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REPORT FROM THE COMMITTEE ON ASBESTOS

A STUDY OF THE HEALTH EXPERIENCE IN TWO U.K. ASBESTOS FACTORIES

BOHS COMMITTEE ON ASBESTOS (1977–1982)

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Abstract—Radiological, physiological and clinical data from two asbestos factories have been examined in an effort to establish what cumulative exposure to asbestos dust is associated with the first signs of adverse pulmonary effects. Persons included in the present study had been exposed to asbestos for at least 10 yr and had all started work with asbestos after 1950, by which time regular recording of dust concentrations had become established. The type of asbestos involved was predominantly chrysotile, but in both factories some crocidolite had been processed at some stage during the study period. Three physicians made independent assessments of 'early' and 'late' chest radiographs from 295 men from Factory A and 351 men and women from Factory B. Lung function and other medical data were supplied by the Medical Officers of the factories concerned. The dust data from Factory A made possible an assessment of the relationship of cumulative exposure to the onset of adverse pulmonary effects. The nature of the data from Factory B precluded such an exercise.

The radiological results from Factory A showed an association between the occurrence of parenchymal changes (profusion of combined opacities) and estimates of cumulative exposure. The evidence from Factory B generally supported this finding. Lung function measurements indicated that levels of FEV_1 and FVC among men who had accumulated relatively high exposures in Factory A were lower than for those who had received only low exposures. The correlations with dust exposure were significant at the 6% level.

Investigations were carried out into the relationships between dust concentrations measured by present-day methods and those used in earlier years. The estimated exposures involve many uncertainties but are probably the best available for such a retrospective study of asbestos-related disease. They relate to static sampling, not personal sampling.

The results indicated that, at Factory A, the probability of occurrence of any one of seven defined Adverse Effects in association with a cumulative exposure of less than 25 fibre-yr/ml was less than 2%, based on static sampling by the membrane filter method. For exposures less than 50 fibre-yr/ml the figure was 7% and for exposures up to 100 fibre-yr/ml it was 17–20%. This does not necessarily imply that asbestos dust exposure caused the observed effects.

Cancer risks were outside the scope of this particular study.

* The Committee wishes to record with deep regret the death of Dr C. G. ADDINGLEY in October 1978.

1. INTRODUCTION

THE U.K. HYGIENE standard for chrysotile asbestos adopted for use with THE ASBESTOS REGULATIONS (1969) was based on a report published by the BRITISH OCCUPATIONAL HYGIENE SOCIETY (1968) describing a study on a cohort of men in an asbestos textile factory (Factory A), first employed since 1 January 1933 and still employed on 30 June 1966, with at least 10 yr service in asbestos areas. The recommended standard was in the form of a total integrated exposure (dust concentration in fibres per millilitre of air multiplied by the time of exposure in working years) considered to carry a 1% risk of a worker exhibiting the earliest signs of the possible effect of asbestos exposure. The figure arrived at was 100 fibre-yr/ml, giving an exposure of 2 fibres/ml (by the counting procedures then current) over a working life of 50 yr, and it is this limiting concentration which has been quoted in the literature of many countries. It is unusual, of course, for any individual to be exposed for so long a period in modern industrial practice.

This 1968 standard has been the subject of a number of criticisms over the years, the main ones being the following:

(a) The cohort was biased in that persons fulfilling the cohort definition, i.e. at least 10 yr service since 1933, were not included if their exposure had ceased prior to 30 June 1966 as a result of leaving asbestos areas or death.

(b) Similarly, persons reaching 10 yr service after 30 June 1966, even by as little as one month, were also excluded.

(c) The earliest sign of adverse effect was taken to be the presence of persistent basal rales, but this is not always so. There are other early signs which might well precede rales in certain cases.

(d) The data had been collected from one asbestos textile factory only.

(e) During the period covered by the study, some crocidolite had been used in the factory, exposure to which may have influenced the findings.

(f) Asbestos-associated cancer risks had not been considered.

More recently, a good deal of extra information has become available on the adverse effects of exposure to asbestos. Diagnostic methods have improved, in particular by the extensive use of lung function measurements and the adoption of an agreed classification for the assessment of asbestos workers' X-ray films (INTERNATIONAL LABOUR OFFICE, 1972). In addition, considerably more experience has been gained in dust sampling and analysis for the measurement of exposure and some additional data have become available from a second factory (Factory B).

