of the passage of the Occupational Safety and Health Act and the Clean Air Act. The initial standard was based on the light microscopical count of fibers of a length of 5 μm, collected by mechanical means. A concentration of five fibers per cubic centimeter of air, averaged over an eight-hour period, was deemed permissible, with stipulations for transient excesses above that concentration. In 1976 the contemporary standard of two fibers per cubic centimeter was established, and more recently a level of 0.5 fiber per cubic centimeter has been proposed.

Is the current limit of two fibers per cubic centimeter sufficiently rigorous to prevent disease in the future? Is it appropriate to base regulation exclusively on determinations of fibers of >5 μm when the bulk of the dust in air consists of fibers of a shorter length? Because standards are based on extrapolations from data accumulated among workers exposed to relatively heavy concentrations of dust in the past, predictions must be based on analyses that assume that there are no thresholds below which the disease fails to occur. Within the ranges usually found in the occupational setting, there appears to be linearity in the dose-response relation, at least with regard to bronchogenic carcinoma. However, the likelihood that cancer will occur is influenced substantially by cigarette smoking, since the risk in the nonsmoker who has heavy exposure to asbestos is increased only a few fold. Thus, the risk for the nonsmoking asbestos worker is substantially lower than the risk for a member of the general population who smokes two or three packs of cigarettes each day.

The conclusion that asbestosis fails to develop below a certain threshold dosage is based on physical examinations and radiologic studies of workers and not on pathological examinations. By these criteria, it is probably impossible to be certain whether a fibrotic lesion in the lung is due to asbestos. With mesothelioma, the data are more controversial. Although a dose-response relation appears to exist, the threshold may be determined by the life span of the person exposed, because the latency period for these tumors is protracted. Since the problem cannot be answered with contemporary epidemiologic and experimental approaches, it must be resolved by practical rather than theoretical considerations.

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EXPOSURE TO ASBESTOS AND HUMAN DISEASE

DURING the past two decades, ill health resulting from exposure to asbestos has been the subject of intensive observation and research[1] — probably more intensive than research on any other environmental agent.[2] In the most direct target organ, the lung, and in its pleural coverings, there is a wide spectrum of response after exposure; not only acute and chronic inflammatory diseases but also cancer of these organs may occur. Research has been stimulated by the belief that the more complete our understanding of the mechanisms of pathogenesis, the better will be our ability to control the continued use of this mineral in today's complex technologic world.[3]

The review by Craighead and Mossman of the pathogenesis of asbestos-related diseases in this issue of the *Journal*,[4] which covers recent work in cell biology, is set in the context of pathology but also discusses the use of these minerals and regulatory considerations; it complements other recent reviews of the epidemiology of these diseases,[5] their impact on public health,[6] and current clinical issues.[7] Also important is a recent report that provides criteria for grading the pathologic changes in the lungs associated with asbestos exposure.[8] Systematization of pathological assessments can only enhance the pooling of experience from different centers or countries by maximizing the comparability of studies. The international classification of radiographs of pneumoconiosis[9] by the International Labour Office is an example of such systematization, and the dividends associated with its use are generally recognized.

Perhaps the major contribution of the review by Craighead and Mossman (and this may surprise readers not familiar with the field) is the emphasis placed on the shortcomings of our present knowledge of the pathogenesis of asbestos-related disease. Considering first the fate of inhaled fibers in the lung, it is now evident that the dust burden of the lung is primarily in the form of uncoated asbestos particles,[4] whether or not these conform to the definition of a fiber (i.e., a particle with a length-to-width ratio of 3:1). This definition probably originated rather arbitrarily from a need to standardize what was considered a fiber for purposes of industrial hygiene[6]; it is now widely believed that a much higher ratio, perhaps 10:1, would have been a better choice. Both fiber length[10] and mineralogic type[11] are important determinants of whether a fiber becomes coated and so takes on the familiar appearance of the asbestos body. Most asbestos bodies found in human lungs contain an amphibole fiber as a core,[11] even though chrysotile accounts for the greatest use and presumably the most exposure.[7] What permits some particles to lie apparently dormant in the lungs for long periods before evoking an organ response is not known, and there is no good explanation for the fact that all the disease consequent to asbestos exposure (including fibrosis of the lungs and

pleura as well as cancer of these organs) may appear long after exposure has ceased.

