PATHOLOGY OF MALIGNANT MESOTHELIOMA AMONG ASBESTOS INSULATION WORKERS

YASUNOSUKE SUZUKI, M.D. • I.J. Selikoff, M.D.
Mount Sinai School of Medicine
New York, NY, USA

ABSTRACT

An epidemiological investigation of a cohort of 17,800 asbestos workers has revealed a high incidence of malignant mesothelioma among these workers during the period covered by this study (1975–1986). 278 consecutive cases of definite (234) and probable (44) mesothelioma in the cohort group were pathologically characterized. Data was derived from; 113 (40.7%) autopsies, 153 (55.0%) biopsies, and in 12 (4.3%) cases, there was a combination of autopsy and biopsy. The site of the tumor was 160 (57.5%) peritoneal, 97 (34.9%) pleural, 18 (6.5%) pleural and peritoneal, 1 (0.4%) pleural and pericardial and 2 (0.7%) pleural, peritoneal and pericardial. Cell type was 178 (64.0%) epithelial, 25 (9.0%) fibrous and 75 (27.0%) biphasic. The presence or absence of both diffuse interstitial fibrosis and asbestos bodies in the lung sections were ascertained in 137 of the 278 cases. Fibrosis was seen in all but 6 (95.6%). All but 6 cases were positive for the presence of asbestos bodies (95.6%). There were no deaths at age 39 or younger; between 40 and 49, 28 (10.1%); between 50 and 59, 99 (35.6%); between 60 and 69, 89 (32.0%); between 70 and 79, 50 (18.0%) and $\geq$ 80 years, 12 (4.3%). It was possible to calculate years from first exposure to death in 273 of the 278: none among 9 years or shorter; 1 between 10 and 19 (0.4%); 50 (18.3%) cases between 20 and 29; 129 (47.3%) between 30 and 39; 58 (21.2%) between 40 and 49, and 35 (12.8%) were 50 years and longer.

INTRODUCTION

Since January 1, 1967, we have been conducting an extensive prospective mortality study of a cohort of 17,800 asbestos insulation workers in the U.S.A. and Canada. The study continues; however, significant initial important data have been obtained, and have been published.[1] Data 1967-1976 revealed that in 2,221 consecutive deaths, approximately 20% of the insulation workers died from lung cancer, approximately 7% died from malignant mesothelioma: other cancers such as esophagus, colon, rectum, larynx, kidney and stomach were also higher in incidence among these workers in comparison with the general population.[1] Further experience (1967-1984) has shown that malignant mesothelioma in approximately 10% of the insulators (356/3,500) have died from malignant mesothelioma and the incidence of the tumor has increased with extension of years after first exposure to asbestos.[2]

Since 1975, one of us (YS) has evaluated all pathological materials of the study. 278 cases of the malignant mesothelioma were reviewed. It was found that these could be categorized as definite (234) and probable (44) (1975-1986). Here, our objective is to clarify the pathological characteristics of these 278 cases of malignant mesothelioma, and to study relationships of the tumor to other factors, such as the severity of pulmonary fibrosis (revealed by histopathological study), age at death, years after first asbestos exposure to death, and to cigarette smoking.

MATERIALS AND METHODS

278 consecutive cases of malignant mesothelioma in which pathological diagnosis was established (YS) between 1975 and 1986, were used as materials.

Pathology slides (histopathology) from various hospitals, additional slides systematically stained at our laboratory, autopsy and surgical pathology reports, and operative reports were thoroughly reviewed: type of specimens, primary site, cell type and the presence of pulmonary asbestosis were investigated.

