Fiber Levels and Disease in Workers from a Factory Predominantly Using Amosite

A. R. Gibbs,†, M. J. Gardner,* F. D. Pooley,‡ D. M. Griffiths,* B. Blight,§ and J. C. Wagner†

†Environmental Lung Disease Research Group and Pathology Department, Llandough Hospital, Penarth, South Wales, UK; ‡MRC Epidemiology Unit, Southampton, UK; *School of Engineering, Department of Materials and Minerals, University of Wales, College of Cardiff; §DataStat, London, UK

The Cape Boards Plant at Uxbridge produced insulation board containing predominantly amosite since 1947 but with usage of small amounts of very short chrysotile fiber (grades 6 or 7). Since 1973 amosite has been the only type of asbestos used. In 1981 Acheson et al. reported five mesotheliomas (four pleural and one peritoneal), four of which they associated with work at the factory (1). In a further study they described the mortality experience, up to the end of 1980, of 5,969 men employed at the same factory and found a doubling of the risk of lung cancer, five mesotheliomas and nine deaths from asbestosis (2). However, epidemiological studies of workers from plants that were considered to have been exposed to only one type of asbestos fiber have not always been accurate. For example, mineralogical examination of the lung tissues of autopsied workers from the Rochdale textile plant who were initially thought to be mainly exposed to chrysotile asbestos (3) surprisingly showed substantial amounts of crocidolite (4). It later became apparent that in fact significant amounts of crocidolite had been used at that plant.

We obtained lung tissues from workers at the Uxbridge plant who had come to autopsy and examined the pathological changes in relation to mineral content; no similar study of a predominantly amosite facility has been reported. Also, the tissue fiber studies would indicate the relative amounts of the different types of fiber used.

Materials and Methods

Pathology

Pathologists and coroners provided 143 paraffin blocks of lung tissue from 48 subjects. From one additional subject, histological sections only were available. Histological sections were cut and stained from each block and the degree of fibrosis and ferruginous bodies were graded numerically as follows (5):

- **Fibrosis**
  0. Absent
  1. Slight degree of reticulin or collagen accumulation around respiratory bronchioles.
  2. Fibrosis around respiratory bronchioles extending into adjacent alveolar ducts, atria and alveoli but not extending to adjacent respiratory bronchioles.
  3. Fibrosis linking adjacent respiratory bronchioles.
  4. Widespread fibrosis with or without honeycombing.

In some cases the degree of fibrosis was not assessed because adequate samples of lung tissue had not been taken away from tumor.

Ferruginous Bodies

0. Absent
1. Average of one or less per section.
2. More than one per section but requiring careful search to find them.
3. Easily found but forming only occasional clusters.
4. Easily found with numerous clusters.

In addition, any tumor present was classified and additional histochemical and immunohistochemical procedures performed, particularly periodic acid-shift procedure (PAS) with and without diastase, cytokeratin, and carcinoembryonic antigen (CEA).

Mineralogy

Appropriate tissue for mineral analysis was available for 43 cases only. The paraffin wax was removed from the tissue blocks by xylene and the tissue was digested in 40% potassium hydroxide, washed, then ashed.
at 350°C for 3 hr in an oxygen atmosphere. The final extract was suspended in distilled water and aliquots of known volume were filtered onto Nucleopore filters. These were carbon coated, the filters were dissolved in chloroform, and the carbon films were mounted onto gold electron microscope support grids for transmission electron microscopy. Between 100 and 200 fibers were counted and analyzed by energy dispersive X-ray analysis for each case (6).

Results
The entire population consisted of 49 subjects, 14 lung cancers, 14 mesothelioma cases, and 21 asbestos cases. The mineral analysis results (given in millions of fibers per g of dried lung tissue) were dominated by the amosite fiber levels (Table 1). All results for total fiber count and amphiboles followed the same pattern, so only amosite results will be presented in the later tables.

Chrysotile was analyzed separately but due to the low levels did not reveal any results of significance. Three of the 49 cases, all lung cancers, had very high counts and could be considered as outliers—they had amosite counts of 6476, 7853, and 3313 (millions per g dried tissue) and were each graded 4 for fibrosis and ferruginous bodies. Where appropriate, analyses were performed both with and without these cases. There was a definite positive relationship between the amosite levels and grades of fibrosis and asbestos bodies. (Tables 2, 3).

