CONFERENCE

on

BIOLOGICAL EFFECTS OF ASBESTOS

Monday, October 19,
Tuesday, October 20, and
Wednesday, October 21, 1964

THE NEW YORK ACADEMY OF SCIENCES
SECTION OF BIOLOGICAL AND MEDICAL SCIENCES
2 East Sixty-third Street
New York, N. Y. 10021

The evening session on October 20
will be held at the Academy Building

ALL OTHER SESSIONS WILL BE HELD AT

The Waldorf-Astoria
Park Avenue at 50th Street
New York, N. Y.

A number of new techniques are described which enable (1) the tagging of individual fibers with fluorochromes in vivo for a period of at least one month and (2) facilitate the detection of otherwise "invisible" individual asbestos fibers and mineral particulates by electronic ashing of sections.

These techniques were designed for use (a) in experimental studies in animals to locate individual fibers in situ shortly after respiratory exposure and (b) in human biopsy or autopsy specimens in the absence of asbestos bodies.

Localization by electronic ashing has proven highly satisfactory. Variations in technical factors allow for correlation of fiber location with histological structures. Studies of the effect of ashing on asbestos bodies are also described. The advantages of the contomitant use of phase microscopy were demonstrated.

The results of the fluorochromes experiments raise the question of mechanical fixation of particulate carcinogens in tissue, as well as the adsorption and concentration of dilute carcinogenic agents.

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SESSION 1, PAPER 4

IDENTIFICATION OF THE SEVERAL VARIETIES OF ASBESTOS FIBERS IN HUMAN LUNG TISSUE

by
A. Vorwald
Wayne State University, Detroit, Mich.

(Abstract not received)

SESSION 1, PAPER 5

SOME OBSERVATIONS ON THE DUST CONTENT AND COMPOSITION IN LUNGS WITH ASBESTOSIS, MADE DURING WORK ON COAL MINERS PNEUMOCONIOSIS

by
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Safety in Mines Research Establishment, Sheffield, England

In the course of studies, made at the Sheffield Laboratory of S.M.R.E. during the last 15 years, of various types of lung dust diseases, and mainly of pneumoconiosis of coal workers, a few observations have been made on lungs with asbestosis.

After a review of the literature, methods of isolating and identifying different types of asbestos (chrysotile, crocidolite, amosite) will be discussed.

Results will be presented for about 20 lungs with asbestosis, obtained from the London Pneumoconiosis Panel, which were studied several years ago. The types of asbestos which had caused the disease are not known and several types may have been involved. Preliminary data will be given for a number of asbestosis lungs with exposure to single known types of asbestos obtained from, and studied in cooperation with the Pneumoconiosis Research Unit of South Africa.

The main tentative conclusion is the following: Whereas in the pneumoconiosis of coal miners and in classical silicosis there is on average a clear positive correlation between amount of dust in the lungs and severity of fibrosis, this does not appear to be the case in asbestosis. This suggests that products of dissolution, perhaps polysilicic acid, cause the fibrosis. The data also suggest that in the lungs chrysotile is more soluble than crocidolite, and amosite may be less soluble than crocidolite.

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SESSION 1, PAPER 6

ASBESTOS DUST DEPOSITION AND RETENTION IN ANIMALS

by
J. W. Skidmore and J. C. Wagner
M.R.C. Pneumoconiosis Research Unit, Glamorgan, Wales

In previous animal dusting experiments it has been established on histological grounds that there was a difference in the fibrogenic properties of different types of asbestos. Following the intrapleural inoculation of varieties of asbestos dust and silica into rats it has been shown that it is possible to induce pleural mesotheliomas with chrysotile, crocidolite, amosite and silica. The amount of dust inoculated into these animals was 20 mg. This appeared, by histological examination, to be greatly in excess of the amount found in the majority of human cases of pleural mesothelioma. Following the experiences of human cases in South Africa, it was expected that the mesotheliomas would occur in animals inoculated with crocidolite. In an attempt to clarify the position a series of dusting experiments were planned.

It was desirable, therefore, to produce an experimental method by which a known amount of dust could be deposited in the lungs of rats by an inhalation method. In addition, it was necessary to know whether the various types of asbestos were retained and had a similar histological distribution.

Groups of rats have been exposed to airborne dust clouds of chrysotile, crocidolite, amosite or powdered glass which served as a control inert and insoluble non-fibrous dust. Reasonably constant and equal weight concentration of dust in the aerodynamic range which could reach the pulmonary regions

RHEUMATOID FACTOR IN SERUM OF INDIVIDUALS EXPOSED TO ASBESTOS

by
B. Pernis and E. C. Vigliani, University of Milan, Milan, Italy, and
I. J. Selikoff, The Mount Sinai Hospital, New York, N. Y.

