Follow up study of workers exposed to man made mineral fibres

Janet M Hughes, Robert N Jones, Henry W Glindmeyer, Yehia Y Hammad, Hans Weill

Abstract
A survey of workers in seven man made mineral fibre (MMMF) production plants, the subject of a previous report, was conducted, with other blue collar workers serving as regional comparisons. Based on the median reading of chest radiographs by five readers, a low prevalence of small opacities, all at the 1/0 and 1/1 profusion levels, was again found: for workers with MMMFs, 23/1435 (1-6%); for comparison workers, 2/305 (0-7%). Spirometric measurements indicated generally healthy populations, and were not related to presence of opacities. Ninety three per cent (21/23) of MMMF workers with opacities worked at the two plants with the highest exposures to fine fibres, resulting in a dose-response relation across plants. For one location, the prevalences of opacities for the MMMF and comparison workers were not significantly different (5-9% (13/220) v 3-1% (2/65)). No comparison x ray films were obtained for the MMMF plant with the highest prevalence (6-6%), so a second phase of the study was conducted, with pre-employment films from these two plants. On this second reading, the prevalence of opacities was lower; there were no significant differences between the two groups of films, and no relation between opacities and exposure indices. There was considerable inter and intrareader variability. These results indicate no adverse clinical, functional or radiographic signs of effects of exposure to MMMFs in these workers.

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A 1979–80 study of male production workers in seven United States man made mineral fibre (MMMF) production plants examined tests of lung function and readings of chest radiographs in relation to indices of exposure to MMMF. A low prevalence of radiographic small opacities was found, all at the lowest International Labour Office (ILO) profusion levels (6-7% at 0/1 (63/941), 2-7% at 1/0 (25/941), 0-6% at 1/1 (6/941). The prevalence of opacities ≥ 1/0 was highest, however, among employees at the two plants manufacturing both ordinary (nominal fibre diameter > 3 μm) and fine (nominal fibre diameter 1–3 μm) fibres (7-5% (22/292) compared with 1-4% (9/649) of the other plants combined). None of the 86 workers from the very fine fibre (< 1 μm) plant had small opacities ≥ 1/0, but these workers had been employed, on average, for shorter durations than those in the other plants. Presence of small opacities was related to age and cigarette smoking. Among current smokers, after accounting for age, pack-years of smoking, and two plant categories (ordinary or fine fibre or not), presence of small opacities (profusion ≥ 0/1) was related to several measures of fibre exposure, including cumulative exposure to fine fibres. There were no significant factors among ex or never smokers, possibly because of the few cases (n = 33).

Respiratory symptoms and measurements of pulmonary function indicated a generally healthy population, and were unrelated to either type of fibre or amount of fibre exposure. Radiographic small opacities were, however, associated with lower lung function.

The 1979–80 survey led to the conclusion that the minimal evidence for respiratory effects among these workers could not be considered clinically significant, and that the results were encouraging as regards potential health effects of exposure to MMMFs. Nevertheless, the possible relation between the occurrence of small opacities and exposure to fine fibres indicated the need for continued surveillance of these workers.

About seven years after the initial survey, a follow up was conducted to reassess the respiratory health of workers in these plants, to determine if there was progression of the radiographic indica-
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tors, and to consider the question of whether the apparently increased prevalence of small opacities at two plants was indicative of a fine fibre effect or was an artefact, possibly reflecting factors related to geographic region or radiological laboratory.

Methods

STUDY DESIGN

The present study consisted of two phases: the first or primary phase, which included workers from all seven plants; and a second phase, which included workers from only two plants. The first phase, a cross sectional survey, was similar to the earlier study, but with these exceptions: (1) no minimum duration of employment was required for workers in the seven MMMF plants (in 1980, either five or 10 years of employment, depending on the size of the plant, was required); (2) at each geographic location, other blue collar workers, without exposure to fibre or other materials known to be hazardous to respiration, were recruited to serve as regional comparison populations; and (3) the number of x ray film readers was increased from three to five.

During the first phase of the study, radiographs of comparison workers could not be obtained at two locations. As will be described in the results section, this lack of comparison films, as well as the small number of comparison workers at one other location, made the interpretation of the radiographic findings difficult. Consequently, a second phase of the study was implemented in which chest radiographs taken for pre-employment screening at two plants were obtained to serve as (additional) comparison films.

DESCRIPTION OF THE MMMF PLANTS AND INFORMATION ON EXPOSURE

Descriptions of the seven MMMF plants, their processes, and the available information on exposure are provided in the report on the 1980 study.1 There are five fibrous glass and two mineral wool manufacturing plants. These produce primarily insulation and building materials. The five fibrous glass plants included two producing only ordinary fibres, two producing both ordinary and fine fibres, and one producing only very fine fibres.