Conclusions were unaffected by the inclusion or exclusion of the three outliers. Regressions of grades on amosite, chrysotile, and time of exposure verified the significant relationship between amosite levels and grades but indicated that time of exposure affected the grades to a lesser extent. There was no evidence that the levels of chrysotile affected grades but the amounts of chrysotile were small (Tables 2, 3). There were higher levels of amosite fibers in lung cancer cases than in mesothelioma cases, and higher levels in mesothelioma cases than in the other cases (Table 4). Nonparametric (Wilcoxon Rank Sum) tests on these data and standard (parametric) t-tests on the log data were performed with similar results and levels of significance for both. Only the results of the nonparametric tests are given in Table 4. The comparison of mesothelioma with “other” cases is significant at the 10% level for a 2-tailed test and at the 5% level for a 1-tailed rest. There is no significant difference between the mesothelioma and lung cancer values. The major difficulty with the data is the lung cancer group, which contains three cases whose very high counts make it difficult to draw any firm conclusions in comparing them with the other two categories. The main feature that distinguishes the lung cancer group from the other two groups is that it contains the three very high counts. The positive relationship of grades to amosite fiber levels was much the same for mesothelioma and lung cancer cases; but there were more lung cancer cases than mesothelioma cases for the higher grades of fibrosis and asbestos bodies.

Discussion
In general, the fiber counts were high in these subjects and similar to those reported in a study of an East London asbestos factory that used crocidolite, amosite, and chrysotile (7). Measurements of airborne samples in the late 1960s within the Uxbridge plant showed some areas to con-

| Table 1. Mean fiber counts (x 10^4) for 43 subjects. |
|-----------------------------------------------|
| Variable          | Mean   | Median | SD    | Number with zero levels | Maximum |
|-------------------|--------|--------|-------|-------------------------|---------|
| Asbestos          | 784.9  | 106.3  | 1603.9| 2                       | 7852.9  |
| Crocidolite       | 22.5   | 0.1    | 72.7  | 19                      | 397.3   |
| Chrysotile        | 12.1   | 1.1    | 24.3  | 14                      | 135.5   |
| Mullite           | 8.6    | 3.9    | 14.2  | 9                       | 309.3   |
| Anthophyllite     | 0.7    | 0      | 4.8   | 42                      | 31.6    |

| Table 2. Amosite and chrysotile fiber levels (x 10^4) by grade of fibrosis. |
|-------------------------------|
| Grade | Amosite | Chrysotile |
|-------|---------|------------|
|       | Mean    | SD         | Mean   | SD    | Cases |
| 0.0   | 3.9     | 4.2        | 3.4    | 4.2   | 3     |
| 0.5   | 5.1     | 5.6        | 3      | 4     | 5     |
| 1.0   | 321.3   | 343.6      | 24.7   | 27.7  | 4     |
| 1.5   | 469.9   | 821.5      | 4.7    | 8.6   | 6     |
| 2.0   | 671.5   | 510.6      | 9.6    | 14.4  | 3     |
| 2.5   | 1606.6  | 2342.3     | 15.2   | 23.6  | 4     |
| 3.0   | 194.7   | 175.2      | 26.6   | 16.8  | 4     |
| 4.0   | 1916.3  | 2693.1     | 19.2   | 41.1  | 11    |

| Table 3. Amosite and chrysotile levels by grade of ferruginous bodies. |
|-----------------|
| Grade | Amosite | Chrysotile |
|-------|---------|------------|
|       | Mean    | SD         | Mean   | SD    | Cases |
| 0.0   | 1.4     | 2.7        | 1.5    | 2.4   | 10    |
| 1.0   | 28.9    | 19.2       | 1.7    | 1.1   | 3     |
| 2.0   | 272.9   | 436.3      | 33.5   | 57.6  | 5     |
| 2.5   | 395.3   | 656.5      | 0.1    | 0.2   | 3     |
| 3.0   | 484.5   | 650.2      | 24.4   | 17.9  | 9     |
| 4.0   | 1951.9  | 2497.4     | 8.7    | 16.4  | 13    |

| Table 4. Fiber count (x 10^4) by type of pathology. |
|-----------------|
| Pathology       | Total | Amosite |
|                 | Mean  | SD      | Mean  | SD    | Cases |
| Mesothelioma    | 1035.0| 1038.9  | 1000.7| 1012.9| 5     |
| Lung cancer     | 1483.3| 2567.9  | 1433.8| 2590.1| 14    |
| Other           | 396.0 | 489.9   | 296.9 | 463.4 | 24    |