(Abstract not received)

OBSERVATIONS ON THE PATHOGENESIS OF ASBESTOSIS

by
E. C. Vigliani and B. Pernis
University of Milan, Milan, Italy

(Abstract not received)

ASBESTOSIS IN GREAT BRITAIN

by
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Ministry of Pensions and National Insurance, London, England

A whole new literature relating to asbestos appeared in Great Britain between 1927 and 1932. The Report by Merewether and Price in 1930 was outstanding and established the occupational origin of asbestosis. It was made clear that the principal safeguard against the ill effects of asbestos dust on the lungs was to be found in improved ventilation and dust suppression. Asbestosis became a compensatable disease. Initial and periodical examination of workers in certain scheduled processes were instituted and specific instructions were issued regarding exhaust ventilation, dust prevention, etc. Case finding arises in two ways: from the statutory periodical medical examinations and from applications for compensation under the Workmen's Compensation Acts and from applications for benefit under the Industrial Injuries Act which superseded the Workmen's Compensation Acts in 1948. This is probably the only source of information about the prevalence of asbestosis in the country. Tables give the number of cases diagnosed each year since 1931 and a special breakdown of 248 cases diagnosed between 1955 and 1963. These show that 169 of these 248 cases entered the industry after 1933. They show the numbers resulting from periodical medical examinations and from applications. The clinical, radiological and pathological features of the disease are described and diagnostic criteria indicated. The effects of asbestosis, e.g. disablement, morbidity, liability to other pulmonary and pleural disease, and mortality are discussed. Against this background the value of periodical examinations is examined.

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ASBESTOSIS AMONG INSULATION WORKERS IN THE UNITED STATES

by
I. J. Selikoff, J. Churg, and E. C. Hammond
The Mount Sinai Hospital, New York, N. Y.

Large scale studies of asbestosis in the past have been restricted to workers employed in asbestos textile factories. This was true both of the important basic investigations of Merewether in Great Britain (363 employees) and of Dreessen and his colleagues in the United States (541 employees).

There have been scattered reports of pulmonary asbestosis and its complications in workers exposed to asbestos in industries other than textile. However, the absence of satisfactory epidemiological data has made it difficult to assess the risk of such exposure. Yet such assessment is important since it is likely that asbestos textile workers now represent only a minority of those exposed to asbestos in industry.

Investigations reported here were concerned with 1,522 members of the International Association of Heat & Frost Insulators and Asbestos Workers, in the New York-New Jersey Metropolitan area, a union of insulation workers. This study included every individual who was a member of this union December 31, 1942 or who joined by December 31, 1962.

264 men were dead on January 1, 1963; 43 have died since. Each death has been studied. 1,258 were alive; 1,117 were examined (89.9%), including 133 of 169 no longer working in the trade and 984 of the 1,086 working members. Clinical, radiological and pulmonary function examinations were made.

1. Prevalence of asbestosis: Correlation of radiological abnormality with lapsed time from onset of exposure.

demonstrate significant changes in a chronological series of films. Pulmonary function studies have become an important technique in diagnosis and assessment of disability.

In a small group of 10 cases with 10 controls matched for age, sex and length of exposure, the evidence for the influence of pulmonary infection has proved inconclusive.

The changes in pathology of asbestosis are noted by comparing two series of post-morten reports on workers from the same factory. In 1949 Wyers published the findings in 115 cases of asbestosis at death. The present series of 71 post-mortems since 1957 shows much less frequency of tuberculosis as a complication but increased occurrence of malignancy of the lungs. Emphysema has become less common. Primary malignancy of the pleura and peritoneum occurs with a frequency unsuspected in the earlier reports.

The mean age at death has risen from 40.8 to 57.3. The average duration of the disease has lengthened from 6.4 to 10.9 years. The longest interval between last exposure and diagnosis is 38 years, one year before post mortem.

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SESSION 2, PAPER 5

OCCUPATIONAL AND NON-OCCUPATIONAL EXPOSURES TO ASBESTOS

by
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The enormous rise in the production and industrial use of asbestos during the past 50 years has resulted in markedly widened exposure to asbestos dust for a greatly increased number and variety of workers. Some of them, moreover, sustain such contacts incidentally either when being employed in various capacities in operations where asbestos products are processed, used, or handled or when working in plant areas in which an environmental pollution of the air with asbestos exists. The harmful effects of such growing exposures to asbestos during the past two decades are reflected not only in a growing number of reports on the occurrence of asbestosis and asbestos cancer in a variety of asbestos workers, but also in the fact that such reports originate from a rising number of countries in some of which such observations were made only recently for the first time. Information on the number and variety of exposed workers and on the occurrence and incidence of asbestosis and of asbestos cancers among them is most fragmentary in all countries, especially in the United States and Canada, one being the principal consumer of asbestos and the other the chief producer of this mineral. It is for this reason that regrettably, the original plan of having a recent epidemiologic survey on these aspects of asbestos production in Canadian mines and mills be undertaken under the aegis of the National Cancer Institute of Canada was not adhered to, and that this study was carried out as an industry-dominated venture which yielded highly controversial negative results. The principal worker groups exposed to respiratory contact with asbestos are employed in the asbestos mining and milling industries, in the production and commercial use of asbestos cement and plaster and their numerous secondary products, in the production and application of asbestos for insulating purposes and in the processing of asbestos and its manufacture into textiles. Protection of asbestos workers against occupational health hazards related to respiratory and cutaneous contact with asbestos by workmen's compensation laws are in many countries and States more or less defective and, therefore, inadequate.