As in the 1980 survey, estimates of exposure are based on a University of Pittsburgh survey,3 which classified all jobs as either involving no fibre exposure or to one of four categories of fibre concentration: 0·0032, 0·032, 0·32, or 1·5 fibres per millilitre of air (f/ml), based on fibre counting with electron microscopy.

Job histories and exposure estimates for individual workers were updated throughout 1986 when most of the radiographs were obtained.

EMPLOYEE ELIGIBILITY, MMMF PLANTS

In the seven MMMF plants, only male production workers with less than one month ever assigned to the batch or binder areas (where exposures to crystalline silica or potential carcinogens were possible) were eligible. In all plants, women constituted less than 5% of production workers and were excluded. For the five plants with 250 or fewer eligible employees, all were targeted for participation; in the two larger plants, all participants from the 1980 survey and a random sample of the other eligible employees were targeted.

COMPARISON WORKERS

For each of the six communities in which the seven MMMF plants were located (the two ordinary fibre plants, plants 1 and 2, were located in the same city), blue collar comparison workers were identified and agreement reached with management personnel for the employees’ participation. These six comparison groups consisted of city workers (for plants 1 and 2), glass products manufacturing workers (plant 3), city workers (plant 4), employees of two plastic container manufacturing plants (plants 5 and 6), and metal cabinet manufacturing workers (plant 7). Comparison workers ever employed as electricians, welders, sandblasters, or any other job with potential respiratory hazards were not included.

Workers in all six of these comparison groups participated in the spirometry and interview phase of the survey. Despite all recruitment efforts and release time from work, the two groups of plastic container workers (corresponding to MMMF plants 5 and 6) refused to have chest x ray films taken. With only a few industries in these rural areas, no other comparison workers could be enlisted.

RESPIRATORY HEALTH ASSESSMENT

The procedures used in the MMMF and comparison plants were identical. The same technicians travelled to each location to administer the spirometric testing and interview, which was a modified version of the American Thoracic Society/Division of Lung Diseases questionnaire.4 Spirometry was performed with a portable testing device developed by the Informed Corporation to the researchers’ specifications.

Plant personnel scheduled workers to have chest radiographs taken at a local radiological laboratory, usually providing release time from work and transportation. The two plants located in the same city used the same facility.

After removal of identifying marks other than a coded study number, the assembled films were thoroughly shuffled. Five readers experienced in the use of the ILO 1980 classification in epidemio-
logical studies were employed. These were JC Gilson, ITT Higgins, RN Jones, WKC Morgan, and EN Sargent. Each reader was provided with the set of ILO standard radiographs and worked independently of the others and without knowledge of patient site or whether the individual films were those of exposed or reference workers. Batches of 50 to 60 films were presented in random order to each reader. Early batches contained certain study films, preselected for the possibility of divergent judgements as to quality or lung abnormality, for use as "trigger films". After the reader's initial classification of trigger films, which were not identified to the reader as such, they were inserted into later film batches. At subsequent readings, the recording clerk informed the reader that a trigger film was just classified, telling the reader how it was previously classified. The intention of trigger films is to provide feedback, so that readers can detect any drift in sensitivity over the course of a long reading exercise.

Films judged unreadable by three of the five readers were excluded from analyses. For each film, the median of all readings was used as the summary reading.

Radiographs from participants in the 1980 study were included in the random readings. After completion of the random readings, the films were paired and read side by side, in known order, to determine progression. Comparability was rated as good, fair, or impossible, and pairs receiving a majority rating of impossible were excluded from analysis. A seven part scale for change was used: no change, and three categories (possible, probable, and definite) for progression and regression. No change was scored as zero, possible regression as -1, possible progression as +1, etc, and the mean of all readers' scores was assigned as the progression score for the film pair.

PHASE TWO OF THE STUDY
As previously stated, no x ray films for comparison workers were obtained for plants 5 and 6. In the earlier survey, none of the 86 plant 5 workers and only one of the 32 plant 6 workers had small opacities profusion 1/0 (none higher); therefore, the lack of comparison x ray films at these locations was initially considered unlikely to be a serious limitation.

Increased prevalences of small opacities, at minimal profusion levels, were subsequently found for MMMF workers at two plants: plant 5, for which no comparison workers were available, and plant 3, for which only 65 comparison workers had participated. Because comparison films were considered essential for interpreting minimal radiographic findings, radiographs taken as part of pre-employment screening at these two plants were obtained. To maximise comparability, an individual worker's pre-employment radiograph was included only if it was taken at the same radiological facility during 1985-7 (the years during which the study films were taken), and if the person had been hired by the plant (only a very few subjects with a pre-employment film were not subsequently hired). None of the workers with pre-employment radiographs from these years had participated in the main part of the study.

