01-ASBEST-QWXP



# MINERAL FIBRE CONTENT OF HUMAN LUNG TISSUE AS AN INDEX OF PAST EXPOSURE TO ASBESTOS TYPES

A. J. Rogers

Commonwealth Institute of Health
The University of Sydney, NSW, 2006



Presented at

International Academy of Pathology
XIV International Congress
15 October, 1982

ABSTRACT

Prolonged occupational exposure to high levels of asbestos may result in an increased incidence of clinical cases of asbestosis, bronchogenic cancer and mesothelioma. The diagnosis of these diseases and the association with asbestos as an aetiological factor is usually made from a knowledge of the patient's occupational history. Often such evidence is weak or may be entirely absent. Quantitative analytical microscopic examination of the asbestos content of the lung provides information for an estimation of degrees of past exposure to asbestos.

The range of values of asbestos found in the lungs of the unexposed Sydney community, cases of bronchogenic cancer and cases of mesothelioma are presented.

A reasonable association is found when fibre levels are matched against past occupational history, often however the lung fibre levels provide the missing evidence of association with asbestos exposure. The data provided by such examinations has been most valuable in supplementing and substantiating evidence used for epidemiology and compensation purposes.

# MINERAL FIBRE CONTENT OF HUMAN LUNG TISSUE AS AN INDEX OF PAST EXPOSURE TO ASBESTOS TYPES

The pathological observation of accumulated dust in lung tissue as an aid in confirmation of pneumoconiosis and some environmentally induced malignancies has been attempted with various levels of success since the start of this century.

Historically major surveys of mineral content of lung tissue has been conducted in

- South African gold-mines (notable work by Watkins-Pitchford 1916)
- British coal mines (Nagelschmidt 1950s)
- Badham in 1936 investigated the lungs of N.S.W. coal, metalliferous and sandstone miners.

For asbestos exposed individuals, the observation of "curious bodies" in the lungs of asbestotics produced interest from Cooke in the 1930s who by microscopic examination and XRD linked these bodies with the dust generated from the asbestos process. His major pathological concern was

"Are the curious bodies diagnostic of pulmonary asbestosis"? (Cooke 1929).

The extrapolation of this comment to other asbestos related diseases resulted in the development of numerous semi-quantitative techniques for the examination of asbestos bodies resident in the human lung.

Specimen examination may be based on preparations of

- sputum
- smears of incised lung
- histological sections
- micro-incineration of histological sections
- chemical and enzymatic digestions.

Each technique varies in its sensitivity, reproducibility and correlation with actual asbestos content of the lung.

The Australian Mesothelioma Surveillance Programme was faced with the situation of implementing techniques to quantify past asbestos exposure by recording a detailed occupational history from the patient with confirmation of the asbestos exposure obtained by examination of residual asbestos in the lung. Many methods available in the literature were quantitatively unsuitable for our purposes although each possessed many good analytical aspects. With funding provided by the New South Wales Dust Diseases Board, eighteen months were spent in developing, testing and modifying a suitable technique (the results are currently awaiting publication in the journal "Analytical Chemistry").

The methodology is designed around the following steps:

1. Chemical digestion of the lung tissue using sodium hypochlorite
2. Dispersal of the residual mineral fragments using detergent
3. Concentration of the residue on membrane filters
4. Preparation of the filters for microscopic analysis
5. Quantitative examination of the mineral residues
   - light microscopy - quantitative counting and sizing (Differential Interference Contrast X 500)
   - Transmission Electron Microscopy - additional information on asbestos types by use of EDAX.

LAM 025896

The interpretation of results obtained using the method has been made difficult since non-occupationally exposed individuals accumulate in their lungs low levels of mineral fibres from natural and man made airborne contamination.

Comparison of the actual results obtained from other authors is of little value since the percentage of instances in which bodies are found and their quantitative levels varies considerably with the analytical technique used in the investigation, the amount of lung tissue examined and the experience, diligence and persistence with which fibres are sought. For investigators using the most sensitive techniques it is obvious that the presence of asbestos fibres and asbestos bodies appears to be almost ubiquitous in the general population.

Baseline Population

To develop baseline data, thirty matched pairs of lung cancer and control specimens (Australian born males, Sydney residents age $>40$) were selected from 430 consecutive necropsy and 64 resected lung samples. Statistical comparison of the mineral fibre levels found in the two groups indicated there was no difference in fibre level distribution between groups when tested at the 95% level of confidence. Using this information the two groups of matched pairs could be regarded as coming from the same homogeneous population and the results combined to form the basis for levels in the male Sydney population.