Fibrosis of the lung (asbestosis) was recognized by the first decade of this century and has been the subject of much research in animal models. Nevertheless, Craighead and Mossman conclude that the pathogenesis of asbestosis remains to be established,[4] as does the importance of exposure dose as compared with individual "susceptibility" in the initiation and the progression of the fibrotic reaction. The finding of an acute inflammatory response in some early human lesions[4] raises the issue of whether there is a reversible component to the acute response in human beings, as suggested by work in animals.[12] Long-term studies in sheep[13] may help to answer this question. As for whether asbestos acts as an initiator or as a promoter of lung cancer, the authors of the review[4] favor the latter view; perhaps particles act as physical carriers of other environmental carcinogens to the basal epithelial cells. It is also possible that more than one mechanism is involved.[7]

There is perhaps even more uncertainty about the pathogenesis of pleural reactions than there is about parenchymal lesions. For instance, it is not clear how often acute exudative reactions, such as effusions (presumably usually clinically silent), precede the more chronic diffuse or localized fibrotic reactions of visceral or parietal pleura. It is also unclear how fibers reach the parietal pleura and concentrate there in such a way as to evoke plaque production after a long delay while leaving the visceral pleura intact; an adequate hypothesis for the pathogenesis of pleural plaques is needed to explain all these features.[14] Perhaps even more puzzling is what determines whether the pleural reaction will be benign or malignant. Not all would agree with the view expressed in the article[4] that malignant mesotheliomas are pathognomonic of asbestos exposure: these tumors were described by European pathologists in the 19th century — long before major commercial exploration of the asbestos minerals[15] — and there is little evidence even today that asbestos is responsible for many cases in men or women outside industrial centers.[3,15] What are described in the present review as "casual" exposures (i.e., usually domestic or neighborhood) are exposures that are intermittent but have often turned out to be to very heavy dust clouds of fine particles.[3]

In spite of considerable current interest in the topic,[7] the issue of whether asbestos exposure is associated with airway abnormalities is not addressed by Craighead and Mossman. The involvement of small airways in the early stages of asbestos-related lung fibrosis has in all likelihood its clinical counterpart,[7] although there is no evidence about whether these abnormalities are reversible or not. The association between asbestos exposure and other forms of airway response, such as bronchitis or emphysema in the absence of asbestosis, also remains to be clarified, as do the confounding effects of cigarette smoking.

Finally, there is the question of whether there are differences in the pathogenic potential of the various fibers in this mineral group. Of particular concern is whether chrysotile (which has accounted for over 90 per cent of commercial uses during the past several decades) differs from the two amphibole fibers, crocidolite and amosite, which were used extensively during World War II and in the postwar building boom. The issue has been bedeviled by problems of comparing like with like,[5] by the difficulty of sorting out the relative contributions of exposure (duration, level, and particle size) and fiber type, and by the differences between exposure in the mining and milling of fiber and the secondary application of fibers in manufacturing. Thus, although it is clear that the rates of mesothelioma are different in different exposed populations, it has usually not been possible to assess the extent to which these differences are due to fiber type or to other factors. Some clarification has come from the application of modern methods of lung-dust analysis to autopsy material. In two case-control studies of mesothelioma, an excess of amphiboles (amosite in North America and crocidolite in the United Kingdom) was found in the lungs of the cases, whereas chrysotile contents were similar in cases and controls.[5,16] In a study of chrysotile miners in Quebec, almost as much tremolite (an amphibole contaminating some of the mined rock deposits) was found in the lungs as chrysotile, although the latter was clearly the main environmental contaminant.[17] These results are consistent with what has long been believed on the basis of more tenuous evidence — that there is preferential clearance of chrysotile, as compared with amphibole fibers, from body tissues and that this may contribute to the differences in the pathogenic potential of the minerals.

Epidemiologic evidence for a fiber gradient in pathogenic potential is strongest for mesothelioma, with crocidolite more strongly implicated than chrysotile, and amosite probably in between. The evidence is also reasonably strong for lung cancer, with crocidolite again more strongly implicated than chrysotile. For pleural reactions (pleural plaques and fibrosis), there may also be a fiber gradient, although other factors are almost certainly involved; for parenchymal fibrosis the evidence for a fiber gradient is minimal. At present it is believed that the biologic activity of asbestos particles relates to the degree of penetration and the amount of deposition in the lower respiratory tract, both of which depend mainly on their physical characteristics, including their aerodynamic properties. Particle size (and particularly length and fineness) may also determine oncogenicity. However, biologic activity is likely to be modified by the length of time that particles survive in the lung without denaturing, which may be related to their chemical characteristics. The most plausible explanation for differences in the pathogenic potential of various fibers is that these differences result from differences in both the physical and chemical properties of the fibers.

What is the clinical importance of the issues raised by the review in the *Journal*? Perhaps the most impor-

tant is that health risks in relation to exposure to asbestos vary according to environmental factors. Some of these factors (such as exposure dose, particle size, and fiber type) are known, but there are undoubtedly others not yet recognized. Host characteristics probably also influence the response to exposure. Thus, in considering the individual patient with a disease known to be related to asbestos exposure, the wise clinician should avoid regarding any particular exposure as too short, too remote, or at too low a level (even if environmental counts were in compliance with the present regulations) to have accounted for the disease. Assessment of the importance of particular environmental exposures is often outside the clinician's expertise; it should be referred to appropriate consultants in industrial hygiene, engineering, or physics. In lung cancer the statistical probability that a given case is attributable to asbestos exposure may be estimated from exposure-response data,[18] which for practical purposes can probably be assumed to be linear, provided that the data available are applicable to the industry in which the subject was employed. Finally, the unpredictable clinical course of these diseases demands vigilance by the clinician with respect to past exposures, and the most powerful indicator remains the careful, complete, and precise occupational history.[7]

