PLAINTIFF'S EXHIBIT
DUP-84

Brit. J. industr. Med., 1965, 22, 165.

REPORT AND RECOMMENDATIONS OF THE WORKING GROUP ON ASBESTOS AND CANCER

Convened under the auspices of the Geographical Pathology Committee of the International Union against Cancer (U.I.C.C.)

Preface

The Geographical Pathology Committee of the International Union Against Cancer (U.I.C.C.) convened a Working Group on 22 to 23 October, 1964 in New York to discuss evidence of an association between exposure to asbestos dust and cancer. Forty delegates from eight countries attended, and separate panels on epidemiology, pathology and experimental pathology, and physics and chemistry met and, at the final session, under the Chairmanship of Dr. Harold Stewart (U.S.A.) prepared the Report and Recommendations published below.

Terms of Reference

I 'demiology

To investigate the incidence of mesothelial tumours of the pleura and peritoneum in groups and/or regions where exposure to only one type of asbestos fibre has occurred.

B. To investigate the risk of bronchial carcinoma in populations exposed to asbestos dusts where the incidence of asbestosis is known, or believed, to be low.

C. To investigate the incidence of other tumours.

II. Pathology and Experimental Pathology

A. To establish criteria for the diagnosis of mesothelial tumours, to assemble material to assist in the standardization of diagnosis, and to form consultative panels.

B. To develop a standard of grading of fibrosis of the lung due to asbestosis.

C. To develop a standard method of assessing semi-quantitatively the amount of asbestos fibres and or bodies in sputum, fresh lungs, and fixed tissue.

D. To collate work done in various countries.

III. Physics and Chemistry

A. To investigate the usefulness of providing in one centre a set of standards of the main types of asbestos fibres and their extracted organic matter for distribution to centres investigating the biological, physical, and chemical properties of this material; if it is regarded as useful and practical, to suggest a centre

B. To suggest a minimum list of characteristics by which differences between these samples should be identified.

C. To suggest standard methods for the identification of types of asbestos in the lung in (*a*) large samples, and (*b*) tissue sections.

Association of Exposure to Asbestos Dust and Cancer

The main types of asbestos of commercial interest are amosite, anthophyllite, chrysotile, crocidolite, and tremolite. There is evidence of an association between exposure to asbestos and malignant neoplasia. This has been established mainly on information from Germany, Italy, South Africa, the United Kingdom, and the United States of America.

The types of tumours which have been shown to be associated with exposure to asbestos dust are (1) carcinoma of the lung, and (2) diffuse mesothelioma of the pleura and peritoneum.

There is some suggestion of an association also with gastro-intestinal carcinoma, and possibly ovarian tumours.

The latent period between first exposure to the dust and detection of the related tumours is many years, usually 20 or more. Instances up to 60 years have been reported. For this reason, further cases of these associated tumours are expected to occur for many years to come, even if dust exposures are now greatly reduced.

Present evidence indicates that the associated carcinoma of the lung is not limited to exposure

DUP 1141919

to any one type of asbestos fibre. However, further investigations are urgently needed to establish whether the degree of risk is importantly related to the type of fibre inhaled.

In the case of mesotheliomata, evidence from several countries suggests that exposure to crocidolite may be of particular importance, but it cannot be concluded that only this type of fibre is concerned with these tumours, and further investigation of this problem is needed.

Certain types of asbestos fibres in the virgin state have been found to contain oils, waxes, and other organic matter. In addition, asbestos fibres absorb hydrocarbons subsequent to mining. Small or trace amounts of various elements such as nickel and chromium are also found associated with some types of fibre. The possible role of such associated materials in the development of tumours after exposure to asbestos dust is not yet clear.

These findings, when considered in relation to the great increase in the use of asbestos for many purposes in all countries, suggest that a more serious and widespread hazard from exposure to asbestos dust may exist than is widely appreciated.

Recommendations on Problems Requiring Epidemiological Study

1. That the Importance of Fibre Type on the Risk of Developing Asbestosis, Carcinoma of the Lung, and Mesothelial and Other Tumours be Investigated.—International and intranational comparative studies of mining and other populations exposed to only one type of fibre are recommended. Among the countries in which and between which studies should, if possible, be made are Australia (crocidolite), Canada (chrysotile), Cyprus (chrysotile), Finland (anthophyllite), Italy (chrysotile), South Africa (amosite, chrysotile, and crocidolite), the United States of America (chrysotile and tremolite), and the Union of Soviet Socialist Republics (chrysotile).