Levels of diagnostic certainty of malignant mesothelioma has been classified into 5 categories, definite, probable, possible, unlikely and definitely not.[3] Classification of diagnostic certainty was decided by comprehensive pathological analysis of the tumor[4] consisting of gross appearance (from atuopsy or surgical pathology reports or the operative report), histology, histochemistry, immunocytochemistry and electron microscopy. Gross appearance and histology were used as the essential components in the comprehensive analysis in all cases, and both histochemistry (PAS with and without diastase, colloidal iron with and without hyaluronidase) and immunoperoxidase for CEA and cytokeratin were used in the large majority of the cases. Electron microscopy of the tumor was also available for the diagnosis in a small number cases.

Pulmonary asbestos was evaluated by histopathology of non-

neoplastic lung parenchymal sections. The presence of diffuse interstitial fibrosis has been accepted as the histopathological criterion of pulmonary asbestosis, particularly if associated with ferruginous bodies, when adequate material is available for study of the latter. The severity of asbestosis was classified as none/minimal, mild, moderate and severe, as reported previously.[5]

Age at death, years after first exposure to death, and smoking history were investigated in each of the cases.

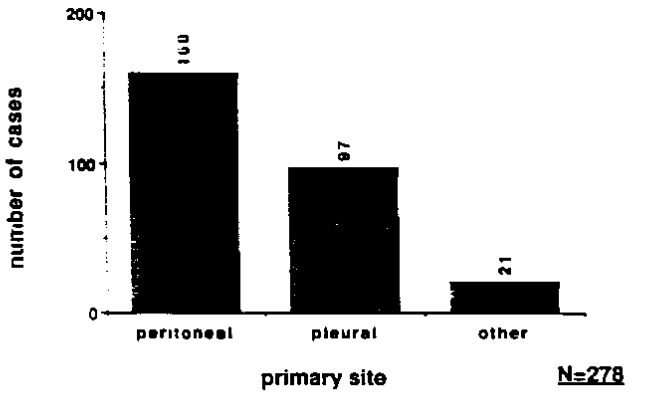
RESULTS

Based on the foregoing diagnostic criteria, the 278 cases were classified as 234 definite mesothelioma (84.2%) and 44 probable (15.8%). Although 30 additional cases were "possible" mesothelioma, these 30 cases were excluded for the present study. Derivation of the pathology specimens consisted of 153 (55.0%) surgical, 113 (40.7%) autopsy and 12 (4.3%) both autopsy and surgical. The primary site of the tumor was 160 (57.5%) peritoneal, 97 (34.9%) pleural and 21 (7.6%) other (Table I). The primary site of the 21 "other" cases could not be ascertained since the tumor was spread along two or three body cavities (pleura and peritoneal or pleura and pericardium or pleura, peritoneal and percardium) at autopsy. The ratio of the incidence between the pleural and peritoneal mesotheliomas was 4 to 6. Cell types were classified as 178 epithelial (64%), 75 biphasic (27%) and 25 (9%) fibrous (Table II). The ratio of the 3 cell types was quite similar between the pleural and peritoneal mesotheliomas. Age at death was; none in 39 years and younger, 28 between 40 and 49 years old (10.1%), 99 between 50 and 59 (35.6%) and 151 in 60 years old and older group (54.3%). Years from first exposure to death was; none in 9 years or shorter, 1 between 10 and 19 years (0.4%), 50 between 20 and 29 years (18.3%), 129 between 30 and 39 (47.3%), 58 between 40 and 49 (21.2%) and 35 in 50 years and longer (12.8%). Such long latency is similar to lung cancer among insulators.[5]

Histological evaluation of pulmonary asbestosis was done in 137 of the 278 cases (in which pulmonary parenchyma slides or paraffin blocks were submitted). Diffuse interstitial fibrosis and ferruginous bodies were seen in 131 of the 137. The degree of diffuse interstitial fibrosis was 6 (4.4%) none, 31 (22.6%) mild, 39 (28.5%) moderate and 61 (44.5%) severe. Ferruginous bodies were 6 none (4.4%), 41 small in number (29.9%), 36 moderate (26.3%) and 54 large (39.4%). It is to be noted that, in general, it may be difficult or impossible to detect ferruginous bodies in standard 5 μ sections. Indeed, we were rather surprised to see them as frequently as we did. Pulmonary asbestosis (diffuse inter-