The first attempt to up-date the 1968 data was made by a reconstituted Sub-Committee between 1974 and 1976, using a group from Factory A extended to include men who had completed 10 yr service between 30 June 1966 and 31 December 1972. Men who had left the factory between those dates were also included. The results of this study were described by BERRY *et al.* (1979).

2. THE WORK OF THE PRESENT BOHS COMMITTEE

It was decided in May 1977 to further reconstitute a BOHS Committee on Asbestos to review the information available up to 31 December 1976. The following steps were taken:

(a) In addition to the cohort from Factory A (all of them men), a second cohort was studied comprising men and women from Factory B. Some members of the second cohort had worked on the production of textiles and others on friction materials.

(b) Both cohorts were confined to people who had not been exposed to asbestos before 1 January 1951, because no dust measurement results were available prior to that date, and who had at least 10 yr accumulated exposure by 31 December 1976. Efforts were made to trace those who had left before that date so that they could return for an X-ray and clinical examination and, in the case of those who had died, the cause of death was ascertained as far as possible. By doing so, it was hoped to meet some of the criticisms of the 1968 study. It should be noted that, while chrysotile was by far the most predominant fibre used, some crocidolite was processed at both factories at some time during the study period. It is not possible to estimate what proportions of the respective cohorts were exposed to this latter fibre.

(c) Efforts were made to calculate the dust exposure for each individual in each cohort, year by year, adjusted on an agreed basis to take into account the changes in dust sampling and analysis which had taken place over the 25 yr period of the study.

(d) At the outset, the object of the Committee was to review the hygiene standard for chrysotile asbestos dust, but the health experience over recent years has indicated that such a review would be of limited value if it did not take some account of malignancy. Long-term, wide-ranging prospective epidemiological studies of cohorts followed throughout their lives would be needed to support a hygiene standard designed to reduce the incidence of malignancy attributed to asbestos exposure and, since malignancy has multifactorial causes, parameters other than asbestos exposure would need also to be recorded and considered. The outstanding factor is cigarette smoking and there is evidence that smoking potentiates the risk of lung cancer in asbestos-exposed workers; the effects are not simply additive. In the cohorts studied by the Committee detailed mortality records were not generally available. The Committee therefore decided to confine itself to a study of morbidity data with a view to obtaining a better understanding of the adverse effects of asbestos exposure during life, bearing in mind that an ongoing mortality study had been established for many years at Factory A, last reported by Peto *et al.* (1977).

(e) The work of the re-constituted BOHS Committee was to some degree overtaken by events. An Advisory Committee on Asbestos was set up by the Health and Safety Commission (HSC) in 1976 and a Medical Working Group of that Committee was given the task of reviewing all the available information on asbestos and health and making appropriate recommendations. Although the BOHS Committee's study was still at an early stage, it provided the HSC Medical Working Group with an interim statement in April 1978, outlining the progress which had been made up to that time and this was no doubt taken into account by the HSC Medical Working Group when reporting to its parent Advisory Committee on Asbestos. When the Advisory Committee on Asbestos issued its Final Report in October 1979, it recommended that the term 'hygiene standard' should be replaced by 'control limit' for the assessment of exposure to asbestos dust, because, in its view, there is no apparent threshold below which exposure entails no risk to human health. It states that 'this new concept is intended to represent a realistic level of airborne concentration of dust, closely associated with the relevant legislation, above which no persons should be occupationally exposed' (HSC, 1979).

3. THE MEDICAL DATA

The medical information which has been analysed for the BOHS Committee is described in detail in Appendix 3. The main features were:

(a) Pairs of chest radiographs comprising the earliest post-1950 film and the latest pre-1977 film for each person. These, along with 'control' films, were presented in turn to three physicians of acknowledged expertise in this particular field who were asked to classify them independently in accordance with the ILO U/C (1971) International Classification of Radiographs of Pneumoconioses.