Whether the dust concentrations permitted by current regulations will in fact eliminate the future risk of asbestosis, as Craighead and Mossman suggest,[4] remains to be established. Similar suggestions in the 1930s proved to be premature. Evaluation of the impact of present controls on health issues is an urgent matter for research. Furthermore, a total ban on use seems unlikely in technologic societies,[3] in which it may be considered preferable to retain these versatile minerals for certain uses. Until it is established that asbestos substitutes do not carry health risks,[19] research into the mechanisms by which asbestos particles produce ill health should be vigorously pursued.

McGill University
Montreal, PQ H3A 2B4,
Canada

MARGARET R. BECKLAKE, M.D.

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SOUNDING BOARDS

AFTER LAETRILE, WHAT?

LAETRILE was moribund before Moertel et al. laid it to rest with the recent report of their prospective clinical trial.[1,2] It had been replaced in popularity by an approach unusual in the annals of unorthodox cancer therapy — one that represents more of a challenge than did Laetrile or its predecessors. This is the "natural" approach to malignant disease, which emphasizes cure through purification and the body's capacity to heal itself. The currently popular alternative approach is rooted in homeopathic and naturopathic beliefs, Indian and Oriental philosophy, and 19th-century theories of intestinal putrefaction. Promoters often evoke the time-worn conspiracy dogma, which states that the medical system, the Food and Drug Administration, and the federal government withhold true cures from the public, thereby perpetuating therapeutically useless and biologically harmful cancer treatments in order to further the Establishment's economic interests.[3,4]

Alternative cancer therapies in vogue today differ importantly from Laetrile and from other unproved remedies of the past. Previous unorthodox treatments were "medicines" or at least "medicinal." Examples were Dr. Bye's Combination Oil Cure, Dr. Chamlee's remedy for removing cancer viruses from the blood, Dr. Leach's Cancerol, Dr. Koch's glyoxylide, and many others that attained great prominence in their day.[5] They came in ampules, vials, or syringes, mimicking standard medications, and they were sold and administered in the usual clinical fashion by people in white coats.

Today's alternative remedies explicitly reject association with standard treatments, environments, and paraphernalia. These are anti-medicines, emphasizing purification through dietary regimens, detoxification

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Asbestos

Highlights of This Issue

AMA MODIFIES RESOLUTION WHICH MIGHT HAVE RESTRICTED OCCUPATIONAL PHYSICIANS:

Without public notice or fanfare (but with plenty of behind-the-scenes negotiation led by Dr. Bruce Douglass of Mayo Clinic), the American Medical Association's House of Delegates recently adopted a modified resolution which generally leaves intact the right of occupational physicians to conduct on-site medical examinations of workers in keeping with the Code of Ethics of the American Occupational Medical Association.

The hassle began last December when the American Society of Internal Medicine, without prior consultation with occupational health officials, submitted to the AMA House of Delegates a proposed resolution, which stated:

"Whereas, many corporations, businesses and employers have recently, in the interest of their employees' health, arranged for comprehensive examinations which are done by prearrangement with clinics or other physicians; and whereas these examinations are well motivated, but frequently leave the patient with the impression that his health has been taken care of;

"And whereas these examinations do not provide for any follow-up or continuing care in those cases in which medical problems have been uncovered, and whereas such examinations would best be performed by physicians who are interested in following patient and taking care of any problems that arise;

"Therefore, be it resolved that it be the policy of the American Medical Association that comprehensive physical examinations which are done in the interests of maintaining employees' health should be performed wherever possible by a qualified personal physician who is in a position to continue to care for the patient and to take immediate action with regard to any abnormalities or medical conditions which are uncovered by such examinations."

Dr. Douglass, who is AOMA's representative to AMA, immediately huddled with AOMA and the American Academy of Occupational Medicine in an effort to sidetrack what was considered, rightly or wrongly, as a restriction on the right of industrial medical departments to conduct initial and follow-up examinations. Occupational physicians sometimes conduct only the initial exam and refer patients to specialists for continuing care.

In fact, complaints were heard that this might be a reincarnation of past turf battles between industrial physicians and private practitioners—an issue long thought to have been laid to rest. But as a result of intense lobbying, the final version adopted by the AMA House of Delegates read as follows:

"The American Medical Association encourages employers who provide or arrange for special or

comprehensive medical examinations of employees to be responsible for assuring that these examinations are done by physicians competent to perform the type of examination required. Whenever practical, the employee should be referred to his or her personal physician for such professional services.

"In the many instances in which employees do not have personal physicians, efforts should be made to assist them in obtaining one, with emphasis on continuity of care. This effort should be aided by the local medical society wherever possible."

The resolution adds that the AMA's "Guiding Principles of Medical Examinations in Industry," last revised in 1973, should be updated. That will probably be done this year or next.