Table I

Malignant Mesothelioma Insulation Workers—Primary Site



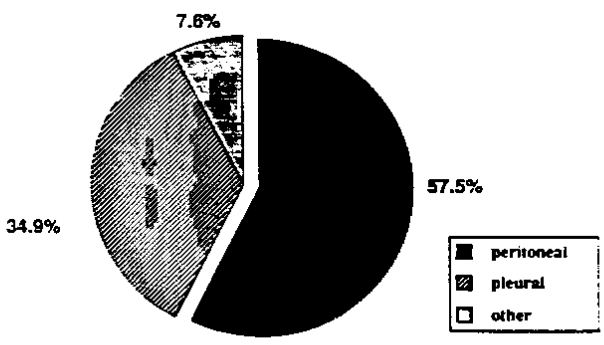
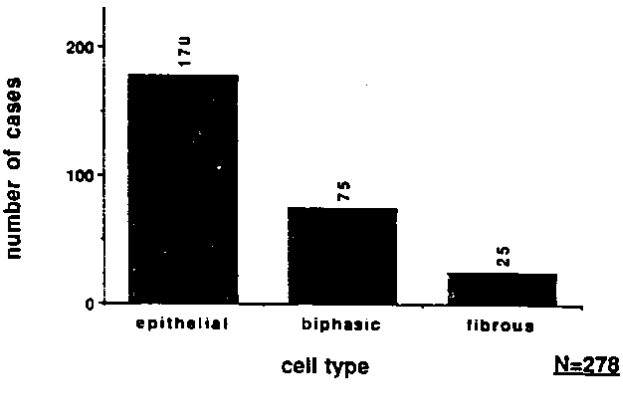
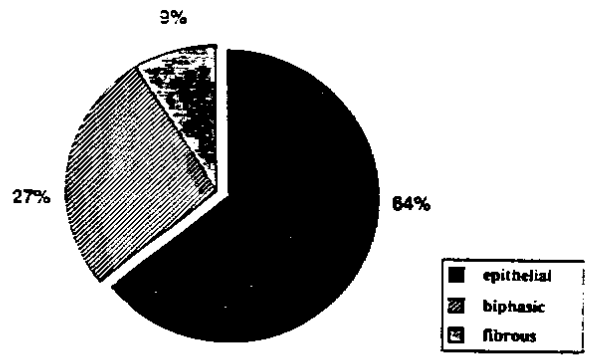


Table II

Malignant Mesothelioma Insulation Workers—Cell Type





stitial fribrosis with ferruginous bodies) was present in 95.6% of the 137 mesothelioma cases. The severity of asbestosis (represented by the degree of diffuse interstitial fibrosis) was compared between the pleural and peritoneal mesotheliomas; proportionally, severe interstitial fibrosis was higher in incidence in pleural mesothelioma (48.2% to 36.5%). The degree of asbestosis was compared between the 137 malignant mesothelioma and the insulators' lung cancer (415 consecutive cases; unpublished data). The severity of asbestosis was proportionally milder in the mesothelioma cases (44.5% vs. 56.0% in severe, 28.5% vs. 36.3% in moderate, 22.6% vs. 6.5% in mild, and 4.4% vs. 1.2% in none/minimal. (Table III).

Smoking history was available in 185 of the 278 mesothelioma cases. There were 144 present and ex-cigarette smokers (77.8%), 17 pipe and/or cigar smokers and tobacco chewers (9.2%) and 24 who had never smoked (13%). This smoking history data were compared with that of the insulators' lung cancer cases (532 in which smoking history was known): present or ex-cigarette smokers were smaller in proportion (77.8% vs. 91.6%) in the mesothelioma group, and the non-smokers were larger in proportion in the mesothelioma group (13% vs. 1.3%). (Table IV).