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SESSION 2, PAPER 6

ASBESTOS AND THE URBAN DWELLER

by
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University of Cape Town Medical School, Cape Town, South Africa

The extent of inhalation of asbestos fibres by urban dwellers was investigated by counting asbestos bodies in smears from the lung bases from 500 consecutive autopsies in subjects over the age of 15 in Cape Town, South Africa, and 500 in Miami, Florida. The results were similar in the two cities and no less than 30% of the males and 20% of the females showed asbestos bodies. In 80% of the positive cases the bodies were scanty, were not associated with pulmonary changes, and were regarded as the result of contamination of the urban atmosphere. In 6% of the males the bodies were numerous and were presumably of occupational origin.

The tendency for asbestos fibres too long to be phagocytosed to move downwards by gravity before they become asbestos bodies leads to concentration at the lung bases, and small doses can have a cumulative effect. An increase in the amount of urban air contamination would seem inevitable in view of the increasing consumption and diversity of uses of asbestos and of its virtual indestructibility, and an increase in basal asbestosis is suggested as a possible future development. As a limited basal asbestosis may be associated with malignant mesothelioma of pleura and peritoneum an increase in this tumour is forecast as the main ground for regarding asbestos as a potential urban hazard. While that view is conjectural, the finding of abundant asbestos bodies in the lung bases of 1 in 17 of the male hospital population suggests that the occupational hazard from asbestos is greater and more diversified than is at present realized.

The main object of this work is to draw attention to the effects of a relatively new development,

Asbestos fibres 50 microns and longer are found in alveoli, whereas few of the particles of near spherical shape present have diameters greater than 10 microns. There is no inconsistency here as the effectiveness of each of the two mechanisms, sedimentation and inertial precipitation, operating to deposit particles in the upper respiratory tract is determined by particle falling speed, which depends on shape and density as well as "size." For a fibre it is the diameter and not the length which mainly determines falling speed. Asbestos fibres can be long and yet be so fine that deep penetration of the respiratory system becomes possible.

Measurements of falling speed, diameter and length, on glass fibres, chosen for their exact cylindrical form, have provided the relationships between these parameters. For a given diameter, increasing the length/diameter ratio from 1 to 10 results in a fourfold increase in the falling speed. For higher length/diameter ratios the falling speed is proportional to the square of the diameter and almost independent of the length. Results of similar measurements on the less uniform fibres of amosite, chrysotile and crocidolite show the same tendencies. The falling speed of an asbestos fibre, for example, 3 microns in diameter, 300 microns long, is comparable to that of a unit density sphere 10 microns in diameter.

The possibility of long fibres penetrating to the pulmonary space has necessitated consideration of their capture in fine airways. The rate of capture by virtue of length has been calculated for places where it is likely to be significant, for example, on the nasal hairs and at branching of airways.

Some aspects of dust sampling asbestos particles are discussed in the paper.

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SESSION 3, PAPER 2

A COMPARISON OF IMPINGER AND MEMBRANE FILTER TECHNIQUES FOR EVALUATING AIR SAMPLES IN ASBESTOS PLANTS

by

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In the United States the threshold limit value of 5 million particles per cubic foot for asbestos is based on samples taken by impinger and counted in liquid by use of a microscope with a 16 mm objective. Dust concentrations in the asbestos textile industry have been evaluated by this method for 30 years. It is recognized that the measurement is only an indirect estimation of the potential hazard from asbestos in that asbestos fibers comprise only a very small fraction of the dust count.

In an environmental study of the asbestos handling and processing industries now under way samples have been taken both by impinger and membrane filter. Companion samples by the two methods have been used to determine the relationship between impinger dust counts by the "standard method" and fiber counts on transparentized membrane filters by use of a microscope with a 4 mm phase contrast objective. In spite of the large variances associated with each of these counting methods, a relationship between results they yield was developed. In general, more fibers were associated with a given impinger dust counting in carding operations than in other operations. The relationships of fiber count to impinger count and the count of fibers longer than 10 microns to the impinger count are presented by operation in this paper. Tentative results suggesting a fiber count equivalent to the present threshold limit are also presented and discussed. In addition, size distributions and determinations of "respirable" dust are briefly discussed.

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SESSION 3, PAPER 3

DEVELOPMENTS IN DUST SAMPLING AND COUNTING TECHNIQUES IN THE ASBESTOS INDUSTRY

by

S. Holmes

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Due to the fibrous nature of asbestos dust, the sampling and analysis of factory atmospheres in the asbestos industry has presented special problems which have been the subject of continuous investigation over the past 20 years, first by the individual manufacturing companies and later as part of the research program of the Asbestosis Research Council. The aim of this work has been to agree on a sound and reliable method of sampling and counting which will enable true comparisons to be made between dust conditions at different processes and in different factories.

This paper traces briefly the development of sampling and counting methods leading up to the long running thermal precipitator and membrane filter techniques. The relative merits of these two methods are discussed and reasons are given to show why the membrane filter is now preferred. Colored membrane filters suitable for dry counting are described, as well as the more usual white membranes which can be cleared for wet counting. Results using the two systems are compared.