Four of the readers returned for a second reading. Regrettably, Dr Gilson died before the second reading took place, requiring the enlistment of another experienced reader (J Wiot). Readers were told that the second reading was necessitated by the lack of comparison films for two locations.

This second reading included 157 pre-employment films, as well as the 342 from these two plants obtained for the main phase of the study (to control for possible changes in readings over time). These were shuffled together, and the set was independently read by each reader, without knowledge of film sources, date, or whether the subject was an exposed worker or a control.

STATISTICAL ANALYSIS
Multiple logistic regression analysis was used to examine the presence of symptoms and x ray film opacities in relation to possible determinants—for example, age, smoking habit, exposure indices. In these analyses, the actual values of continuous variables, such as age and most of the exposure indicators, were used for each worker. Multiple regression was used for relating spirometric values to determinants after confirming the approximate normality of these distributions.

Results
DESCRIPTION OF THE POPULATION
Overall, about 76% of the targeted MMMF workers provided a chest x ray film for the study. Of the 941 participants with x ray films from the earlier survey, only 64% (602) were still employed; of these 522 (87%) again participated. Overall, 1441 workers provided spirometry data; of these, 25 (1.7%) were judged non-repeatable and excluded from analyses of spirometry.

For several MMMF plants there were substantial numbers of workers who refused the spirometry and respiratory health questionnaire phase of the study but later agreed to have a chest x ray film taken. For the MMMF plants combined, 1449 workers provided a chest x ray film, but only 1030 had (repeatable) spirometry. Among comparison workers, 305 had an x ray film and 386 provided repeatable spirometry assessments.

For each location, the mean ages and percent-ages of smokers for the MMMF and comparison
workers were similar (table 1). The most pronounced difference was in the percentage of smokers in plant 7 (74%) compared with the comparison manufacturing workers (55%).

The MMMF workers had been employed in the plants for an average of 14-7 years. For three plants (3, 5 and 6), the mean duration was less than 10 years; for the other four plants, the means ranged from 14 years (plant 7) to 20 years (plant 2).

There were substantial differences across the MMMF plants in the mean concentration of exposure to airborne fibres, with plant 3 (ordinary and fine fibres) and plant 5 (very fine fibres) considerably higher than the others.

Overall, 14% of participants reported previous occupational exposure to asbestos (for a mean of six years), 10% previous mining experience (two years), and 17% sandblasting (one year). The prevalences of previous exposures were similar for MMMF and comparison workers, with the exception of sandblasting (20% for MMMF workers, 7% for comparison).

**Table 1** Description of participants by location*

<table>
<thead>
<tr>
<th>MMMF workers</th>
<th>Comparison workers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMMF plant</strong></td>
<td>**Age (%)</td>
</tr>
<tr>
<td>(category)†</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>1 (Ordinary)</td>
<td>313 (208)</td>
</tr>
<tr>
<td>2 (Ordinary)</td>
<td>269 (174)</td>
</tr>
<tr>
<td>3 (Ordinary/fine)</td>
<td>220 (155)</td>
</tr>
<tr>
<td>4 (Ordinary/fine)</td>
<td>335 (210)</td>
</tr>
<tr>
<td>5 (Very fine)</td>
<td>122 (128)</td>
</tr>
<tr>
<td>6 (Mineral wool)</td>
<td>86 (81)</td>
</tr>
<tr>
<td>7 (Mineral wool)</td>
<td>99 (74)</td>
</tr>
<tr>
<td>Total</td>
<td>1444 (1030)</td>
</tr>
</tbody>
</table>

*Description of workers who participated in any phase of the study (x ray film and/or spirometry/interview).
†Nominal fibre category for MMMF plants.
‡Number of workers with chest x ray films. Number with both a health interview and repeatable spirometry in parentheses.
§Mean years employed in MMMF plant; conc = mean concentration of fibre exposure in f/ml.

SYMPTOMS AND SPIROMETRY

As expected, most respiratory symptoms were significantly related to cigarette smoking and age, and, among current smokers, to pack-years of smoking after accounting for age.

For MMMF plants 2 to 5, symptom prevalences were similar for the MMMF and comparison workers (see table 2 for prevalences of selected symptoms). For plant 1 (ordinary fibre) and the two mineral wool plants, several symptom prevalences were higher among MMMF workers.

In the two mineral wool plants, the higher prevalence of asthma among MMMF was largely accounted for by asthma diagnosed before working at the plants (14 of 17 cases diagnosed before hire, with 12 diagnosed in childhood). After accounting for smoking category (current, ex, never), none of the differences in symptoms between MMMF and comparison workers was statistically significant.