A more detailed study of the many other intermediate films would be necessary to pin-point the first evidence of radiological changes more clearly. At Factory A workers had chest radiographs taken every 3 yr from 1951 to 1967 and annually thereafter. At Factory B workers had chest radiographs taken every 2 yr from 1951 and in some cases more often.

(b) All available information on medical examinations and lung function measurements carried out over the period covered by the study was provided by the medical officers of the respective companies. At Factory A, lung function tests were introduced in 1967 and had been carried out every 2 yr. At Factory B, lung function tests had been carried out every 2 yr since 1960.

In order to arrive at an agreed interpretation of all these data, the medical members of the Committee were asked to meet as a Working Group under the chairmanship of Dr W. J. Smither 'to advise on the first medical indication or indications of adverse effects on the lungs'. A report of their deliberations is given in Appendix 1.

4. DUST CONCENTRATIONS

An extensive account of the history of dust measurement techniques employed in the asbestos industry is given by WALTON (1982).

(a) *Factory A*

The Casella Thermal Precipitator (TP) was used at Factory A from 1951 to 1960 and all monitoring was 'static'; that is, the sampling was conducted with a free-standing sampling instrument having the air inlet at head height and the instrument placed on a stand in a fixed position, near the operative, but without interfering with his movements in carrying out his task. The samples after 'ashing' of the coverslips were counted at high magnification (800–1000 ×) under dark-ground reflected light using a 4 mm objective.* Fibres were not looked for specifically and all particles judged to have a projected diameter of 0.5 μm and above were included in the count.

Between 1960 and 1964, the Long Running Thermal Precipitator (LRTP) was used and, again, monitoring was static. With this instrument fibres were counted at about 500 × magnification and the results were expressed in fibres/ml, using the convention that only fibres greater than 5 μm long and having an aspect ratio greater than 3:1 were counted. Later, when guidance notes on counting were published (ASBESTOSIS RESEARCH COUNCIL, 1971), a further convention limiting the count to fibres less than

* In the earlier report (BOHS, 1968) it was stated, incorrectly, that the Thermal Precipitator samples were counted using a 2 mm objective.

3 μm in diameter was adopted. This latter convention is not considered to have affected the Factory A counts to any significant degree.

From 1964 to 1974, static monitoring continued, but using a membrane filter sampling instrument or a Royco Automatic Particle Counter. The membrane filter samples were counted for fibres at about 500 × magnification under phase contrast conditions. The Royco instrument detects both particles and fibres but was set to produce results comparable with membrane filter fibre counts.

After 1974, membrane filters were used exclusively and a change in technique was introduced in that counting was restricted to the area within a British Standard Graticule (BS 3625, 1963) mounted in the microscope eyepiece, instead of covering whole microscope fields of view. This had the effect of increasing the numbers of fibres counted per unit area of the slide by a factor of about 2 (BECKETT *et al.*, 1976), so the fibre concentrations calculated in the 1960s (used in the 1968 BOHS study) would need to be multiplied by 2 to compare them with counts taken today.

In an attempt to relate the early figures to 1977 membrane filter counts, an investigation was carried out at Factory A, running all instruments side by side (Appendix 2A). The samples obtained from the older instruments were counted using identical techniques to those employed in the factory when those instruments were in use. The following approximate relationships were found, all relating to static sampling:

1977 Membrane Filter = 0.07 TP
1977 Membrane Filter = 2.2 LRTP
1977 Membrane Filter = 2 × 1964–1974 Membrane Filter

These conversion factors were used in calculating the dust exposures in the present study of Factory A and it should be realised that they are different from those used in the 1968 BOHS study. Bearing in mind that considerable extrapolation was necessary and that conditions and processes in the factory are very different today, it will be realised that considerable uncertainty must be attached to such factors.

(b) *Factory B*

The Owens Jet dust counter was in use at Factory B in 1951 and continued to be used routinely until 1959. Up to 1956, the 'ashed' coverslips were counted at a magnification of 900–1000 × and no differentiation was made between fibres and particles. After this date, the count was limited to particles of size greater than 1 μm and from January 1958 fibres longer than 5 μm were recorded as well. Between 1958 and 1961 the Long Running Thermal Precipitator (LRTP) was used on an experimental basis for comparison with the Owens Jet.