A description is given of the microscopic techniques used in sample counting and attention is drawn to the difficulties which can arise due to the crystalline nature of asbestos dust. One result of this is that care must be taken in choosing a liquid of suitable refractive index to clear the membrane and a number of such liquids are mentioned.

Brief reference is made to recent work in which, by clearing the membrane with a liquid of high dispersion, use can be made of the dispersion staining technique in viewing the sample. In this way, it is possible that the individual components of samples containing mixed asbestos dusts may be identified.

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RADIOLOGICAL CLASSIFICATION OF PULMONARY ASBESTOSIS

by
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Every classification is imperfect, even more so regarding asbestosis. The classifications now in use are not quite identical, but they mainly divide the radiological appearances into three fluently changing stages, of which especially the second is illogically defined and not to be produced efficiently. Because the national differentiation between the compensation rules only a mere radiological classification can be taken into consideration for international agreement. The fact of this conference taking place at all proves that new international agreements about a practicable classification for pulmonary asbestosis are necessary. If experts agree that linear opacities are also disseminated shadows and that the radiological appearances of pneumoconioses can be only either disseminated or squared opacities, it would seem appropriate to adopt these two kinds of appearances as a base for new classification. Doing so, considerable approximation to already existing classifications (Sydney 1950; Geneva 1958) would be gained as well. For intensifying the reproducibility of the X-ray film and, on the other hand, enlarging the distinctness of the codified X-ray findings, we suggest not to use the unalterable symbol "L" (Geneva 1958), but to introduce another symbol "f" for linear patterns, chiefly occurring in asbestosis, and to combine it with the quantitative categories for small opacities (Geneva 1958). The large opacities might be characterized by the symbol "A" for beginning confluence and by "B" and "C" for opacities having longer diameter than 5 cm. The additional symbols (Geneva 1958) would mean welcome for further accommodation of the findings code to individual, local or national peculiarities. Extensive reconstruction of the radiological appearances, even without the film in question, would be possible when adopting the symbol suggested. It is unimportant whether this proposition is adopted or not; it is exceedingly important that some international agreement should be attained which would be really practicable.

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SESSION 4, PAPER 4

ROENTGENOLOGICAL STUDIES OF PLEURAL CALCIFICATION IN ASBESTOSIS

by
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The Mount Sinai Hospital, New York, N. Y.

Although scattered instances of pleural calcification had been noted 25 years ago (Gloyne, Vigliani), these were considered coincidental or ignored. Such evaluation was strengthened by the negative findings of A.R. Smith in 1952.

Recently, attention has again been called to the association of pleural calcification with exposure to asbestos under industrial conditions (Jacob, Bohlig, Muller) and following environmental community exposure (Kiviluoto).

Data are presented here which demonstrate that pleural calcification is frequently found among asbestos insulation workers and suggest that asbestosis is perhaps the most common cause of pleural calcification in industrial countries at present, especially when such calcification is bilateral.

1. Analysis was made of the results of x-ray examinations of 1,117 asbestos insulation workers (see Selikoff, Churg and Hammond, this conference).

Pleural Calcification on X-Ray Examination of 1,117 Asbestos Insulation Workers

Lapsed time from onset of exposure	No. Examined	Pleural calcification — Extent of calcification			
		0	1	2	3
40+ years	121	51 (42.1%)	37	20 (57.9%)	13
30-39 "	194	127 (65.4%)	46	15 (34.5%)	6
20-29 "	77	69 (89.6%	8	0 (10.4%)	0
10-19 "	379	374 (98.9%)	5	0 (1.1%)	0
0-9 "	346	346	0	0	0
	1,117				

Data is presented to indicate that both total exposure in years and lapsed time from onset of exposure are of importance, with the latter probably of greater consequence.

2. Almost half of the instances of calcification were bilateral (73 of 150). This tendency especially noted in more extensive calcification (29 of 35 Grade 2 and 19 of 19 Grade 3). When radiologically unilateral, the left side was more commonly involved (49) than the right (28).

3. Illustrations will be given of the variable location of plaques (diaphragm, costal, anterior and posterior mediastinal, pericardial, apical, interlobar fissures), their appearance and radiological demonstration.

PULMONARY FUNCTION IN ASBESTOSIS: SERIAL TESTS IN LONG TERM PROSPECTIVE STUDY

by
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Ten years ago, a group of 17 actively employed asbestos factory workers was evaluated clinically, radiologically and by means of pulmonary function tests. The plant in which the men were employed discontinued operations at this time; therefore, they had no further industrial asbestos exposure. Nevertheless, they were maintained under observation to study the natural history of established pulmonary disease uncomplicated by further exposure. Annual clinical, radiological and pulmonary function studies were undertaken, as well as management of intercurrent illnesses.

During the baseline studies, pulmonary function examinations, when abnormal, revealed the classic findings of the alveolar capillary block syndrome; uniform decrease in lung volumes, well preserved maximum breathing capacity, decreased arterial oxygen saturation (especially on exercise), normal pCO_2 values, and decreased diffusing capacity. Hyperventilation at rest and exercise occurred in more than half the cases, and while dead space ventilation was increased, alveolar ventilation was also increased. The most sensitive index of impaired function was arterial oxygen saturation. Slight reduction at rest was found in six and reduction below 92% was found in half the workmen on exercise. Poor correlation existed between impaired function and intimacy and duration of exposure. Better but still not parallel correlation was found with radiographic findings.