Dr. Douglass and others believe that much of the objectionable language in the original ASIM resolution has been diluted through 16 revisions and that the right and ethics of occupational physicians to conduct exams remains intact. The experience suggested to him, however, that occupational health authorities must necessarily involve local practitioners, whether through educational or other means, in the continuing care of workers.

KELLOGG AWARDS $621,546 TO EXPAND OCCUPATIONAL HEALTH CLINIC IN CALIFORNIA:

The W.K. Kellogg Foundation has awarded a three-year grant of $621,546 to the University of California, San Francisco, to expand a multi-disciplinary training program for students and professionals in occupational health. The training program is based in the occupational health clinic at San Francisco General Hospital. Also participating in the project is the University of California at Berkeley.

"Expansion of the program will help ease the severe shortage of health professionals trained to treat work-related health problems," said Dr. Richard H. Fine, medical director of the Adult Health Center at SFGH and UCSF associate clinical professor of medicine. "It will also help to meet the growing demand by organized labor for occupational health care services. Standard medical training devotes little time to occupational medicine. At present, only about 70 physicians nationwide are in postgraduate training programs in occupational medicine."

A similar shortage of training programs exists in the nursing field. Expansion of the clinic will significantly strengthen the quality of the educational experience for occupational health nurse practitioner students at UCSF, said Barbara Resnick, coordinator of the occupational health nurse practitioner training program at UC-San Francisco, and clinical professor of nursing.

The SFGH Occupational Health Clinic was founded in 1979. It is currently open twice a month but under the grant will be expanded to four or five half-day clinics a week. It will also offer group screenings of workers.

Workers from public and private, union and non-union work sites throughout Northern California receive care at the clinic. It has ties with the Northern California Occupational Health Center, which is sponsored by UC-San Francisco, UC-Davis and the Berkeley School of Public Health, and is linked with the SFGH Center for Municipal Occupational Safety and Health. Its activities are overseen by an advisory board, which includes representatives of business, organized labor and various training programs.

The clinic is said to be the only one of its kind on the west coast to use an interdisciplinary team to treat patients. The team includes physicians, nurses, industrial hygienists, health educators, patient advocates and lawyers. Under the grant, the following services will be established or expanded:

* The clinic will provide occupational health care to many more workers. A number of labor unions and small businesses are expected to contract with the clinic for services. This will include individual and group assessments for work-related disease.

* Students from the medical, nursing, industrial hygiene and postgraduate residency programs of the professional schools at UC-Berkeley and UC-San Francisco will have an opportunity to train at the clinic.

* The clinic will offer continuing medical education seminars and training opportunities for community professionals so that they can care for patients, using the specialized information needed to treat occupational disease.

* It will encourage community health centers, particularly those serving ethnic or geographic neighborhoods in the Bay area, to develop their own occupational health programs.

* An industrial hygiene consultant service will be established. Its staff will visit the workplace and recommend changes to improve health and safety. The consultation service will allow small businesses and

worker groups access to sound industrial hygiene evaluation and will provide a field training opportunity for students in the environmental health sciences program at UC-Berkeley School of Public Health.

* Clinic staff will provide speakers, fact sheets and audio-visual materials on occupational health and safety on request to worker and professional groups.

"Occupational health problems are difficult to identify and treat without specialized training, because of long latency periods," said Robert Spear, Ph.D., director of the Northern California Occupational Health Center and a member of the clinic's advisory board. "Occupational illness is especially challenging because, at least in theory, it can be completely prevented.

In addition to the Kellogg Foundation grant, expansion of the occupational health training program at SFGH is being supported by a $10,000 grant from the L.J. and Mary C. Skaggs Foundation of Oakland, Cal.

The Kellogg Foundation, located in Battle Creek, Mich., has distributed more than $585 million in grants in the last five decades in support of self-help programs in health, education and agriculture. The Foundation is among the largest private philanthropic organizations in the United States and supports programs in the U.S. and Canada, Europe, Latin America and Australia.

OSHA PROPOSES EXTENDING STAY OF COTTON DUST STANDARD IN KNITTING INDUSTRY:

OSHA has proposed extending the temporary stay of the 1978 cotton dust standard in the knitting industry until October 31 as it completes its over-all review of the regulation.

The agency proposed the extension following a final report submitted to the agency by Cotton, Inc., on the basis of research at the University of North Carolina indicating that cigarette smoking rather than dust was the major cause of pulmonary impairment among workers in the knitting industry. The study was contracted for by industry. The data was supplied to the UNC investigators by ELB Associates, Inc., Chapel Hill, N.C.

Preliminary analysis of the data indicates that cotton dust at current exposure levels is not a significant health threat to knitting industry workers, OSHA said. Pending its review, however, OSHA said it will continue to enforce its pre-1978 exposure limit to cotton dust (1mg per cubic meter of air) in the knitting industry.