The studies of the effect of exposure to different types of fibre within a country are likely to be of special value, but studies of groups exposed to apparently similar fibres in different parts of the same country are also likely to be informative.

2. That the Relationship of Dust Dosage (including Concentration and Duration of Exposure), and the Composition and Physical State of the Dust to the Incidence of Asbestosis, Carcinoma of the Lung, Mesotheliomata, and Other Cancers be Studied.—Comparative studies in factory populations in the asbestos textile and other manufacturing processes using asbestos are likely to be useful, especially when there are records of past dust measurements. In any prospective studies of new entrants, the measurement of dust by a standardized method should be regarded as an essential part of the investigation.

3. That the Effects of Removal from Further Exposure to Asbestos Dust be Investigated.—It is important to establish the subsequent morbidity and mortality from asbestosis, and the mortality from cancers associated with exposure to asbestos, in population groups no longer exposed to the dust.

4. That Further Investigations be made of Past and All Future Cases of Diffuse Mesothelial Tumours of the Pleura and Peritoneum to establish Any Association with Asbestos and Other Factors.—These tumours should be diagnosed on the criteria suggested by the Panel on Pathology (see below) and reviewed by a Panel of Pathologists with experience of these rare tumours. The tumour and lung should be investigated for the presence of asbestos by physical and chemical methods (see below).

5. That Studies of Morbidity and Mortality be Extended to Asbestos-exposed Populations that have not so far been widely Investigated.

1. It is recommended that special attention be directed to surveys in (*a*) the insulating industry, including that in ships; (*b*) the asbestos cement industry; (*c*) asbestos products industry; and (*d*) other plants in which asbestos is regularly used, such as certain paper, paint, and plastic factories.

2. It is also recommended that, since incidental exposure to asbestos dust may occur in certain trades and occupations, attention be directed to (*a*) handling and transporting asbestos; (*b*) the building industry; (*c*) pipe fitting; and (*d*) ship building and breaking.

3. It is recommended that surveys be made to study environmental and community exposures, including populations near mines and factories and elsewhere.

4. It is recommended that general population surveys be made nationally and internationally to establish by standardized methods, in areas of presumed high and low exposure to asbestos dust, the prevalence of asbestos bodies and fibres.

5. It is recommended that surveys of asbestosis in domestic and wild animals be extended to areas of high and low exposure.

6. Epidemiological Methods

1. *General*

(*a*) In addition to the usual information about the individual collected in such surveys, special attention should be directed to a detailed, social (including smoking habits), occupational, environmental, and

DUP 1141920

medical history from early childhood to elucidate any possible exposure to or association with any type of asbestos or other dusts. A study of the family unit or household may be of interest in view of the occasional reports of significant neighbourhood and household exposures.

(*b*) In view of the association between exposures to asbestos dust and pulmonary fibrosis and its complications, it is important to obtain as much information as possible about morbidity and mortality from *all* causes with particular attention to asbestosis, chronic bronchitis and emphysema, bronchiectasis, diffuse interstitial fibrosis, pneumonia, tuberculosis, cor pulmonale, carcinoma of the lung, diffuse mesothelial tumours of the pleura and peritoneum, gastro-intestinal tumours, and ovarian tumours.

(*c*) The principal epidemiological surveys likely to be used are retrospective, cross-sectional, and prospective, or a combination of these. In most of the surveys one or preferably more control groups will be needed. It is strongly urged that early and full consultation with statisticians be made at all stages from planning to an analysis of the findings.

2. *Clinical Criteria.*—The need to establish the minimal clinical information to be obtained in surveys of workers exposed to asbestos was agreed. A small panel met informally after the main working party and their recommendations are as follows:

(*a*) Symptoms: It was agreed that in all surveys the presence or absence of cough, sputum, dyspnoea, and chest pain should be recorded as a minimum. This should be recorded using a standardized questionnaire.

The British Medical Research Council Questionnaire on Respiratory Symptoms (1960), with the additional questions relating to chest pains in the W.H.O. Questionnaire on Cardiovascular Disease (Rose, 1962), is suitable for this purpose; these questionnaires have been widely used internationally for interview surveys. The Cancer Society Questionnaire in the Cancer Prevention Study has been widely applied in the U.S.A. It contains questions about a wide range of symptoms and diseases and was designed for self-completion.