After trials, the membrane filter sampler came into use in July 1961 and in June 1963 phase contrast was introduced, increasing the counts by a factor of about 1.6. The use of an eyepiece graticule in the form of a 7 mm Miller Square began in 1971 and this was replaced by a circular graticule, 6 mm in diameter, in 1974. In contrast with the experience of Factory A, no increase in fibres counted per unit area was observed as compared with counting full microscope fields.

In addition to membrane filters, the Royco Instrument was widely used from 1963 onwards. With careful calibration of the instrument against membrane filter, the Royco can be more reliable than microscope counting.

(c) *Personal sampling*

Towards the end of the period covered by the study, from about 1974 onwards, 'personal' sampling was used increasingly instead of static methods. 'Personal' means that the sampling head was attached to the lapel of an individual worker. As experience was gained, it became apparent that the results from personal samples did not generally equate with the results from static samples in the same working area, even for samples taken simultaneously. The Committee therefore made a study of the information available in this field, as detailed in Appendix 2B, and came to the following conclusions:

(i) When identical sampling instruments are deployed simultaneously at personal and static sampling points and the distances between them are reasonably small, most of the personal sampling results obtained in a given location are higher than those obtained from static sampling.

(ii) The differences between the two types of result tend to be particularly great when the static sampling points are relatively remote from dust emission points, for example, when background static sampling is adopted.

(iii) In certain cases results from personal sampling may be lower than those from static sampling, owing to factors such as the positioning of the static sampling point with respect to air extraction systems.

(iv) The correlation coefficient between personal and static measurements is statistically significant but, even so, no consistent relationship of great practical utility could be found in the limited data available.

In the light of the above, the Committee decided to use only the results from static samples in calculating exposures.

5. THE GROUPS STUDIED

(a) *Factory A*

Three hundred men* from Factory A met the criteria for inclusion in the study, but no medical records were available for five of them. The present study is therefore concerned with the remaining 295 men. It was recognised that the 10 yr restriction might have resulted in bias if many persons with less than 10 yr exposure had suffered adverse health effects because of such exposure. A random 5% sample was therefore taken of all those who had commenced work in the factory during the 26 yr covered by the study. This gave 850 names, but, when women and those who had never worked with asbestos were excluded, 487 men were left, 15 of whom had worked with asbestos for more than 10 yr; 14 of these were in the study group, one having been inadvertently omitted in the original record search. Of the remaining 472, 71% had less than 1 yr exposure up to the end of 1976 and only about 6% had worked for between 5 and 10 yr. Of 16 men who had left the factory for medical reasons, one had worked with asbestos for 3 yr and the remaining 15 had less than 1 yr exposure. The conclusion reached from this sampling exercise, therefore, was that it seemed unlikely that the criteria for admission to the study had excluded many who had adverse health effects arising from their exposure to asbestos dust at the factory.

* Men only, following the pattern of earlier studies at this factory.

(b) *Factory B*

Although at least 499 persons from Factory B met the criteria for inclusion in the study, some had to be excluded because of incomplete medical and radiological data. In the end, the 351 persons for whom two serial chest radiographs were available were considered, comprising 323 men and 28 women. Information was provided for 3361 persons who had been exposed since January 1951 but for less than 10 yr. The distribution of exposure periods in these groups was different from that of Factory A, 22% having worked with asbestos for less than 1 yr, as against 71% for Factory A, and 72% for 1–5 yr, as against 22% for Factory A.

There was also a considerable contrast between the factories in the sub-groups who had left asbestos areas on medical advice. In Factory B, of 171 such persons, 106 (62%) had only worked with asbestos for from 1 to 5 yr. One very laudable reason for this was that in Factory B a number of people were advised to leave asbestos areas in the early 1960s on the appearance of early suggestive signs of lung fibrosis. Some 70 people were removed from exposure between 1963 and 1965 because of adverse lung function results. Many more were recommended for transfer to non-dusty departments. They included persons with bronchitis, old TB scarring, kyphoscoliosis and persistent cough. The survivors of the 70 or so removed because of lung function abnormalities are being followed up by the company. The main reason for their exclusion from the BOHS study was that the early dust records associated with these people were not acceptable as being valid for that purpose. Nevertheless, these people were lost to the study, although some may have developed abnormalities as a result of their exposure to asbestos dust. It is also possible that some had completed more than 10 yr exposure at the time of withdrawal.