COMMENTS

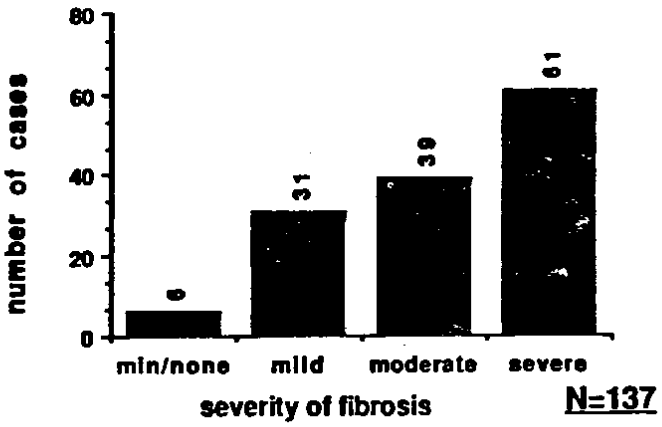
To the present, no specific single method has been available to establish a definitive diagnosis of malignant mesothelioma. Consequently, comprehensive pathological analysis of the tumor is still the best approach to establish such a definite diagnosis.[4]

It has been reported that the incidence of peritoneal mesothelioma was higher than that of pleural mesothelioma among insulation workers.[1,2] The present study has confirmed these initial reports. Presently, no clear explanation has been available as to why the incidence of the malignant peritoneal mesothelioma is so high among insulators.

The comparative proportion of cell types (epithelial, biphasic and fibrous) of the insulators' mesothelioma is similar to that of mesothelioma in general. Pulmonary asabestosis was almost always present (95.6%) in the insulators mesothelioma cases. It is known however, that pulmonary asbestosis is occasionally absent in the lung sections of malignant mesothelioma patients who had been mildly exposed to asbestos by environmental asbestos exposure or family contact to asbestos. It was interesting, when the severity of pulmonary asbestosis between malignant mesothelioma and

Table III

Malignant Mesothelioma Insulation Workers
—Interstitial Fibrosis



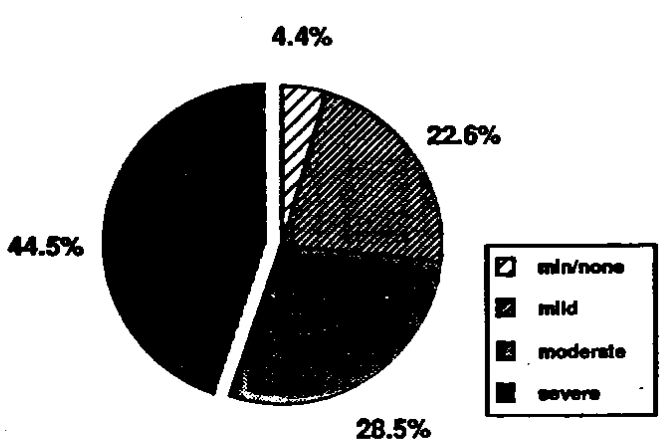
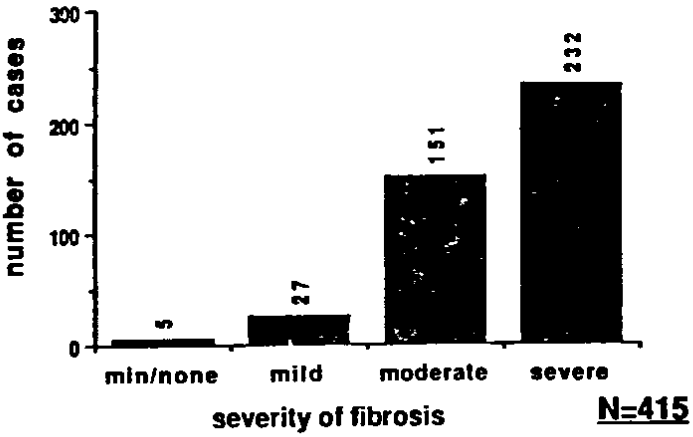