Workers in MMMF plant 1 had a significantly higher prevalence of symptoms than the comparison workers (after accounting for smoking and

**Table 2** Prevalence of selected symptoms and mean FEV<sub>1</sub>, by location

<table>
<thead>
<tr>
<th>MMMF workers</th>
<th>Comparison workers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMMF plants</strong></td>
<td><strong>Symptom prevalence‡</strong></td>
</tr>
<tr>
<td>Not</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>1</td>
<td>208</td>
</tr>
<tr>
<td>2</td>
<td>174</td>
</tr>
<tr>
<td>3</td>
<td>155</td>
</tr>
<tr>
<td>4</td>
<td>210</td>
</tr>
<tr>
<td>5</td>
<td>128</td>
</tr>
<tr>
<td>6</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>74</td>
</tr>
<tr>
<td>Total</td>
<td>1030</td>
</tr>
</tbody>
</table>

*See footnote, table 1, for fibre type category.
†Number with both a respiratory health interview and repeatable spirometry.
‡Prevalences of chronic bronchitis, chronic cough, dyspnoea > level 3 (having to stop when hurrying on level ground), current asthma respectively.
Although these differences remain unexplained, it is considered unlikely that these higher prevalences are due to mineral fibres, as this plant had the lowest estimated levels of exposure to fibres. The spirometric measurements, expressed as percentage of predicted (and incorporating the OSHA recommended adjustment of 0.85 for black subjects), indicated generally healthy populations: the mean values for forced expiratory volumes in one second (FEV₁), forced vital capacity (FVC), FEV₁/FVC, and forced expiratory flow (FEF₂⁵₋₇₅) were 101, 103, 95, and 78, respectively for the MMMF workers overall and 103, 104, 96, and 81, respectively for comparison workers. Functional values showed the expected relation with cigarette smoking—for example, mean FEV₁ values of 105, 102, and 99 for never, ex and current smokers respectively. There were some workers whose values were surprisingly low for an actively employed population—for example, five MMMF workers with FEV₁ (% predicted) less than 40. However, most of these low values were in workers with active asthma or previous chest surgery.

Among MMMF workers, there were significant differences in functional values across the seven plants; the highest mean values were found for workers from plant 5, the very fine fibre plant (109% predicted for FEV₁), the lowest for those from plants 1 and 2, the two ordinary fibre plants (96 and 99% predicted for FEV₁). Functional values were not related to any of the exposure indicators, either across or within plants. For some plants, there were significant differences between MMMF and comparison workers; however, when asthmatic workers and workers with previous chest surgery were omitted from the analyses, none of the differences remained significant.

CHEST X RAY FILMS
There was considerable variability between the five readers. For film quality, four of the readers were in close agreement, finding from 0% to 1% unreadable, but one reader judged 8% to be unreadable. The percentages of readable films judged to have small opacities ≥ 1/0 were: 1%, 2%, 2%, 6%, and 11%.

Based on median reading for quality, nine of the 1749 films (0.5%) were judged unreadable and 244 (14%) of poor quality. The median assessments of quality differed substantially across the six radiological laboratories, with 26%, 2%, 1%, 5%, 5%, and 39% of the films judged to be poor or unreadable. For each, however, the distributions by quality were similar for the MMMF and comparison workers.

As in the 1980 survey, there was only a low prevalence of small opacities, all at the lowest profusion levels. Of the 1435 readable films for MMMF workers, median readings categorised 14 (1-0%) and 9 (0-6%) as 1/0 and 1/1 respectively; for the 305 comparison films, one (0-3%) was categorised as 1/0 and one (0-3%) as 1/1. The primary type of opacity was irregular for 96% of these films. No films had large opacities.

Presence of opacities was not related to mean spirometry measurements among either the MMMF or comparison workers. Of the 1435 MMMF workers with a chest x ray film 956 had also performed repeatable spirometry. Mean FEV₁ values (% predicted) for the 938 without and the 18 with opacities (≥ 1/0) were 101.3 and 103.9 respectively; corresponding FVC values were 103.4 and 107.2.

For films taken for this survey, presence of opacities (≥ 1/0) was significantly related to film quality, with 2-9%, 1-1% and 0-4% of films of optimal, good, and poor quality having opacities respectively. Opacities were not related to cigarette smoking (prevalences of 1-2% and 1-6% among never and ever smokers), nor to previous occupational exposures such as asbestos, mining, and sandblasting.

Among MMMF workers, the two ordinary fibre plants (plants 1 and 2) had similar (and low) prevalences of small opacities, as did the two mineral wool plants (plants 6 and 7). These two sets of plants are combined in the summaries of x ray film findings by location.

Plants 3 (5-9%) and 5 (6-6%) had higher prevalences than the other five plants (table 3). Film quality could not account for these differences: the same patterns in prevalences across plant were seen for each grade of film quality.