The UNC investigators were Drs. Brian Boehlecke and Mario Battigelli. Their report, based on data provided by ELB Associates as a result of its medical surveillance programs of knitwear and hosiery manufacturers, was sent to Cotton, Inc., Raleigh, and then transmitted to OSHA.

The investigators analyzed pulmonary function and respiratory questionnaire data collected by six knitwear and six hosiery manufacturers on 2287 knitting room workers exposed to cotton dust. Current respirable dust levels were reported to be less than 500 micrograms/m^3 for all workplaces in the study. They concluded:

"We found no excess of chronic cough, chronic phlegm or mild dyspnea in the knitting workers over that reported for a group of blue collar workers without exposure to respiratory hazards. Prevalence of byssinotic symptoms was less than 2 percent and was similar to that reported for workers processing synthetic fibers or wool.

"A review of 480 sets of spirometry tracings, approximately 12 percent of the data, showed 93.5 percent to be of acceptable technical quality. The decrement of FEV_1 with age for non-smoking knitting workers estimated from a linear regression analysis was similar to that predicted for a healthy non-smoking population. Cigarette smoking was significantly associated with more rapid loss of lung function with age.

"In linear regression analyses on a subset of 1396 workers for whom an estimate of years of knitting work was available, no significant effect of duration of knitting work on FEV_1 was demonstrated. The knitting workers had on average a small acute decrement in FEV_1 over the work shift which was similar to that reported for workers processing synthetic fibers or wool.

"Over-all, there was little evidence in these data of a significant chronic effect of knitting room exposure on the respiratory system. Determination of whether these findings are applicable to the entire industry may require consideration of additional information regarding the representativeness of the study group."

They said that after controlling for the effect of smoking, they were unable to demonstrate a significant chronic effect of knitting room dust exposure on pulmonary function. The small acute decrement in lung function over the workshift in these workers was no greater than that reported in workers exposed to

dust from synthetic fibers or wool and may represent a non-specific effect of knitting room dust, they commented.

"The consistency of results among several types of analysis supports the conclusion that knitting room work was not associated with important adverse effects on the respiratory system in the workers in this study," they reported. "Although we have presented some information suggesting that the study group was a reasonably representative sample of workers in the knitting trades, additional information would be useful before forming a final judgment on this question."

The standard was first issued in 1978 and was stayed for the hosiery knitting industry on December 30, 1980, after petitions from the industry. It was stayed for the rest of the knitting industry on March 31, 1981, by the current Administration. At that time, industry trade associations had argued that OSHA had not demonstrated that cotton dust posed a significant health risk to knitting workers, that industry data and experience showed there was none and therefore the rule was an unnecessary burden.

The stay has since been extended several times to give the industry time to conduct detailed analysis of its data, submit its report to OSHA and for the agency to review the study.

Eric Frumin, health and safety director of the Amalgamated Clothing and Textile Workers Union, called OSHA's most recent action unfair, saying "you shouldn't stay a law just because industry complains about it."

OSHA, PREPARING NEW NOISE STANDARD, EXTENDS AUDIOGRAM TESTING DEADLINE:

OSHA, which is nearing completion of a new noise performance standard, has deferred the August 22 deadline by which employers were to have completed baseline audiograms on their employees as required by the hearing conservation program. The deadline will be deferred until the publication of the comprehensive noise standard (it's called "hearing conservation" in the current Administration parlance).

The hearing conservation program, an amendment to OSHA's noise standard, went into effect last August 22, with several of its provisions stayed pending review while others were to be phased in at various dates over a two-year period.

The provision calling for a baseline audiogram for all employees exposed to noise equal to or greater than an eight-hour time-weighted average level of 85 dB was to become effective one year after the effective date of the amendment.

The permissible worker exposure limit under the current noise standard remains at the time-weighted average of 90 dB.

In March 1981, the U.S. Chamber of Commerce asked the Administration to postpone indefinitely a proposed national program by OSHA calling for noise measurements in U.S. workplaces and regular hearing data tests for workers at risk of excessive noise exposure (*OCCUPATIONAL HEALTH & SAFETY LETTER*, March 8, 1981).

A letter to Assistant Secretary of Labor Thorne G. Auchter from Mark A. de Bernardo, labor law attorney and staff executive for the Chamber's OSHA task force, stated:

"The U.S. Chamber of Commerce has long espoused the maintenance of effective hearing conservation programs, the use of personal protective equipment in lieu of engineering controls when reasonably equivalent in degree of hazard abatement, and a policy of business concern and vigorous effort to protect the safety and health of American workers. In turn, we have also worked to protect the rights of employers in their efforts to comply with OSHA rules and regulations. In this context, we have strong reservations and recognize significant flaws in the exposure amendment.

"We believe many of the amendment's flaws are the result of agency failure to adequately solicit and adhere to the recommendations of responsible industries and industrial groups with technical expertise in the occupational noise abatement area."