Table III

Lung Cancer-Insulation Workers
Interstitial Fibrosis



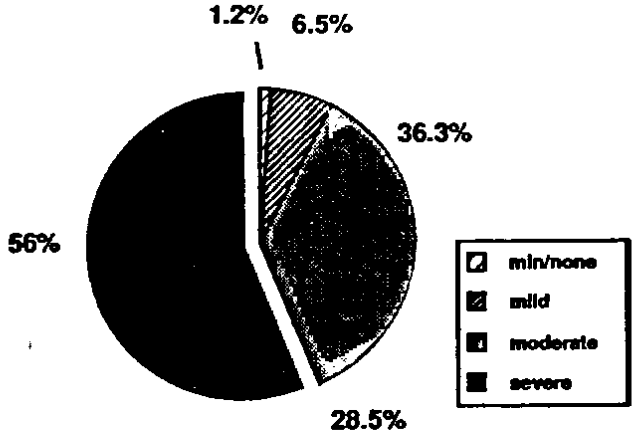
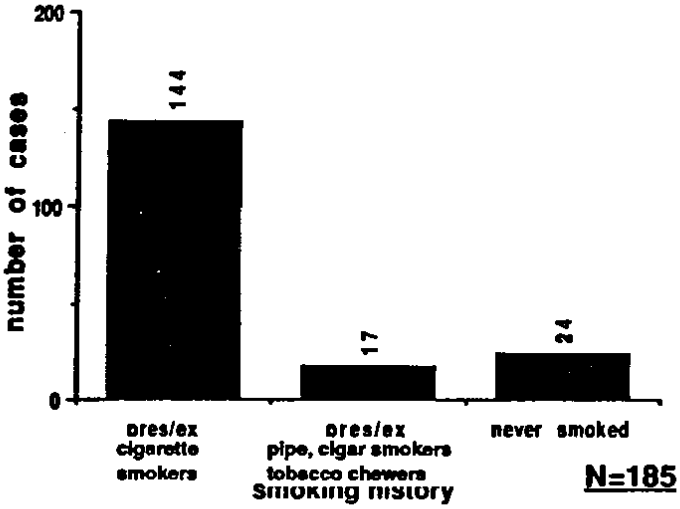