The post-employment serial evaluations were made in terms of x-ray progression, development or worsening of dyspnea on exertion and further measurements of pulmonary function.

Follow-up observations were limited by complications of the disease being studied.

1. 8 men are dead: 2 of lung cancer, 1 of pleural mesothelioma, 2 of gastric carcinoma, 2 of pulmonary asbestosis (cor pulmonale) and 1 of myocardial infarction.
2. 9 are alive, 1 following resection of lung cancer.

With this limitation, long term follow-up results are described with correlation with clinical and radiological features. Original observations on pulmonary compliance and pulmonary airway resistance in these men are discussed with relation to vital capacity and maximum breathing capacity.

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SESSION 4, PAPER 8

ROUTINE LUNG FUNCTION STUDIES ON 830 EMPLOYEES IN AN ASBESTOS PROCESSING FACTORY

by
Ross Hunt
British Belting and Asbestos, Ltd., Yorkshire, England

Routine work in this field was started in July 1960 in an asbestos textile plant in the North of England. The aim was to create a set of normal figures for lung compartment volumes, gas transfer factor coefficients, 90% mixing indices, ventilation on exercise, and forced breathing capacities. The subjects used in these tests were volunteers of both sexes in varying age and stature groups from departments other than those processing asbestos. These results were then analysed statistically and the regression formulae obtained applied to the results of men and women working in 'scheduled' and 'exposed' occupations. The conclusions drawn from these results were aligned with the X-ray and clinical findings in each case. Pulmonary function tests were also used as a screen to prevent people with lung impairment from taking up work in departments where asbestos dust was prevalent. Some difficulties were encountered in the beginning, both in subject response and sampling technique, but these were overcome and this paper deals in the main with the technique and results obtained over the past 3 years. The evidence points to a significant decrease in gas transfer and vital capacity before any radiological or clinical signs are evident.

The work continues as a routine test procedure carried out in the firm's medical centre. Approximately eight people are examined each day, the intention being to examine all 'scheduled' and 'exposed' personnel once a year at least, and more often if their results give cause for concern. A modified single-breath-holding sampling technique is used and is described in the paper.

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SESSION 4, PAPER 9

THE DISCRIMINANT VALUE OF PULMONARY FUNCTION TESTS IN ASBESTOSIS

by
M. L. Thomson, Anne-Marie Pelzer and W. J. Smither
London School of Hygiene and Tropical Medicine, and
Cape Insulation and Asbestos Products Ltd., London, England

A clinical, radiographic and pulmonary function evaluation has been made on 19 workers in an asbestos factory certified as having asbestosis, and on a further 9 exposed, but uncertified workers. The clinical and radiographic assessments were made, using a 2 or 4 point scale, by one of the authors without knowledge of the pulmonary function results.

Of the clinical features, radiography, dyspnoea and rales have the greatest discriminating

In addition to the oils naturally associated with certain types of asbestos, secondary contaminating oils may sometimes be found. Experiments have shown that asbestos fibers may absorb up to 75% of jute oil from the jute sacks in which the asbestos is commonly stored or transported. Trace amounts of polycyclic aromatic hydrocarbons were found in samples of jute oil and at least one sample was shown to possess tumor-promoting activity after tests on the mouse skin. In some cases, oil emulsions are added intentionally to fibers to facilitate processing.

Since the biological activity of asbestos may be due, at least in part, to the metal-complex nature of its structure, analyses for iron in asbestos and other minerals were carried out. Correlations are being sought between the content of ferrous and ferric iron and the biological activity of different minerals. Spectrographic analyses have shown the presence in chrysotile of relatively high concentrations of chromium and nickel, both of which are recognized as carcinogenically active.

As part of this project, the elution of metals by serum under defined experimental conditions has been investigated.

Methods for the identification of asbestos fibers in histological preparations and tissues have been developed.

####

SESSION 5, PAPER 3

PREPARATION OF ASBESTOS FIBERS FOR EXPERIMENTAL USE

by

M. S. Badollet, Fairleigh Dickinson University, Madison, N. J., and
W. A. Gantt, State Department of Health, Trenton, N. J.

Asbestos in its natural state in the form of ore contains impurities associated with the ore body. These impurities may be part of the wall rock or occluded in or embedded in the crystal formation between layers of asbestos.

For fundamental investigations of biological effects of asbestos, it is essential to eliminate impurities that are not part of the asbestos molecule. To accomplish this, we have removed bundles of fibers from original unrefined ores, split them along the fiber planes with a knife into sections 1/16 to 1/32 inch thick, which were then cut with scissors into lengths of 1/8 inch or less, removing visible pieces of rock wall. This material was transferred to a Waring Blendor, a motor-driven rotating series of sharp blades in a vertical jar. The jar was half-filled with distilled water containing 2 to 3 grams of the hand-cut fibers. The Blendor was run until desired fiber length distributions were obtained. Samples with fiber lengths in ranges below 100 microns were thus prepared. The slurry was filtered through paper on a Buchner funnel, washed with water, alcohol and ether, then air dried. This preparation sharply decreased the hydrocarbon content of the material, as measured by estimation of several specific polycyclic hydrocarbons in a sample of amosite.