(*b*) Signs: It was agreed that when physical examination was possible, the minimal observations should include the presence or absence of *clubbing of the fingers, cyanosis, and basal rales in the chest.*

It was agreed that the measurement of sputum volume (first hour on rising) and degree of purulence recorded in a standard way (Miller, 1963) were useful in association with the questionnaires for assessing the prevalence of bronchitis, and this may be relevant the disability caused by asbestosis.

The epidemiological usefulness of examinations of sputum for asbestos bodies and fibres is at present uncertain but needs investigation.

3. *Classification of Chest Radiographs of Asbestos-exposed Individuals.*—There is no international or national standardized classification of the radiological appearances of asbestosis. It is recommended that a scheme based if possible on an extension of the I.L.O. Classification (1959) be developed.

Possible means of doing this were presented at the New York Academy of Sciences Symposium on the Biological Effects of Asbestos (1965) by Finnish, German, South African, and British contributors. The aim should be to specify separately and record semi-quantitatively the principal radiological features seen in asbestos-exposed groups, but exposure to mixed types of dust is not uncommon, and the appearances may therefore include those caused in part by other pneumoconioses.

The classification should be purely descriptive of the radiological features and should not imply pathological change or the extent of disability. It is probable that the type and severity of alterations in radiological features, such as pleural plaques, etc., vary with the type of dust exposure and other factors so that a classification based on the principles in the I.L.O. Classification for Pneumoconiosis, in which there is a semi-quantitative assessment of several qualitatively different types of abnormality, may be expected to be useful.

It is recommended that a working group be set up to develop and test a new international classification.

4. *Lung Function Assessment.*—The preferred lists of lung functions to be used will vary according to the type of survey and the facilities available. A list of minimal and additional tests likely to be of use is as follows:—

Minimal
- Forced vital capacity (F.V.C.)
- Forced expiratory volume over 1 sec. ($F.E.V._{1\cdot0}$)

Additional
- Transfer factor (diffusing capacity) of lung for carbon monoxide—single breath method
- Lung compliance
- Standard exercise test
- Peak expiratory flow
- Airways resistance.

Recommendations on Pathology and Experimental Pathology

1. Diagnosis of Asbestosis

(*a*) *Macroscopic Examination:*

(1) At necropsy the parietal pleura should be

DUP 1141921

stripped if possible with the thoracic contents. It is desirable that at least one lung be inflated with fixative and whole lung sections be prepared.

(2) It is recommended that special note be made of the following:—

The pleurae should be examined for thickening and plaques (defined as localized areas of stiff horn-like material (Gloyne, 1933)). The site and size of all pleural lesions should be recorded.

The lungs should be examined for the presence of interstitial fibrosis, bronchiectasis, cystic change, tuberculosis, pneumonic consolidation, and tumours. The site of any tumour should be recorded as precisely as possible.

Mediastinal tissues should be examined for evidence of neoplastic infiltration and for tuberculosis.

Parietal and visceral fibrosis in the peritoneum, such as parietal plaques and 'sugar-icing' of the spleen, should be recorded.

(*b*) *Microscopic Examination.*—It is recommended that at least six sections be examined from the lungs before the degree of asbestosis is decided, and these blocks should be taken from specific sites and identified in the following standard manner: (1) Apex of right upper lobe, pleural surface; (2) right middle lobe, lateral pleural surface; (3) right lower lobe, middle of, basal surface; (4) left upper lobe, central section; (5) lingula, central section; and (6) left lower lobe, central basal section. In addition, sections should be taken from the bronchi and peritracheal and peri-bronchial lymph glands.

It is presumed that all examining pathologists will take further sections of any suspicious or abnormal tissue.

(*c*) *Assessment of the Severity of Asbestosis.*—The need to assess this in some standard way was agreed. It was recommended that the assessment should be based on the severity of interstitial fibrosis and the amount of tissue involved. The proposed scheme is as follows:

Extent of Lung Involvement	*Degree of Asbestosis*	*Degree of Interstitial Fibrosis*
Slight	Slight	Slight
Moderate	Moderate	Moderate
Marked	Marked	Marked

A category of *minimal* asbestosis is also proposed to describe slight focal fibrosis in the region of the respiratory bronchioles associated with the presence of asbestos bodies; such changes are common, confined to sections taken from the bases of the lower lobes.

This scheme puts more emphasis on the extent of the lesions than the degree of fibrosis (which should be averaged for the six sections). Thus, a lung with moderately extensive disease but only slight severity of fibrosis is graded as 'moderate asbestosis'. The use of an average assessment of the six sections makes it impossible to have a grading of slight involvement and moderate or marked degree of fibrosis.