For three of the four groups of comparison workers with x ray films, no opacities (≥ 1/0) were seen; these findings are comparable with those for the corresponding MMMF plants, indicating no differences between the MMMF and comparison workers at these locations.

The 5-9% with small opacities for MMMF workers at plant 3 was higher than the 3-0% among the 65 comparison workers who were employed in the manufacture of glass products. This difference, however, was not significant, either alone or after accounting for possible differences in age and smoking between the two plants (one tailed p > 0.14). There were no comparison workers for MMMF plant 5, which had the highest prevalence of opacities (6-6%).

The distributions of readings for opacities across plants were similar for the individual readers; all...
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Table 3  Profusion of small opacities by plant

<table>
<thead>
<tr>
<th>Plant (fibre)</th>
<th>MMMMF workers</th>
<th>Comparison workers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No 1/0 1/1</td>
<td>No 1/0 1/1</td>
</tr>
<tr>
<td>1,2 (Ordinary)</td>
<td>576 1 (0-2)* 0</td>
<td>123 0 0</td>
</tr>
<tr>
<td>3 (Ordinary/fine)</td>
<td>220 8 (3-6) 5 (2-3)</td>
<td>65 1 (1-5) 1 (1-5)</td>
</tr>
<tr>
<td>4 (Ordinary/fine)</td>
<td>334 0 1 (0-3) 9 (0-6)</td>
<td>84 0 0</td>
</tr>
<tr>
<td>5 (Very fine)</td>
<td>122 5 (4-1) 3 (2-5)</td>
<td>0 — —</td>
</tr>
<tr>
<td>6,7 (Mineral wool)</td>
<td>183 0 0</td>
<td>33 0 0</td>
</tr>
<tr>
<td>Total</td>
<td>1435 14 (1-0) 9 (0-6)</td>
<td>305 1 (0-3) 1 (0-3)</td>
</tr>
</tbody>
</table>

*Number as a percentage of films from plant.

five read substantially higher prevalences for MMMF workers at plants 3 and 5, and for the comparison workers corresponding to plant 3.

FACTORS RELATED TO SMALL OPACITIES AMONG MMMF WORKERS
Most (21/23) of the MMMF workers with small opacities were employed in plants 3 and 5, which had the highest average concentrations of exposure (table 1) and cumulative exposures (not shown). Considering all MMMF workers combined, each of the following exposure indicators was significantly related to the presence of opacities after accounting for film quality, smoking, and plant: cumulative exposure (p < 0.001), time in jobs > 0.32 f/ml (p < 0.01), time in jobs at 1.5 f/ml (p < 0.01), and average concentration of exposure (p < 0.01).

After allowing for a plant category effect, however (plants 3 and 5 vs the others combined), the only significant indicator of exposure was duration of exposure (one tailed p = 0.04). On the other hand, after allowing for all exposure indices (as well as age, smoking, and film quality), plant category remained highly significant (p < 0.0001), indicating increased prevalences of opacities at these two locations not accounted for by the available exposure indices.

WORKERS AT MMMF PLANTS 3 AND 5
When only workers at plants 3 and 5 were included in the analyses (thereby including 21 of the 23 workers with opacities), after accounting for age, smoking, and film quality, the prevalences of opacities did not differ between the two plants, and the only exposure indicator that was significant was duration (one tailed p = 0.04).

For plant 3 workers alone, after accounting for age, smoking, and film quality, the presence of opacities was significantly related to cumulative exposure (p = 0.02), time at 0.32 f/ml (p= 0.02), and duration of exposure (p = 0.04). For workers at plant 5 only, after accounting for age and smoking, no exposure variables were significant (one tailed p > 0.16).

Table 4 shows the prevalences of opacities among workers in these two plants by quartile of employment duration. Whereas the trend among workers at plant 3 was statistically significant, this trend held for profusion 1/0 but not for 1/1. In fact, two of the five workers with profusion 1/1 had been employed for only short periods (12 and 19 months).

As with the MMMF workers overall, presence of opacities was not related to the spirometry measurements among workers at plants 3 and 5; the mean FEV1 values (% predicted) for those without opacities were 102.5 (n = 125) and 108.7 (n = 114), respectively and the corresponding means for those with opacities were 102.0 (n = 9) and 111.1 (n = 8).