Some other methods for reduction of sizes are ball mills, fiberizers and disintegrators, The Blendor method has advantages which are two fold: it allows the operator to observe the grinding action, it can be stopped at intervals and samples quickly withdrawn for size measurement. Size is a function of time of grinding.

Fibers prepared by this method have been injected into hamsters and rats by Smith and Miller as reported elsewhere at this conference.

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SESSION 5, PAPER 4

TESTS FOR CARCINOGENICITY OF ASBESTOS

by

W. E. Smith and Llonas Miller
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Asbestos samples were prepared from water slurries with a rotary knife according to a method described by Badollet and Gantt in a preceding paper at this conference. Soft chrysotile ore, harsh chrysotile ore, and a commercial sample of amosite were processed to average fiber lengths of 67, 36 and 18 microns, respectively. Single intrapleural injection was made into the right chest of golden Syrian hamsters (15 animals per sample). Each injection contained 25 mgms. of sample suspended in 0.5 cc. of 0.9% sodium chloride.

Extensive granulomatous and fibrous pleural adhesions resulted in each treatment group. Large intrathoracic tumors were found in 2 hamsters at 244 days and 358 days, respectively, after injection of commercial amosite, and in 2 other hamsters at 419 and 527 days after injection of harsh chrysotile No tumors have yet been found in hamsters given the sample of soft chrysotile. In each group, several animals are still living. The tumors showed local invasion and distant metastases. One was transplanted through 3 serial generations of new hosts in which it formed solid tumor masses up to 6 cm. in diameter.

In other experiments, 180 hamsters and 270 rats have been given weekly or biweekly intratracheal injections of four types of asbestos prepared by the rotary knife method (soft chrysotile, harsh chrysotile, amosite and crocidolite) in suspending medium (saline). Pneumonia and fibrosis but no tumors have been found in animals thus far examined. A majority of animals in these intratracheal tests are still living.

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Detailed occupational and personal data were obtained from 1,117 men (of the 1,258 who were alive on January 1, 1963) who were examined. Union records were available for similar analysis for those men who were dead (264) or who failed to appear for examination (141). 43 men have died since the onset of the study.

We have previously demonstrated, using age-specific death rates in a prospective study of 255 consecutive deaths among this group of men 1943-1962, that total deaths were increased (observed 255, expected 204) as were deaths caused by cancer of lung and pleura (observed 45, expected 7) and stomach and colon (observed 29, expected 10).

We now report an analysis of the 307 consecutive deaths among these insulation workers January 1, 1943-August 30, 1964.

307 CONSECUTIVE DEATHS AMONG 1,522 ASBESTOS INSULATION WORKERS 1943-64

	(264) 1943-62		(43) 1963-64		TOTAL
Cancer of the lung	42		11		53
G.I. Cancer	30		5		35
Esophagus		1		0	
Stomach		11		2	
Colon-Rectum		18		3	
Mesothelioma, Pleura	3		1		4
Mesothelioma, peritoneum	2		3		5
Other neoplasms	20		7		27
Bladder		3		1	
Generalized		5		2	
Oro-pharynx		1		2	
Neck		3		0	
Pancreas		1		1	
Asbestosis	12		5		17
Pulmonary infection	7		0		7
Pulmonary tuberculosis	4		0		4
Cardiovascular	104		10		114
All other causes	40		1		41
	264		43		307

We have been particularly interested in analysis of those deaths due to intra-abdominal neoplasms (G.I. tract and peritoneum). For a variety of reasons, accuracy of diagnosis of such neoplasms is often insecure. In 2/5 of the 49 such deaths analysis of all available data showed the diagnosis to be presumptive only; this was especially true of stomach cancer (8 of 13) and generalized abdominal cancer (6 of 7). Therefore, it is possible that peritoneal mesothelioma may be even more common than the 5 of 307 deaths recorded.

In addition to the neoplasia among the recorded deaths, there are 3 men alive with known neoplasms (1 lung cancer, 1 pleural and 1 peritoneal mesothelioma) as well as one apparently cured of tongue cancer, one of cancer of the colon, and three following successful resection of localized lung cancer found in this survey.

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SESSION 5, PAPER 8

COHORT ANALYSIS OF CHANGES IN INCIDENCE OF BRONCHIAL CARCINOMA IN A TEXTILE ASBESTOS FACTORY

by

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R. S. Doll, M.R.C. Statistical Research Unit, London, England

An association between asbestos dust inhalation and pulmonary fibrosis was first recorded in Great Britain at the turn of the century, but until further cases were reported 20 years later no official action was taken on prevention. A survey of the asbestos industry in Great Britain was carried out by members of the Factory Department of the Home Office in 1928-29 and a Report laid before Parliament in 1930. In a sample of 363 workers pulmonary fibrosis was found in greatest proportion in those employed for 20 years and upwards. These workers were principally employed in the asbestos textile industry.