(*d*) *Detection and Significance of Asbestos Bodies and Fibres*

(1) Sputum: The presence of asbestos bodies and fibres is an indication of exposure to asbestos dust and not evidence of asbestosis. It is therefore suggested that the bodies should be referred to as 'asbestos bodies' and not by the previously used term 'asbestosis bodies'. Because of their sporadic appearance and, in the case of fibres, their relation to recent dust exposure, the Group were of the opinion that the quantitative assessment of bodies and fibres in sputum was not, in the light of present knowledge, a very useful procedure but might become more useful when further investigated.

In sputum, detection by direct examination under a coverglass and the use of phase contrast, oblique illumination or narrowed condenser diaphragms are proposed. If sputum concentration is used, antiformin or 'Eusol' treatment is recommended. If this technique is used for large-scale comparative epidemiological surveys, the exact method should be standardized.

(2) Lungs: From fresh lungs, the highest positive results are obtained from smears from the base of a lower lobe (of the thickness of a thick blood smear for malarial parasites), air-dried and mounted in balsam. A rough quantitative examination by low-power magnification is easy and practicable. For fixed lungs, the smear technique is of limited value and unstained sections 30 microns thick are recommended.

(3) For investigation of asbestos fibres in lung sections, micro-incineration, acid treatment, and examination by phase-contrast are suggested. Morphologically, the fibres appear as straight rods of varying lengths and thickness, but with longitudinal shredding, and in the thicker fibres smaller fibrils may be recognized. Although there are other structures described as pseudo-asbestos bodies, or curious bodies, it was the view of the Group that in practice little difficulty is found in distinguishing the genuine from the others. These other types usually have a carbon-black centre, a shape which is other

DUP 1141922

than linear, but the body that can mimic an asbestos body completely is the small one found in talcosis, which may be tremolite, a form of asbestos.

(*e*) *Chemical Analysis of Lung Tissue.*—Where possible, blocks of tissue from these six areas chosen for histology should be taken, and the amount of collagen relative to total proteins should be estimated by the standard hydroxyproline methods. The results of collagen estimations should be expressed in absolute amounts and as percentages of defatted dried lung tissue (Harington and Kilroe-Smith, 1964).

2. Diagnosis of Diffuse Mesothelial Tumours

(*a*) *Macroscopic*

(1) The salient characteristic of the diffuse mesothelioma is its predilection to spread along the serosal membrane in which it occurs. In the pleural cavity, the entire surface may become replaced by a continuous layer of tumour due to symphysis of the pleural surfaces. This is uncommon in the peritoneum where the surfaces often remain separate but covered by isolated plaques and nodules or diffuse infiltration. Only those mesothelial tumours in which serosal spread is unequivocal should be termed 'diffuse'. A few benign diffuse mesotheliomas have been described. Almost all diffuse mesothelial tumours show evidence of malignancy by direct infiltration of adjacent tissues and organs and metastases to regional lymph nodes.

(2) The differentiation from metastatic tumour is the main problem in diagnosis and can only be made with complete certainty by the exclusion of all other sources of tumour at necropsy. Because of the tendency of the tumour to surround and infiltrate subserosal organs, these organs most commonly come under suspicion as points of origin. The possibility that the primary growth may have been surgically removed must be borne in mind.

(*b*) *Microscopic.*—Diagnosis is possible because the growth commonly shows histological patterns which are infrequent in other tumours and especially those which might metastasize to serosal membranes. Particularly helpful is the presence in some diffuse mesotheliomata of a mixed structure of malignant elements of both epithelial and mesenchymal character, or other diverse combinations. Growths in which only one type of cytoarchitecture is present may also have a highly distinctive pattern; for example, (1) a tubular or tubulo-papillary pattern in which the tumour cells show marked uniformity and are cubical or flattened; (2) masses of collagen in which there are either (*a*) clef-like spaces lined or occupied by tumour cells, or (*b*) fine hyaline strands which form complex meshworks and laminated bundles. Other examples of these tumours may have an entirely non-specific structure presenting the appearance of a spindle-cell sarcoma or of an anaplastic tumour.

Because of the difficulty in distinguishing clearly on histological grounds alone some of these growths from metastatic tumours, cases diagnosed from biopsy material should be called 'probable mesotheliomas'. In epidemiological studies precise details of the pathological evidence on which the diagnosis was based should be stated.