Table 4  Profusion of small opacities by quartile of years employed, plants 3 and 5

<table>
<thead>
<tr>
<th>Plant</th>
<th>Years employed</th>
<th>&lt; 1.7</th>
<th>&gt; 1.7–&lt; 5.8</th>
<th>&gt; 5.8–&lt; 15.2</th>
<th>&gt; 15.2</th>
<th>All durations</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>220</td>
</tr>
<tr>
<td>1/0 f</td>
<td></td>
<td>0</td>
<td>1 (1-8)†</td>
<td>2 (4-0)</td>
<td>5 (9-4)</td>
<td>8 (3-6)</td>
</tr>
<tr>
<td>1/1</td>
<td></td>
<td>2 (3-3)‡</td>
<td>1 (1-8)</td>
<td>0</td>
<td>2 (3-8)</td>
<td>5 (2-3)</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>25</td>
<td>29</td>
<td>35</td>
<td>33</td>
<td>122</td>
</tr>
<tr>
<td>1/0 f</td>
<td></td>
<td>0</td>
<td>0</td>
<td>3 (8-6)</td>
<td>2 (6-1)</td>
<td>5 (4-1)</td>
</tr>
<tr>
<td>1/1</td>
<td></td>
<td>0</td>
<td>0</td>
<td>2 (2-9)</td>
<td>2 (6-1)</td>
<td>3 (2-5)</td>
</tr>
<tr>
<td>Plants combined</td>
<td></td>
<td>86</td>
<td>85</td>
<td>85</td>
<td>86</td>
<td>342</td>
</tr>
<tr>
<td>1/0</td>
<td></td>
<td>0</td>
<td>1 (1-2)</td>
<td>5 (5-9)</td>
<td>7 (8-1)</td>
<td>13 (3-8)</td>
</tr>
<tr>
<td>1/1</td>
<td></td>
<td>2 (2-3)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>4 (4-7)</td>
<td>8 (2-3)</td>
</tr>
</tbody>
</table>

*Number in group.
†Significant (p < 0.04) relation for profusion ≥ 1/0 (not for 1/1) and years employed after accounting for age and smoking; see text.
‡Number as percentage of films.
§No significant relation for any profusion levels and years employed after accounting for age and smoking; see text.
PROGRESSION OF OPACITIES

There were 512 workers with readable films from both the 1980 and current surveys. For the 1980 films, there was good agreement in the median readings for small opacities for the 1980 study and the current study, with no evidence of a systematic difference: the two medians agreed for 477 (93%), and the current reading was higher than the earlier reading for 18 films and lower for 17.

There was little evidence of progression of opacities, with only 10 pairs with possible progression and one with probable progression. Eight of these 11 workers were employed in plants 5 and 7; the prevalences of progression were 12.5% and 11.5% for workers from these two plants respectively, compared with 1% or lower for the other plants. These readings for progression do not seem to indicate important changes: for seven of these eight workers (including the one with probable progression), both the earlier and later films, when read independently, were read as 0/0; for the eighth worker, his later film was 1/0. Also, only age was a significant factor in progression among the workers from these two plants, with none of the exposure indicators approaching statistical significance.

STUDY EXTENSION, PLANTS 3 AND 5
Pre-employment films from plants 3 (n = 87) and 5 (n = 70) were obtained to provide comparison films for workers from plant 5 and additional comparison films for plant 3. Compared with the 342 workers who had participated in the main part of the study, these 157 hirees were on average younger (33.0 ± 38.5 years), with a lower percentage of ever smokers (44% v 64%).

The median readings for quality for the 157 pre-employment and 342 workers' films were similar.

The 342 films taken in the main phase of the study at these two plants had been read about 18 months previously; there were significant changes in the readings of these films. The second median reading for quality tended to be better than the earlier: the two medians agreed for 78% of the films, the second indicated better quality than the earlier for 14% and worse for 8%. This difference was primarily due to one repeat reader, who assessed the films as significantly better on the second reading, and the fifth reader, who classified the films as significantly better than the reader he replaced.

For the 341 readable films, there were also significant changes in the readings for small opacities. The two median readings agreed for 88% of the films (299/341), but the second reading indicated a lower profusion category than the previous reading for 11% (39/341) and higher for 1% (3/341). Two of the four repeat readers read significantly lower the second time, and the substitute reader read significantly lower than the original reader he replaced.

Because of the lower readings in the second phase, the prevalences of opacities (median readings) were lower for workers in both plants: during the main phase of the study, the prevalences were 5.9% and 6.6% respectively; in the second phase, these prevalences were 3.2% and 0.0% respectively.

In this phase, presence of opacities (median reading) was significantly related to smoking (2.8% (8/287) among ever smokers v 0.5% (1/210) among never smokers). At both plants, there were no significant differences in the prevalences of small opacities between pre-employment and workers' films. At plant 3, the prevalences were 3.2% and 1.1% whereas at plant 5 these were 0% and 1.4% (table 5).