It was found that 95% of the sampled population contained less than 150,000 fibres per gram of dry tissue and less than 100,000 asbestos bodies per gram of dry tissue. On a semi-quantitative scan 83% of the lungs contained some mineral fibres.

TABLE 1. Mineral Fibre Levels Determined in Combined Patients and Controls

Uncoated Fibres

| Fibre count/g dry tissue | Percentage | Cumulative % |
|---|---|---|
| Not detected | 31.6% | 31.6% |
| $<50 \times 10^3$ | 42.1% | 73.7% |
| $50-99 \times 10^3$ | 15.8% | 89.5% |
| $100-149 \times 10^3$ | 8.8% | 98.3% |
| $150-199 \times 10^3$ | 1.7% | 100.0% |
| $200-249 \times 10^3$ | - | 100.0% |

Coated Fibres (Asbestos Bodies)

| Fibre count/g dry tissue | Percentage | Cumulative % |
|---|---|---|
| Not detected | 68.4% | 68.4% |
| $<50 \times 10^3$ | 29.8% | 98.2% |
| $50-99 \times 10^3$ | - | 98.2% |
| $100-149 \times 10^3$ | 1.8% | 100.0% |
| $150-199 \times 10^3$ | - | 100.0% |
| $200-249 \times 10^3$ | - | 100.0% |

TABLE 2. Grade of Mineral Fibre Detected in Lung Tissue

| Grade | | Uncoated fibres/g dry tissue | Coated fibres/g dry tissue |
|---|---|---|---|
| I | normal population | $0-149 \times 10^3$ | $0-99 \times 10^3$ |
| II | elevated amphibole asbestos exposure | $150-299 \times 10^3$ | $100-199 \times 10^3$ |
| III | | $300-599 \times 10^3$ | $200-399 \times 10^3$ |
| IV | increased incidence asbestosis mesothelioma | $600-1199 \times 10^3$ | $400-799 \times 10^3$ |
| V | | $>1200 \times 10^3$ | $>800 \times 10^3$ |

LAM 025898

ABS-006276

Comparison of this data to patients with known occupational exposure to asbestos indicated a geometric progression of lung fibre burden categories (Table 2).

The interpretation of individual cases of degree of asbestos lung burden against this baseline data provides interesting information.

## Samples referred by Outside Pathologists and N.S.W. Dust Diseases Board

Twelve cases were submitted on the basis of suspected asbestosis or lung cancer due to asbestos exposure; fifty-eight percent (7/12) of the samples had higher than normal levels of fibre. Of these 7, three had extremely high levels of fibre in the lung. Due to the limited data available on the occupational history and medical diagnosis of these samples, it cannot be considered feasible for further analysis of these samples other than to say they come from a higher exposed group than the normal population.

Medical officers of the N.S.W. Dust Diseases Board submitted seven cases of lung cancer for lung fibre analysis. Six of the seven had elevated lung fibre content and these fitted fairly well with the recorded history of occupational exposure to asbestos, hence assisting in confirmation of evidence for compensation purposes.

## Samples Obtained from Cases of Mesothelioma

LAM 025899

The first 27 completed confirmed cases of mesothelioma from the Australian Mesothelioma Surveillance Programme were examined for the presence of asbestos fibre in lung tissue by light microscopy:

44% (12/27) had fibre levels same as normal population range

26% (7/27) had fibre levels slightly elevated c.f. normal population

30% (8/27) had fibre levels in excess 3x normal (3x - 12,000x).

Relating the fibre levels determined by light microscopy to the evidence of exposure to asbestos as provided in the detailed occupational history, a reasonable association between the two factors was obtained (Table 3). However, one false positive was detected and five false negatives were detected, indicating the need for caution in the interpretation of aetiology of individual cases.

Most interesting was the point that 26% of the cases provided no evidence of asbestos exposure from occupational history or elevated asbestos levels in the lung. The U.K. Pneumoconiosis Panel's record is that approximately 30% of the U.K. mesothelioma cases also have no available evidence of asbestos exposure.