Table IV
Malignant Mesothelioma-Insulation Workers
Smoking History



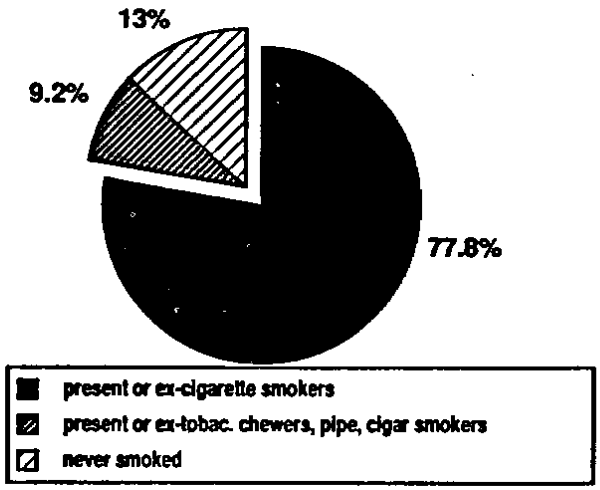
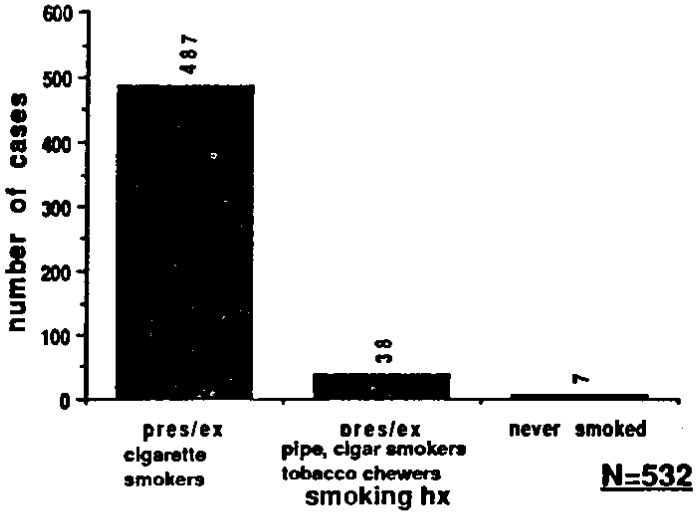
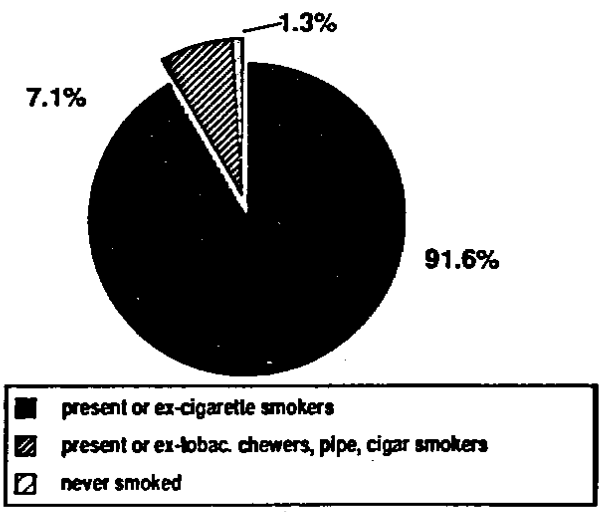


Table IV
Lung Cancer-Insulation Workers
Smoking History





lung cancer among asbestos insulation workers was compared, the former was comparatively milder in the severity.

It has been suggested that malignant mesothelioma may be induced with smaller doses of asbestos, in comparison to asbestos related lung cancer.

Age at death and years from first exposure to death were similar to that seen in other studies, including our preliminary ones of the same cohort.[1,2]

It has been reported that, unlike lung cancer, cigarette smoking does not exert a causal influence in malignant mesothelioma.[6,7] The present study has revealed that the current and ex-cigarette smokers were smaller in proportion in the mesothelioma cases, compared with those in the lung cancer cases among the asbestos insulation workers and that non-smokers were proportionally much higher in the mesothelioma cases (13% vs. 1.3%).

SUMMARY

The pathology and epidemiological features of 278 cases of malignant mesothelioma (234 definite and 44 probable) among asbestos insulators were investigated. These cases were those personally studied since 1975.

1. The primary site was 160 (57.5%) peritoneal, 97 (34.9%) pleural and 21 other (7.6%; 18 pleural and peritoneal, 2 pleural, peritoneal and pericardial, and 1 pleural and pericardial).

2. Cell types were 178 (64.0%) epithelial, 75 (27.0%) biphasic and 25 (9.0%) fibrous. These proportions were quite similar in pleural and peritoneal mesothelioma.

3. Histopathologically, pulmonary asbestosis was found in 95.6% (131/137) of the mesothelioma cases; 44.5% were severe, 28.5% moderate, 22.6% mild, and 4.4% were minimal or none.

4. 89.9% (250/278) were 50 and older at death. None were 39 or younger. Years after 1st exposure to death were 20 years and longer in 99.6% (272/273). None were found in less than 9 years. A single case was seen between 10 and 19 years.