X-RAY CHANGES FOUND IN RAILROAD WORKERS EXPOSED TO ASBESTOS:

NIOSH has found x-ray evidence of asbestosis in six out of 266 current and former railroad workers in Conrail's shop facility in Reading, Pa., but suggested that a higher incidence of asbestos-related diseases might be found in a more representative group of railway workers who had been employed in the steam era

prior to 1950.

A volunteer population of 266 current and former railroad workers underwent chest roentgenograms and, in addition, gave an occupational-smoking history. Seventy-five percent of the participants were over the age of 60, and 80 percent had fewer than 10 years of railroad-related asbestos exposure.

X-ray evidence of asbestosis was found in only six workers, whereas 20 percent of the group had one or more pleural changes, principally thickening.

"While selection factors qualify the results of this study, the findings support the exposure, and suggest a past and future history of asbestos mortality and morbidity among steam-era railway workers," said the investigators, Drs. Martin-Jose Sepulveda and James A. Merchant. Dr. Merchant is currently chairman of the Department of Preventive Medicine and Environmental Health, University of Iowa.

The larger study was prompted by a recent NIOSH investigation which found four cases of diffuse malignant pleural mesothelioma in former workers of the Reading facility.

Pleural abnormalities were the most common finding, and were observed in 20 percent of the workers examined. Among workers with pleural changes, pleural thickening with calcification was more common than diffuse or localized pleural thickening alone. Roentgenographic evidence of pneumoconiosis was found in eight persons.

Boilermakers and machinists had the highest proportion of pleural abnormalities. The proportion of individuals with abnormal films appeared related to age and years from onset of railroad employment; the longer the interval from first employment or the older age group, the higher the prevalence rate of pleural abnormalities.

No difference was found in the prevalence rate of x-ray abnormalities between smokers and non-smokers. In its report, NIOSH acknowledged the limitations of the cohort studied, and suggested that follow-up studies be conducted to reveal the true magnitude of disease. It said:

"The current survey includes a population of railway workers which is not representative of the work force at the facility prior to 1950. Participants are survivors of a worker population whose asbestos exposure ceased 31 years ago. It is expected, therefore, that these individuals are the fittest of the group and the least likely to exhibit the ill health effects of this exposure.

"Additional selective factors operative in this volunteer population include ambulatory health status, current residency in the community, membership in the retired railroaders association, and media recruitment of former workers separated before 1976. The effects of these non-random influences on study results are less clear than the survivor bias but further serve to limit the quantitative aspects of the findings.

"It should also be noted that this survey included posteroanterior (PA) and 45° oblique chest roentgenograms. The enhanced sensitivity of PA and oblique chest films compared to the PA view alone cautions further against comparison of the findings to other occupational groups. . .

"This report serves to document some health effects from asbestos exposure in a volunteer group of railway workers. While selection factors limit the interpretation of the data, the occurrence of asbestos related radiological findings suggest that this occupational group may be at risk for the complete spectrum of adverse health effects from asbestos.

"The magnitude of the workforce employed at similar facilities during the steam epoch would suggest yet another asbestos legacy of disease. The need for better assessment of the health experience of workers in this industry seems appropriate. NIOSH is currently engaged in one such study to evaluate the mortality experience of selected occupations during this period."

CADMIUM WORKERS REPORTED TO SHOW NO EXCESS DEATHS DUE TO PROSTATE CANCER:

A study of nearly 7,000 British cadmium workers has revealed no excess deaths due to cancer of the prostate beyond the rate in the general population.

The findings were reported by Dr. G. Kazantzis and B.G. Armstrong of the London School of Hygiene and Tropical Medicine to the Second International Symposium on Epidemiology in Occupational Health in Montreal.

The results thus dispute the outcome of earlier studies which reported high levels of death from prostatic cancer in cadmium workers. The Cadmium Council, an industry group which made the new report public, said the value of the earlier studies was limited by the small size of the cohorts studied.

"Our detailed review of these 7,000 cadmium workers does not support the evidence for a relationship between cadmium exposure and cancer of the prostate," Dr. Kazantzis said.

Cadmium has been the subject of health investigations by OSHA and EPA. Suspicion was first aroused when four deaths from prostatic cancer were found in one group of cadmium nickel battery workers in England. Less than one had been expected. Other studies have shown similar excesses. In addition, a lung cancer excess was found in a single group of smelter workers with heavy past exposure to cadmium and other contaminants, particularly arsenic.

In 1976 the International Agency for Research *in Cancer* conducted an evaluation and concluded that "occupational exposure to cadmium in some form (possibly cadmium oxide) increases the risk of prostatic cancer in man. In addition, one of these studies suggests an increased risk of respiratory tract cancer."

A working group on the carcinogenic effects of metals of the Permanent Commission and International Association on Occupational Health documented 14 cases of prostatic cancer in Britain, U.S. and Sweden against an expected 5.4 cases, and considered the most reasonable interpretation to be that cadmium had contributed to the development of prostatic cancer. However, the existing epidemiological studies were considered by the WHO study group to be inconclusive because of the small numbers involved. A similar conclusion was reached by a working group of experts for the Commission of the European Communities.