For workers at plant 5, all eight films classified (by median) on the first reading as having small opacities (five at 1/0, three at 1/1) were classified on the second as lacking opacities. For workers at plant 3, all eight films first classified as profusion 1/0 were classified on the second reading as negative; of the five originally classified as 1/1, four remained positive (one at 1/0, three at 1/1), and one was classified as negative (0/1). Also, three plant 3 films originally classified as negative were classified as positive on the second reading (two at 1/0, one at 1/1).

Of the four workers at plant 3 with radiographic profusion 1/1, two had been employed for only one year (the others for 5-6 and 34-3 years). Consequently, when prevalences were examined by quartile of years employed (similar to table 4), there was no evidence of increasing trends; the prevalences for profusion > 1/0 were 3.3%, 3.6%, 2.0%, and 3.8%, respectively (for 1/1 these were 3.3%, 1.8%, 0%, and 1.9%). When analysed by multiple logistic regression, none of the exposure indicators approached significance as factors in the occurrence of opacities.

As with the earlier readings, presence of opacities among MMMF workers was not associated with lower functional values. For example, the mean FEV1 values were 105.4 among those with small opacities, and 106.6 among those without small opacities.

COMPARISON OF X RAY FILM READINGS IN 1980 AND CURRENT STUDY

In comparing the results of this survey with that of the survey seven years earlier, it is appropriate to impose the same minimum employment criteria for participants used in the 1980 study (10 years for plants 1-4, and five years for plants 5-7), primarily because of the relation often found between age and x ray film opacities.

With these restrictions, the prevalences of small opacities (≥ 1/0) in the two studies were low and reasonably similar for the ordinary diameter fibre.
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Table 5 Profusion of small opacities, pre-employment and MMMF workers' films, plants 3 and 5, phase two of study

<table>
<thead>
<tr>
<th>Plant (fibre)</th>
<th>MMMM workers</th>
<th>Pre-employment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age (y) Mean (SD)</td>
<td>1/0</td>
</tr>
<tr>
<td>3 (Ordinary/fine)</td>
<td>220 (63) 39-7 (10-7)</td>
<td>3 (1-4)</td>
</tr>
<tr>
<td>5 (Very fine)</td>
<td>1211 (67) 36-4 (9-5)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>341 (64) 38-5 (10-4)</td>
<td>3 (0-9)</td>
</tr>
</tbody>
</table>

*Number of films *

Discussion

The results of this investigation are consistent with previously reported cross sectional studies that have failed to find persuasive evidence of respiratory effects of manufacture of MMMF. A review of the available studies concluded that, whereas occupational exposure to various types of MMMF may be associated with adverse effects on the respiratory tract, no consistent pattern of such effects has emerged.

This follow up study of MMMF workers, studied previously in 1979–80, again found prevalence of respiratory symptoms and functional values generally consistent with a healthy population. Their radiographs showed small lung opacities only in the lower profusion categories, and in low prevalence. There was no persuasive evidence of radiographic progression during the seven year interval between the two surveys.

There were, however, unexplained differences between prevalences of symptoms of MMMF and comparison workers, but without evidence that these differences were attributable to exposure to fibres. The minimal differences in mean values for lung function were explained by unrelated causes (previous chest surgery and asthma, most of which had been diagnosed before employment at these plants).

If the radiographic observations were available only for MMMF workers, a role for MMMF exposures in the occurrence of opacities could be inferred: almost all (21/23) of the workers with small opacities were employed at the two MMMF plants (plants 3 and 5) with the highest fibre exposures, resulting in an overall exposure-response relation. There were relations between opacities and several exposure indicators among workers at one of these plants (plant 3). There was no evidence of reduced functional values among workers with opacities, however, so a clinically important effect could not be inferred. Also, the relations found for workers at plant 3 were only for profusion 1/0; there were no relations for profusion 1/1.

The design of the study, however, included comparisons of the prevalences of opacities between MMMF workers and reference workers studied in the same radiological laboratories. Radiographs of reference workers were obtained for five MMMF plants (four locations), including plant 3; in all cases, there were no significant differences between the MMMF and reference workers in the prevalences of opacities. Whereas the prevalences of small opacities was higher among plant 3 workers than the reference workers (5-9% vs 3-0%), as this difference was not statistically significant, it could have been a chance occurrence.

There were only a small number (65) of reference workers for plant 3, and none for plant 5. The study was therefore extended with pre-employment radiographs of other workers from plants 3 and 5 as reference films in a second reading for both plants. This second reading showed no persuasive evidence for a difference between workers exposed to fibres...
and the reference group. The only suggestion of a possible difference was for opacities of profusion 1/1 among workers at plant 3. Again there was no evidence of a functional relation with the presence of opacities, nor of a relation between the presence of opacities and indicators of exposure among these workers. In fact, two of the four workers with profusion 1/1 had worked in the plant for only one year.