Following the submission of this Report to Parliament Regulations were imposed in 1931 in order to reduce dust emission in manufacturing processes. Arrangements were also instituted for medical examinations of new entrants to the industry and periodic examinations thereafter. Workers found to be suffering from disability due to pulmonary fibrosis received compensation and might be suspended from further employment in the industry. Coroners were instructed to inquire into the causes of death of workers in the asbestos industry who had been suspended for disability or who were likely to have been affected by their employment. Necropsies were performed in most of these cases and material for study thereby accumulated. In a mortality study of the workers in one factory, excess mortality among workers employed for 20 years and upwards was observed. Lung cancer in association with asbestosis was responsible for a considerable proportion of this excess. A study of a group of workers from the same factory, exposed since the regulations, shows a reduction in mortality rate without excess of lung cancer.

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An association between asbestosis and pulmonary malignancy is now generally accepted. More recent investigations have shown that there is an increased incidence of pleural and peritoneal mesotheliomas occurring in people occupationally or environmentally, exposed to asbestos dust. In some of these cases, the exposure has been extremely slight, and not sufficient to produce the histological features of asbestosis. The only pathological evidence of exposure has been the presence of asbestos bodies or fibres in the air spaces. In South Africa more than 100 cases of this tumour have been confirmed histologically. Nearly all these cases have been confined to one asbestos mining area. The majority of these people were not employed in the asbestos manufacturing industry. Chemical investigations have shown that oils containing carcinogenic hydrocarbons are present naturally in this particular type of asbestos.

At present, the incidence of diffuse mesotheliomas associated with exposure to asbestos dust is being investigated in Britain. Thoracic surgery units and pathology laboratories, who have records of these tumours, have been approached and an attempt is being made to find out how many of these cases have been exposed to asbestos dust. The investigation is only partly complete, and so far, as many cases have been discovered in Britain as were observed in South Africa. Details of these British investigations will be given in the papers that follow, and it will be seen that as in South Africa, the association is mainly between astestos exposure and mesotheliomas, and asbestosis is often not a marked feature of these cases.

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SESSION 6, PAPER 2

EPIDEMIOLOGY OF MESOTHELIAL TUMOURS IN THE LONDON AREA

by
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Two groups of patients who have attended a large hospital in the East End of London have been examined to determine their exposure to asbestos.

The first consisted of 83 patients in whom the diagnosis of mesothelioma had been confirmed at autopsy or by biopsy. In all but 7, past occupational and domestic histories were obtained. In 21 patients the tumour was peritoneal in origin, in 62 pleural. The earliest recorded death was 1917, but only 10 of the series died before 1950. 55% of the males and 42% of the females died under the age of 55. The interval between first exposure and development of terminal illness ranged between 16 and 55 years (mean 37 years).

The second group consisted of 76 patients of the same hospital, matched by sex and date of birth with those traced in the first series.

52.6% of those suffering from mesotheliomata had been exposed to asbestos, as compared to 11.8% of the control group. Three main types of exposure were recognized: work in factories manufacturing asbestos textiles, insulating materials and other products; employment as laggers or insulators, and exposure to dust brought home by relatives working with asbestos. 18 of those employed in factory work and four whose relatives were working with asbestos were employed at one factory. This factory opened in 1913 and was, until recent years, a heavy user of crocidolite; all those whose records could be traced worked with this type of asbestos.

Among the 36 patients with mesotheliomata, with no positive occupational history and no relatives living at home who worked with asbestos, there were 11 who lived within half a mile of an asbestos factory; 5 of the control series also lived in the same area. The difference in the proportion of patients in the two series is statistically significant.

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SESSION 6, PAPER 3

CRITERIA FOR THE DIAGNOSIS OF DIFFUSE MESOTHELIAL TUMOURS

by
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The criteria for the diagnosis of diffuse mesothelial tumour are at present imprecise and the security of the diagnosis often depends more on the degree of certainty with which metastatic tumour can be excluded than on any specific quality of the mesothelioma.

The gross appearances of the diffuse mesothelioma are not specific. It is uncommon, however, for metastatic carcinoma to duplicate the extensive sheet-like serosal infiltration which is especially characteristic of the diffuse pleural mesothelioma.

The diffuse mesothelioma shows remarkable structural variation histologically. The most specific structure is a mixed one resembling that of a carcinosarcoma. The commonly observed well differentiated tubulo-papillary or tubular pattern in which the cells are cuboidal or flattened is also unlikely to be confused with metastatic tumour. A form closely resembling that of a spindle-cell sarcoma is highly specific if the growth is known to be diffuse. Several other types of structure including the presence of clefts lined by tumour cells and the disposition of solitary spheroidal cells in the interstices of dense collagen are also thought to be highly distinctive. The diagnostic value of any of these patterns is greatly enhanced if they are associated with one another. It must be

Asbestos in Lung Tissue: Asbestos bodies were scanty in nearly all positive specimens. They were detected more easily in smears of lung juice. No asbestos bodies were seen within tumour tissue. Pulmonary fibrosis was minimal (no patient had been considered to have "pulmonary asbestosis").