Wilcoxon rank tests for unpaired data

Mean rank

Cases
| 11.20 | 5 Mesotheliomas |
| 9.57  | 14 Lung cancers |
|       | 2-tailed p = 0.5786 |
|       | 1-tailed p = 0.2863 |

Mean rank

Cases
| 22.64 | 14 Lung cancers |
| 17.67 | 24 Others |
|       | 2-tailed p = 0.1830 |
|       | 1-tailed p = 0.0915 |

Mean rank

Cases
| 13.79 | 24 Others |
| 20.80 | 5 Mesotheliomas |
|       | 2-tailed p = 0.0941 |
|       | 2-tailed p = 0.0471 |
The results also showed that increasing fibrosis was related to increasing amosite, but not chrysotile levels. This supports the findings of other studies, which have shown better correlations between fibrosis and amphibole than with chrysotile tissue levels (7,10). Our results are not completely consistent in that the grade 3 fibrosis subjects showed a lower mean amosite level than grade 1 to 2.5 subjects. This probably is explainable by sampling error. Unfortunately, due to the retrospective nature of the study, the geographical spread of the specimens, and the involvement of several pathologists, a systematic sampling procedure of the lung specimens could not be employed. Nevertheless there seems little doubt that, in this series, there was a correlation between fibrosis and tissue fiber levels. There were also correlations of both these factors with the grading of ferruginous bodies. In fact, the appearances of the ferruginous bodies were typical of asbestos bodies. Generally amosite produces proportionately more asbestos bodies than crocidolite, which in turn produces proportionately more than chrysotile (11). In terms of assessing asbestosis, the light microscopic grading of asbestos bodies and fibrosis appears reasonably accurate and useful where the predominant exposure has been to amosite.

The fiber counts were very high in the mesothelioma cases. Only three of the five cases had tissue suitable for the assessment of fibrosis, and these showed moderate to severe asbestosis. The fiber counts were higher in those with asbestos-related disease than in those without.

**Conclusion**

This is a brief report of a pathological and mineralogical study of lung tissues from subjects who had worked at a factory that predominantly utilized amosite. To the best of our knowledge, this is the first mineralogical and pathological study of such a group.

**REFERENCES**

1. Acheson ED, Gardner MJ, Bennett C, Winter PD. Mesothelioma in a factory using amosite and chrysotile asbestos. Lancet 2:1403–1405 (1981).
2. Acheson ED, Gardner MJ, Bennett C, Winter PD, Bennett C. Cancer in a factory using amosite asbestos. Int J Epidemiol 13:3–10 (1984).
3. Petro J. The hygiene standard for chrysotile asbestos. Lancet 1:484–489 (1978).
4. Wagner JC, Berry G, Pooley FD. Mesotheliomas and asbestos type in asbestos textile workers: a study of lung contents. Br Med J 285:603–606 (1982).
5. Hinson KFW, Otto H, Webster L, Rossiter CE. Criteria for the diagnosis and grading of asbestosis. In: Biological Effects of Asbestos (Bogovski P, Gilson JC, Timbrell V, Wagner JC, eds). IARC Scientific Publications No. 8, Lyon:International Agency for Research on Cancer, 1973,54–57.
6. Pooley FD, Clark NJ. Quantitative assessment of inorganic fibrous particulates in dust samples with an analytical transmission electron microscope. Ann Occup Hyg 22:253–272 (1979).
7. Wagner JC, Newhouse ML, Corrin B, Rossiter CE, Griffiths DM. The correlation between the fibre content of the lung and disease in East London asbestos factory workers. Br J Ind Med 45:305–308 (1988).
8. Acheson ED, Gardner MJ, Pippard EC, Grime LP. Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos. Br J Ind Med 38:344–348 (1982).
9. Gilson J. Wyers Memorial Lecture. Trans Soc Occ Med 16:62–74 (1965).
10. Wagner JC, Moncrieff CB, Coles R, Griffiths DM, Munday DE. Correlation between fibre content of the lungs and disease in naval dockyard workers. Br J Ind Med 43:391–395 (1986).
11. Pooley FD, Ranson DL. Comparison of the results of asbestos fibre counts in lung tissue obtained by analytical electron microscopy and light microscopy. J Clin Pathol 39:313–317 (1986).