Dr. Kazantzis' figures included the data from the two earlier studies. By including the data from those studies, one by T. Sorahan of the University of Birmingham, England, and another by Dr. H.A. Holden, BICC Metals Ltd., Armstrong and Kazantzis were able to provide information on the over-all pattern of mortality of English cadmium workers.

The findings of those studies were corroborated, with the exception of deaths from prostatic cancer.

They selected 6,995 men born before 1940 who were first exposed to cadmium prior to 1970. The researchers were able to completely follow 96 percent of the study group in Britain and another 2.6 percent were traced to the point of emigration from England.

A total of 2,056 deaths were reported, and death certificates were obtained for 2,051. They showed that the pattern of mortality of these workers roughly corresponded with the rate that could be expected of a normal working population, Dr. Kazantzis reported.

(Editor's Note: Given the long latency period for prostatic cancer, it is considered possible by some observers that many more deaths related to cadmium may yet occur in the cohort.)

Also reported at the Montreal conference was an excess of deaths due to bronchitis in workers exposed to "very high" levels of cadmium. Workers with a medium level of exposure also showed some suggestive evidence of deaths related to bronchitis.

The study showed some suggestive evidence of an effect of cadmium on deaths from kidney disease. There was no indication that deaths from hypertension were related to cadmium.

OCAW APPEALS FOR LOWER OSHA STANDARD ON RADON DAUGHTERS:

The Oil, Chemical & Atomic Workers Union has petitioned OSHA for a lower standard for worker exposure to radon daughters in underground mines--but fears that OSHA is actually planning to increase the permissible level from 4.0 WLM/year to 4.8, based on the International Commission of Radiation Protection (ICRP) recommendations.

OCAW contends that a *1980 NIOSH report said there is* an increased risk of lung cancer at the level permitted by the existing standards--but Labor Secretary Raymond J. Donovan said that was only one of many such estimates and that it lacked data concerning quantitative risk assessment.

In reply, OCAW president Robert F. Goss criticized Donovan's reliance on the ICRP recommendations. He quoted Dr. Edward P. Radford, chairman of the National Academy of Sciences' Biological Effects of Ionizing Radiation Committee, as characterizing ICRP as "a small self-appointed group of scientists with responsibility to a few governmental atomic energy agencies of various countries which cannot discharge their responsibilities as independent scientists nor are likely to be inclined to reach conclusions on occupational health standards that may make development of nuclear energy more expensive or difficult."

Goss said that "all the evidence points to uranium miners as the only group in the nuclear cycle exposed to extraordinarily high levels of radiation (lung dosages as high as 40 rems under the current MSHA standard, more than 2.5 times the current NCRP recommended lung dosage of 15 rems/year)."

"We hope," the union president said, "that the Department of Labor is not contemplating denying our petition in order to propose a less stringent standard based on incomplete epidemiologic data and dubious theoretical dosimetric calculations. If that is the case, your Department will carry the full responsibility for an increasing and continuous epidemic of lung cancer among the U.S. uranium miners."

Note: It's now Rafael Moure, Ph.D. The OCAW industrial hygienist recently received his doctorate from the University of Cincinnati.

NEW JERSEY SUPREME COURT UPHOLDS LIABILITY OF ASBESTOS MANUFACTURERS:

An historic ruling which paves the way for scores of liability lawsuits against manufacturers and distributors of asbestos has been handed down by the New Jersey State Supreme Court, who upheld the legal right of such suits on the basis of workers' health claims.

A lower court in New Jersey had previously accepted the defense claim of the manufacturers that no one knew or could have known asbestos was dangerous during the period covered by a number of suits.

But the State Supreme Court overturned the lower court's decision in a unanimous ruling, which said:

"Fairness suggests that manufacturers not be excused from liability because their prior inadequate investment in safety rendered the hazards of their product unknowable. . .

"The burden of illness from dangerous products such as asbestos should be placed upon those who profit from its production and, more generally, upon society at large, which reaps the benefits of various products our economy manufactures."

The ruling affects six consolidated cases filed against 10 companies. The cases involve asbestos exposure in the state dating back to the 1930s. The plaintiffs are workers, or survivors, who claim that exposure to asbestos caused many asbestos-related illnesses.

Note: Fred L. Pundsack has taken early retirement as president and chief operating officer of Manville Corp. as part of an effort to reduce expenses of the hard-pressed company. He is being succeeded by John A. McKinney, chairman of the board.

ASBESTOS INFORMATION MEETING SCHEDULED SEPT. 14-15:

The Seventh Industry-Government Conference of the Asbestos Information Association/North America will be held Sept. 14-15 at the Twin Bridges Mariott Hotel near Washington. Top Government speakers are scheduled to address the meeting. They include Dr. R. Leonard Vance, chief of OSHA health standards; Dr. John O. Todhunter, Assistant EPA Administrator for Pesticides and Toxic Substances; Nancy Harvey Steorts, chairman of the Consumer Product Safety Commission, and many others. For further information, contact the Asbestos Information Association, 1745 Jefferson Davis Highway, Crystal Square 4, Suite 509, Arlington, VA 22202; (703) 979-1150.