Occupational Histories (17 mesothelioma cases): Of those giving history of asbestos exposure, 5 were laggers employed by firms of insulation engineers and 2 were boiler makers (ship-building). Two patients employed by sackware manufacturers handled old sacks which had contained asbestos. Only 2 patients had worked in asbestos factories. One patient gave history of close environmental exposure, having worked in the offices of concrete manufacturers using asbestos cement.

Five gave inconclusive histories. Asbestos bodies were present in the lungs of two of these. Each of the other 3 patients had worked in places where they may have handled asbestos but there was no direct evidence (1 boiler maker, 1 ship repairers' apprentice, 1 dock railway labourer).

General Information: Sixteen out of 17 mesothelioma patients have died. Average age was 58 years. There were 12 men and 5 women. Length of exposure ranged from 5 to 43 years. Shortest interval from first exposure to development of tumour was 13 years. Interval from end of exposure to development of tumour from a few months to 40 years.

No attempt was made to ascertain types of asbestos fibre used and no approach was made to industrial firms or other employers.

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SESSION 7, PAPER 1

TRENDS IN THE HEALTH OF THE ASBESTOS WORKER

by
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What is an "asbestos worker"? An attempt is made to define the type of work which would properly classify an asbestos worker. Exposure to multiple toxic dusts is discussed.

There are three main types of asbestos fibers in commercial use today. They are different physically and chemically, and produce disease entities which are different chemically and radiologically. Workers in many parts of the world are exposed to one or another type of asbestos fiber. Should the health experience of a group using only chrysotile be compared with that of a group using only amosite or crocidolite?

The importance of the geographical location of the asbestos deposit is important. Are other factors such as chrome, nickel, radioactivity, etc., associated with some deposits and not others important?

Population characteristics are discussed. Disease incidence in a stable, isolated population is compared with that of an urban floating population.

The association of other diseases with the presence of the asbestos fiber is discussed. Should there be an association of a particular disease with the asbestos fiber when there is no asbestotic fibrosis present?

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SESSION 7, PAPER 2

PROBLEMS AND PERSPECTIVES: THE SEQUELAE OF EXPOSURE TO ASBESTOS DUST

by
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The sequelae of exposure to asbestos dust include the inhalation of the fibres, their deposition and the results of their subsequent retention. During this conference a number of these factors have been clarified, and those problems most urgently requiring investigation defined. In this paper some of the salient features are summarized and certain facets illustrated, and aspects in need of further investigation emphasized.

Logical explanations have been given for the presence of long asbestos fibres in the smaller air spaces. Experimental evidence has been given to show that there is a difference in the retention of various types of asbestos. The formation of the asbestos body has been described and the significance of these bodies and fibres in sputum assessed. The anatomical site at which the lesions of asbestosis originate has been defined and the progression of the disease demonstrated in experimental animals. The variation of the effect of different forms of asbestos fibre is most clearly illustrated in the monkey and the rabbit. The previous concepts of the significant particle size, and the solubility of the respirable dust, have been seriously challenged. However, the exact mechanisms of the pathogenesis of the disease is still unknown and the migration of asbestos fibres including the ultramicroscopic from the respiratory tract requires much further study.

The malignant neoplasms associated with exposure to asbestos dust have been discussed. On current evidence, the earlier view that carcinomata of the lung occur in cases with a significant degree of asbestosis is fully supported, but information is still required to confirm that there is no correlation between exposure per se and these tumours. More information is needed on the association of these tumours with different types of fibre. Mesotheliomas of the pleura and peritoneum seem

NOTES ON PREPARATION OF MANUSCRIPTS

The Academy's Editorial Division has already mailed out notices to the senior authors listed in the program for this conference informing them of the deadline for the submission of manuscripts to be published in the conference monograph; senior authors who did not receive such a notice, or who will have problems meeting the announced deadline, are asked to contact the Editor at the Academy building. Included with this advance notice were a set of Instructions to Authors and a special announcement regarding size of manuscripts and extra charges to authors. It may be helpful, however, to bring out at this time the following points regarding the preparation of manuscripts:

Manuscripts. Manuscripts should be typewritten on white bond paper, double spaced throughout - - including references, Figure captions, footnotes, etc. Submit only the original copy.

References. All references listed must be cited in the text. References can be set up either numerically or alphabetically (see the Academy's Instructions to Authors for further details). If the numerical system is used, references must be cited in the text in ascending numerical order, reference # 1 being the first reference cited, etc.

Art Work. If possible, please avoid submitting over-sized tables or illustrations. For example, photographs (or other artwork) that are considerably larger than the usual 8" x 11" size must be so drastically reduced to fit our page size as to often eliminate a good deal of detail. Remember too that words, numbers or letters within any Figure illustration should be large enough so that if reduction is necessary, such words, numbers or letters will still be legible.

Note to Foreign Authors. All material, except references to foreign publications, must be in English. This requirement includes table titles and column headings and any interior information within a Figure illustration.

Authors who at any time have any questions regarding the preparation of their manuscripts should feel free to contact the Editor at the Academy.