TABLE 3. Association Between Lung Fibre Load and Occupational History

Mesothelioma Cases (Light Microscopy)

LAM 025900

| Evidence of past asbestos exposure | Fibre count | | |
|---|---|---|---|
| | Normal range | Top normal to 2x normal | 3x Normal (3x - 12,000x) |
| No evidence / unlikely | 7 | | 1 |
| Some evidence / possible | 4 | 5 | 1 |
| Good evidence / probable | 1 | 2 | 6 |
| | (44%) | (26%) | (30%) |

The evidence of mesothelioma induction produced by elevated total fibre count is only part of the asbestos story. Epidemiological evidence clearly points to a difference in the potency of mesothelioma induction by the various asbestos types,

i.e. Crocidolite (blue asbestos) $\gg$ Amosite (grey/brown asbestos) $>$ Chrysotile (white asbestos)

ABS-006278

Problems are encountered in reviewing occupational histories for mesothelioma cases since almost no information is provided on the type of asbestos encountered by the patient. Since approximately 95% of asbestos usage is from chrysotile, most information on amphibole exposure is not obtained from occupational history taking. The analytical electron microscope provides a technique for identification of each type of asbestos in the lung.

Once again a study of Sydney urban males (60 - 70 years of age) indicates 95% had fibre counts and types as follows:

TABLE 4. Transmission Electron Microscope Counts $>2\ \mu m$ length (normal male population)

| | Total fibres | Chrysotile | Amosite | Crocidolite |
|---|---|---|---|---|
| Fibres x $10^6$/g dry tissue | <2.0 | <0.5 | <0.5 | <1.0 |

The distribution of crocidolite in the Sydney unexposed population approached that found in populations in North American and in the U.K. (Pooley et al)

For the 27 mesothelioma cases:

67% (18/27) had crocidolite levels within the range of the normal population

11% (3/27) had crocidolite levels 1 - 2x the range of the normal population

22% (6/27) had crocidolite levels >4x normal population.

This data is contrary to our occupational epidemiological concepts and poses the following questions:

1. Is a high proportion of the mesotheliomas not related to past amphibole asbestos exposure? There is some evidence being gathered by overseas studies that a fair proportion of mesothelioma cases fit into a no asbestos exposure category.

LAM 025901

ABS-006279

2. Is the method of predicting past exposure by examination of residual asbestos types in the lung insensitive for the levels of asbestos that may cause increased incidence of mesothelioma? The high level of negative evidence produced from occupational history data tends to discount this approach.

Future work will be based on an extension of this data to see if these trends continue.

## Conclusions

The results obtained from detailed investigations of asbestos fibre load of lung tissue provide some basis for assisting in diagnosis of asbestos related diseases. However, the natural incidence of these diseases associated with no asbestos exposure in our population cause many anomalies in the prediction of the diagnosis and aetiology of individual cases. Conclusions may only be reached on a firm basis of clinical diagnosis, histopathology, lung fibre counts and review of the patient's occupational history by an astute experienced occupational hygienist.

This work was supported by research grants provided by the New South Wales Workers' Compensation (Dust Diseases) Board. Electron microscope facilities were provided by the Director, Electron Microscope Unit, The University of Sydney.

## References


Badham C and Taylor HB. The lungs of coal, metalliferous and sandstone miners and other workers in N.S.W., chemical analysis and pathology. Ann Rept Dept Pub Hlth NSW 1936; p. 100-43.

Cooke WE. Asbestos dust and the curious bodies found in pulmonary asbestosis. Brit Med J Sept 28 1929; p. 578-80.

Watkins-Pitchford W and Moir J. On the nature of the doubly refracting particles seen in microscopic section of silicotic lungs. Rep Sth African Inst Med Res 1916; 1(Sept):000-000.

Nagelschmidt G. The relation between lung dust and lung pathology in pneumoconiosis. Brit J Ind Med 1960; 17:247-59.

Pooley F et al. Mineral fibre content of mesothelial tumours in North America. Inhaled Particles V (in press).

Ibid. A pathological and mineralogical study of asbestos related deaths in U.K. 1977. Inhaled Particles V (in press).

Rogers AJ. Determination of mineral fiber in human lung tissue by light microscopy and transmission electron microscopy. Analytical Chemistry (in press).

HVH AUG 9 1982

This should be kept centrally by IS, available to interested parties — You may wish to advise several that it is on hand; R.D. McIlwaine, C.W. Smith, R.E. Hanson, Harry Bissonet, Bryn Amellius, R.E. Joyner, M.B. Slomka, & D.E. Stevenson, in particular —

Paul D.

P.S. I think it is worth sending a copy of the press release, cover page and table of contents along with the notice — Paul D.

LAM 025893

ABS-006271