FLOW GENERAL RECEIVES PATENT FOR CHEMICAL PROCESS FOR ASBESTOS TREATMENT:

Flow General, Inc., McLean, Va., has obtained a patent on a chemical process for altering the surface of asbestos fibers without materially changing the physical and mechanical properties of asbestos. Objective of the patent is to preserve the commercial value of asbestos while reducing its toxicity.

According to Dr. Earl Flowers, an environmental chemist and industrial hygienist and the Flow General employee who invented the process, the patent involves treating asbestos with a solution of metallic salts, resulting in the formation of a new surface characterized as a "metal-micelle polymer." The new process is said to be simple, rapid and inexpensive and does not substantially alter the usefulness of asbestos in the limited product applications that have been evaluated by Flow General.

Joseph E. Hall, Flow General president and chief executive officer, noted that preliminary tests were "encouraging." A strain of human lung cells provided by NIH which the company exposed to asbestos fibers treated by the patented process during limited in vitro tests multiplied almost as well as lung cells that were never exposed to asbestos, while cells exposed to untreated asbestos fibers did not multiply during the preliminary tests.

CONFERENCE ON TOXICOLOGY LAB DESIGN AND MANAGEMENT SCHEDULED:

The National Association of Life Science Industries will sponsor a national conference on toxicology lab design and management Sept. 26-29 at Hyatt Regency Crystal City, Arlington, Va. Presentations are scheduled on such topics as impact of regulations on future lab design; architectural and mechanical/engineering design perceptions; financial implications; data processing, materials handling and waste disposal; adjunctive and supportive methods of toxicity testing; toxicity evaluation of Defense Department "surety" compounds; toxicity lab management and testing. For further information, contact NALSI, National Conference on Toxicology Laboratory Design and Management for the '80s and Beyond, PO Box 827, Rockville, MD 20851-0827; (301) 468-2590 (Sheri Marshall).

DISCONTINUANCE OF RESPIRATORS AS UNSAFE RECOMMENDED BY GOVERNMENT:

The Mine Safety and Health Administration and NIOSH have advised discontinuance of the SurvivAir Models 0028-00 and 0028-03, 5-minute emergency escape self-contained breathing apparatus (MSHA/NIOSH approval number TC-13F-86).

MSHA and NIOSH have learned that the cylinder airflow activating mechanism in some of the respirators is unreliable. Failure of the activating mechanism results in low or no airflow to the hood assembly. In view of the critical nature of this failure, this respirator should not be used, the Government said.

The respirator is made by U.S.D. Corp., Santa Ana, Cal., which has agreed to discontinue SurvivAir models 0028-00 and 0028-03 respirators and to recall all of them. After recertification by MSHA and NIOSH, SurvivAir will retrofit the respirators in accordance with an MSHA/NIOSH approved plan and will return them to the users.

All owners of the models are urged to contact SurvivAir (Ms. Pam Bixler, U.S.D. Corp., 3323 West Warner Ave., Santa Ana, CA 92702, 714/540-8010, exte. 302) or a SurvivAir distributor for further information.

NIOSH MODIFIES POSITION ON RESPIRATORS FOR FORMALDEHYDE:

NIOSH respirator selection guidelines for formaldehyde recommend the use of organic vapor (OV) respirators in workplaces containing up to 50 ppm of formaldehyde.

However, said NIOSH, recent research has shown that MSHA/NIOSH certified OV cartridges have extremely short service time (duration of use) at the 50 ppm concentration and therefore may be inadequate.

Several chemical cartridge respirators have been certified by MSHA/NIOSH that are specific for formaldehyde. These respirators, said NIOSH, are suitable for use in concentrations of formaldehyde not greater than 30 ppm. The service time of the certified formaldehyde cartridges is much greater than the service time of OV cartridges issued for formaldehyde.

Therefore, NIOSH suggests that chemical cartridges which have been certified by MSHA/NIOSH specifically for formaldehyde be used in preference to the certified OV cartridges.

FRANK GOLDSMITH, LORIN KERR AUTHOR BOOK ON OCCUPATIONAL HEALTH AND SAFETY:

The latest authors in the occupational health and safety field are Frank Goldsmith, Director of the Occupational Health and Safety Program at New York State School of Industrial and Labor Relations, Cornell University, and Dr. Lorin E. Kerr, Director of Occupational Health of the United Mine Workers. Together they have authored a 320-page book, Occupational Safety and Health, with a sub-title of prevention and control of work-related hazards. It will come as no surprise that it is written from the vantage point of labor or labor-related viewpoints, but does contain a large volume of information in the last decade of importance to all segments. The book has an introduction by Dr. Eula Bingham and is available for $26.95 from Human Sciences Press, Inc., 77 Fifth Avenue, New York, N.Y. 10011.