(*c*) *Histochemistry*

(1) Most of the mucoid material within mesotheliomata, although often intimately associated with the surfaces of the tumour cells, is extracellular. Intracellular or intratubular mucin of an adenocarcinoma will usually take mucicarmine or PAS stains. The absence of these reactions in a tumour which contains mucoid material can, when taken with the other features, be useful additional evidence for a mesothelial tumour.

(2) Hyaluronic acid is often present in mesothelial tumours. The demonstration of its removal from the tissue sections by specific hyaluronidase preparations is a useful histochemical test, but since the acid is soluble in water, the test requires that the tissues be fixed in a special precipitating fixative, such as formol alcohol acetic acid (Wagner, Munday, and Harington, 1962). It also appears likely that the quantitative measurement of hyaluronic acid in effusions, where this polysaccharide has been isolated and chemically characterized, may well become a reliable method for assisting in the diagnosis of mesothelioma, but it is emphasized that positive results for both the histochemical and chemical tests for hyaluronic acid are found in only a proportion of cases of mesothelioma, and they should not be used as sole diagnostic criteria.

(*d*) *Exfoliative Cytology.*—The contribution to the diagnosis of diffuse malignant mesothelioma by exfoliative cytology of serous fluids requires that (1) the exfoliated neoplastic mesothelial cells sufficiently resemble exfoliated non-neoplastic mesothelial cells for them to be recognized as having a mesothelial origin, and (2) that they also possess the generally accepted features of malignancy. The latter are not often present so a definite diagnosis of mesothelioma is then difficult.

Usually mesothelioma cells, while atypical, do not appear malignant but still show evidence of mesothelial origin. From cytology of the serous fluid it is possible to be strongly suspicious, and, in a few cases, confident of the diagnosis of mesothelioma, but

DUP 1141923

usually its presence can only be reported as possible.

The diagnosis of malignant mesothelioma by exfoliative cytology requires a familiarity with the non-neoplastic mesothelial cell. Mesothelial hyperplasia and hypertrophy can easily be mistaken for malignant mesothelioma and *vice versa*. It may be imprudent to do more than suggest malignant mesothelioma if there is not good supporting clinical, radiological, or biochemical evidence. The exfoliated malignant mesothelioma cell must also be distinguished from the adenocarcinoma cell, by far the commonest malignant cell recovered from serous fluids. This cell is well described in standard texts of exfoliative cytology.

(*e*) *Use of Tissue-culture in the Diagnosis.*—The various manifestations of mesotheliomata in some cases cause difficulty in distinguishing such tumours from bronchogenic carcinoma, metastatic ovarian carcinoma, fibrosarcoma, etc. It is therefore recommended that where possible biopsy specimens of pleural and peritoneal neoplasms should be studied after short-term passage (*a*) *in vivo*, and (*b*) *in vitro*, to determine whether the rate of growth and/or morphology after transplantation can provide useful criteria for a differential diagnosis of mesotheliomata. To achieve this it is recommended that clinical pathologists who see these tumours should co-operate with workers in experimental carcinogenesis who are using tissue-culture methods.

3. Contribution of Experimental Pathology.—It was agreed that various types of asbestos induce in many species of animals lesions similar to those seen in human cases of asbestosis, mesothelioma, and possible carcinoma of the lung, but the need for more precisely planned experiments was emphasized.

The desirability of using healthy animals of known response to asbestos under quantitative conditions of exposure by inhalation, feeding, and parenteral injection at several sites was agreed. Experiments in great variety are being undertaken in many parts of the world, particularly in Canada, Great Britain, South Africa, and the U.S.A. The prospect of providing standardized samples of chrysotile, amosite, crocidolite, tremolite, and anthophyllite asbestos for experimental work was welcomed.

It was agreed that there was a need for improving methods of identifying the type of asbestos in submicroscopic fibres in tissues. Further studies of the rate of formation and resistance to destruction of asbestos bodies in different species of animals may be useful.

It is recommended that there be closer collaboration between clinical and experimental pathologists and other scientists in the field of experimental pathology, biochemistry, and biophysics, as applie to the problems of the biological action of asbesto

4. Proposal for Pathology Reference Panels.—It recommended that central consultation and referenc panels be set up on regional, national, and inter national levels. These panels will (1) assist in estab lishing standards for the pathological classification c asbestosis; (2) serve as consultation centres for th diagnosis of mesotheliomata and other tumour associated with exposure to asbestos; (3) serve as general exchange of pathological material related t asbestosis and its associated tumours; (4) it is sug gested that a comprehensive atlas on the patholog of mesotheliomata should be prepared.