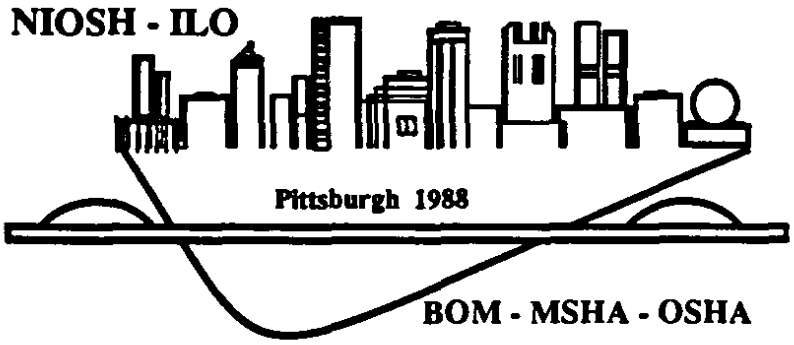
5. There were present and ex-cigarette smokers in 144/185 (77.8%), 9.2% cigar, pipe and chewing tobacco, and 13% (24/185) were non-smokers. Non-smokers were proportionally much higher in comparison with the insulators' lung cancer cases.

REFERENCES

1. Selikoff, I.J., Hammond, E.C. and Seidman, H.: Mortality experience of insulation workers in the United States and Canada, 1943-1976. *Ann. N.Y.A.S.* 330:91-116 (1979).
2. Ribak, J., Lilis, R., Suzuki, Y., Penner, L., and Selikoff, I.J.: Malignant mesothelioma in a cohort of asbestos insulation workers: clinical presentation, diagnosis, and causes of death. *Brit. J. Indust. Med.* 45:182-187 (1988).
3. McCaughey, W.T.E. and Oldham, P.D.: Diffuse mesothelioma: observer variation in histological diagnosis. Biological Effects of Asbestos. Monograph. Edited by P. Bogovski et al. *W.H.O. IARC Scientific Publications:* No. 8 (Lyon), pp. 58-61 (1973).
4. Suzuki, Y.: Pathology of human malignant mesothelioma. *Semin. Oncol.* 8:268-282 (1981).
5. Suzuki, Y. and Selikoff, I.J.: Pathology and epidemiology of lung cancer among asbestos insulation workers. *Proc. Amer. Assoc. Cancer Res.* 29:256 (1988). (Abstract).
6. Hammond, E.C., Selikoff, I.J. and Seidman, H.: Asbestos exposure, cigarette smoking and death rates. *Ann. N.Y.A.S.* 330:473-490 (1979).
7. Berry, G., Newhouse, M.L. and Antonio, P.: Combined effect of asbestos and smoking on mortality from lung cancer and mesothelioma in factory workers. *Brit. J. Indust. Med.* 42:12-18 (1985).

This study was supported by N.I.E.H.S. 0928

Proceedings of the VIIth International Pneumoconioses Conference | *Part* **I**
Transactions de la VIIe Conférence Internationale sur les Pneumoconioses | *Tome*
Transaciones de la VIIa Conferencia Internacional sobre las Neumoconiosis | *Parte*



Pittsburgh, Pennsylvania, USA—August 23–26, 1988
Pittsburgh, Pennsylvanie, Etats-Unis—23–26 aout 1988
Pittsburgh, Pennsylvania EE. UU—23–26 de agosto de 1988

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

CDC
CENTERS FOR DISEASE CONTROL

Sponsors

International Labour Office (ILO)
National Institute for Occupational Safety and Health (NIOSH)
Mine Safety and Health Administration (MSHA)
Occupational Safety and Health Administration (OSHA)
Bureau of Mines (BOM)

September 1990

DISCLAIMER

Sponsorship of this conference and these proceedings by the sponsoring organizations does not constitute endorsement of the views expressed or recommendation for the use of any commercial product, commodity, or service mentioned.

The opinions and conclusions expressed herein are those of the authors and not the sponsoring organizations.

DHHS (NIOSH) Publication No. 90-108 Part I