There are two problems in assessing the results of radiography. Firstly, the finding of small opacities in only the lower profusion categories poses difficulties in interpreting their significance. It is in these same categories that cigarette smoking and ageing, factors known to stimulate the appearances of interstitial fibrosis, have their effects.9

Secondly, the radiographic data in this study show notably large variability, both between different observers and within (some of) the same observers on different occasions. It has been known for a long time, however, that observer variability in grading radiographic lung abnormality is at its greatest when readers are trying to distinguish between normal and suspicious, or suspicious and minimally positive. In 1970, Reger and Morgan10 studied factors influencing consistency of readings and provided six tables showing all pairwise comparisons between four readers who independently classified a set of more than 2000 radiographs. Combining the tables and examining the categories of "zero" (normal), "suspect" (suspicious), and "simple pneumoconiosis" (positive), there were 401 instances in which both readers rated a film as suspicious, but there were 1211 instances of differing judgement as to suspicious vs normal. Agreements at this level of abnormality were thus greatly exceeded by disagreements. At the next higher level, however, agreements far exceeded discordant judgements: 2033 instances of agreement as positive, and only 584 differing as to positive vs suspicious.

As with between-observer variability, within-observer variability was long ago shown to vary with level of abnormality. In 1949, Fletcher and Oldham11 reported a careful study of consistency in radiological judgements, within and among 10 readers of varying experience in pneumoconiosis work. They concluded that "the opinions of these observers were found to differ to a remarkable degree, both amongst themselves, and, to a lesser extent, from the one occasion to the other... The variation of opinion was greatest in films that were neither normal nor grossly abnormal."

It is also likely that systematic differences in the appearances of films from different radiological laboratories would have greater effect on deciding whether minimal changes were or were not present than on the detection of examples of normality or advanced disease. Differences in film quality are not all reflected in gross departures from acceptable quality such as usually arise from errors in exposure settings or from developer malfunctions that produce either very light or very dark films. Less obstructive differences can arise from various film and screen speeds, grids of differing efficiency, and the variations in the quality and maintenance of developers. Readers who often interpret series of films from different sources become aware of systematic differences attributable to technical factors, and try to allow for these to discount spurious appearances and detect only real abnormality. This tendency to compensate is so powerful that it has thwarted attempts to determine the biasing effects of even grossly over and underexposed films. Proof that more subtle differences could lead to over or under reading is thus not to be found in published work. The existence of the phenomenon is so likely, however, that it must be regarded as a potential source of confounding in a study such as this one, where fibre types are segregated by plant, and different plants are served by different radiological laboratories.

Systematic variations in film appearances associated with different radiological laboratories may thus be safely assumed to foster between observer disagreements, owing presumably to the varying efficiency with which different readers can compensate for them. This also furnishes a likely explanation for some of the within observer variability found in the present study. When the films from two sites that were reread in this study were initially read, they were mixed throughout the inclusive set comprising all films from all sites. The readers had less chance to perceive, and so to compensate for, any site specific differences in film quality than when rereading the set restricted to the two sites. According to a hypothesis that compensation for film defects reduces noise in the expression (signal + noise), which constitutes prevalence, a protocol that favours compensation at a second reading would be expected to produce a lower prevalence at the second reading.

In the final analysis, however, confidence in the results of a radiographic survey should rest mainly upon the integrity of the study design, the qualifications of the readers, and the adherence of the investigators to accepted methods of conducting radiographic surveys. In the present study, the design conforms to accepted principles of survey radiography. All readers had long experience in research use of the ILO classification, and all have contributed to publications on radiography of the pneumoconioses. The principles of independent reading, reference to standard radiographs, and blinding to non-radiographic data, were consistently followed. The observer variability found in
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Follow up this study is probably a reflection of very low prevalence of "true abnormality" (or signal), in which case the observed prevalences (signal + noise) are mainly noise. The inherent randomness of noise then produces high rates of between and within observer variability.

The radiographic results of this study show the difficulty in striving to detect effects of exposure at the lower limits of radiographic detectability. Because of reader variability (within and among highly experienced readers), the readings of chest radiographs from such a population are necessarily of limited precision for the lower profusion levels for small opacities. Continued health surveillance of workers in this industry, especially those in fine fibre manufacture, is therefore prudent.

Nevertheless, the limited repeatability of the low level radiographic findings, suggests in itself that the observations are without clinical significance, and this is supported by the lack of a relation between small opacities and spirometry measurements. Moreover, the prevalences of these low profusion level opacities among MMMF workers were not significantly different from regional comparison workers, and for the two fine fibre plants where most opacities occurred, these prevalences exhibited no repeatable, consistent trend with indicators of exposure to fibre.

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