Recommendations Relating to Physics and Chemistr

1. Reference Samples of Asbestos for Experimenta Work.—It is anticipated that there will be a expansion of demand for asbestos of various type for biological and other studies. It is at preser impossible to predict the biological effects o differences in mineral composition, size distributio associated organic matter, and trace metals in diffe ent samples of asbestos. Also fibres from a particula mine may vary in composition and in the amount o absorbed material.

It is therefore recommended that:

(*a*) Standard reference samples, of respirable size of amosite, chrysotile, crocidolite, tremolite, and anthophyllite be prepared from as pure parent material as possible and held at the Pneumoconiosis Research Unit (P.R.U.) in Johannesburg for distribution to centres that require them. (These standards should also serve as references for comparison with larger amounts of material, such as may be required for inhalation or chemical extraction.) It is proposed that samples of chrysotile from different countries, for example, Arizona, Havelock (Swaziland), Quebec, and Shabani (S. Rhodesia) be included in the reference collection.

(*b*) The standard samples be analysed and characterized quantitatively by (1) chemical and spectrographic analysis; (2) optical and electron microscopy for the determination of shape, size distribution, and optical properties, such as refractive indices, extinction angle, etc.; (3) *x*-ray diffraction analysis by the powder technique; (4) specific surface measurement by low temperature gas adsorption and (5) determination of the amount and type of the organic matter present.

(*c*) Oils and waxes isolated from asbestos be prepared and also distributed through the P.R.U. Johannesburg.

DUP 1141924

(*d*) When the standards have been collected and prepared, the P.R.U., Johannesburg, will notify workers of their existence through the U.I.C.C. Bulletin and any other appropriate channels.

2. **Identification and Quantitative Assessment of Asbestos in Tissues.**—In tissue sections it may only be possible to identify the type of asbestos present. For quantitative studies of the amount present in any organ, such as the lung, it is necessary to analyse representative samples of the organs.

It is recommended that:

(*a*) Tissue sections should be treated to remove organic material, for instance by ashing or treatment with active oxygen; but this will not remove the asbestos bodies completely, and chemical treatment may be necessary to free the fibres. The best method for this is not known, but treatment with acetic acid may be useful. Identification of the type of fibre can only be made on free asbestos fibres and not on fibres inside asbestos bodies. It is recommended that methods of distinguishing asbestos from other fibres which may be present should be further investigated. This can probably best be done by phase contrast or polarized light microscopy. It is also recommended that the treated sections be examined by electron microscopy for recognition of sub-microscopic fibres.

(*b*) For large samples of tissue, acetic acid, hydrogen peroxide and formamide methods should be tried as they appear to be superior to ashing, but the best method of extraction of mineral matter from tissue is not yet known and needs further study. However, the quantitative determination of asbestos in the residue obtained in this way is difficult but could be based on chemical analysis, *x*-ray diffraction, or fibre counts. It is recommended that methods for concentrating such asbestos and separating different types of asbestos from each other should be further investigated.

APPENDIX

Consultative Panel of Pathologists in Great Britain

Dr. K. F. W. Hinson, Department of Pathology, The Brompton Hospital, Fulham Road, London, S.W.3

Dr. D. O'B. Hourihane, The Bernhard Baron Institute of Pathology, The London Hospital, Whitechapel, London, E.1

Professor W. T. E. McCaughey, University of Dublin, School of Pathology, Trinity College, Dublin 2, Republic of Ireland

Dr. J. C. Wagner, Pneumoconiosis Research Unit, Llandough Hospital, Penarth, Glamorgan, South Wales

Dr. F. R. Whitwell, Department of Pathology, Broadgreen Hospital, Edge Lane Drive, Liverpool 14

REFERENCES

Gloyne, S. R. (1933). *Tubercle (Lond.)*, 14, 445.
Harington, J. S., and Kilroe-Smith, T. A. (1964). *Arch. environm. Hlth*, 9, 395.
International Labour Office (1959). *Occup. Safety Hlth*, 9, 2.
Medical Research Council (1960). *Brit. med. J.*, 2, 1665.
Miller, D. L. (1963). *Amer. Rev. resp. Dis.*, 88, 473.
Proceedings of the New York Academy of Sciences Symposium on 'The Biological Effects of Asbestos', 1964 (1965). In the press.
Rose, G. A. (1962). *Bull. Wld Hlth Org.*, 27, 645.
Wagner, J. C., Munday, D. E., and Harington, J. S. (1962). *J. Path. Bact.*, 84, 73.

DUP 1141925