6. THE RADIOLOGICAL DATA—FACTORY A AND FACTORY B

The earliest (post-1950) and latest (pre-1977) chest radiographs for the 295 men from Factory A and the 351 persons from Factory B were made available for the study. In addition, 160 chest radiographs from 160 persons employed at the factories, but with no known direct exposure to asbestos, were also provided. These, together with the 1292 films from the exposed groups, were pooled and arranged in random order before presentation to the readers.

7. THE CLINICAL DATA

(a) *Factory A*

Available lung function and anthropometric measurements, information on smoking habits and records of whether or not chest sounds had been heard were taken from the medical records of the 295 men. There were no lung function data available for 56 of them, but all of these had attended for medical examination at least once during the study period. At least two sets of lung function measurements were available for 184 men in this group.

(b) *Factory B*

Similar information to the above was made available for the 351 persons in this group. No lung function data were available for 38 of them. The records indicating the

presence or absence of chest sounds at the latest medical examination were included for study, but earlier assessments of whether this condition had or had not occurred were not studied.

8. THE DUST EXPOSURE DATA

(a) *Factory A*

By using the approximate relationships described in Paragraph 4(a) the records of measured dust levels in the factory were converted to modern membrane filter values for the various job locations.

Using these values and the job histories of the individuals in the cohort, estimates of exposure for each year employed were derived, expressed as fibre-yr/ml, assuming static sampling only. No attempt was made to convert to personal sampling because of the uncertainties attending such conversion [see Paragraph 4(c) and Appendix 2]. Even ignoring any reservations concerning the accuracy of the conversion factors themselves, the estimates of personal exposure could not be precise, as annual average values from static measurements had to be employed and in some cases further assumptions had to be made because job histories were not complete.

(b) *Factory B*

Information was available on the time worked by the persons concerned at the various factory locations and measurements of dust concentrations at some, but by no means all, of these locations were also available. However, taking into account also the uncertainties about the fibre concentration in the 1950s, a close examination showed that the information available might provide reasonably reliable estimates of cumulative dust exposure for only 16% of the group. As will be seen, this put some restriction on the analysis of the Factory B data.

9. ANALYSIS OF THE DATA

(a) *Radiological results*

(i) *Parenchymal abnormalities.* The distributions of film classifications by factory, reader and type of opacity for both the earlier and later films of the pairs revealed systematic differences between the three readers in their interpretation of the distinction between small rounded and small irregular opacities. Less variability was found for 'combined opacities' and this parameter was therefore used in the analysis. One deviation from the general pattern was the relatively frequent assessment of abnormality by Reader 3 among the later films from Factory B. Overall, however, parenchymal abnormalities were noted in a higher proportion of the Factory A group than for Factory B.

(ii) *Pleural abnormalities.* Taking an average of the observations of the three readers, 4.4% of the films early and late showed obliteration of the costophrenic angle, 2.1% showed pleural thickening and 0.4% pleural calcification. More abnormalities were seen on films from Factory A than from Factory B, but it is noteworthy that the differences between readers were larger than the differences between factories. In

neither case were the results distinguishable statistically from assessments of control films.

(iii) *Technical quality of radiographs.* There were large differences between readers in their judgement of the quality of the radiographs, but all three were less satisfied with the films from Factory A than with those from Factory B. That the more frequent assessment of parenchymal change in the Factory A films was not due to this cause alone was confirmed by assessing separately a sub-group of film pairs of good quality. These variations in film quality did not affect the pattern of assessment of pleural abnormalities.

(iv) *Small opacities and smoking habits.* All readers detected small opacities more frequently in Factory A among smokers and ex-smokers than among non-smokers (about 11% higher). Nevertheless, small opacities were also detected on about 12% of the non-smokers' films, indicating that the changes seen in the later films were not wholly attributable to smoking. No such information could be gleaned from the Factory B films, because Readers 1 and 2 judged only a marginally higher proportion of combined opacities in the later films than in the controls. It should be noted, however, that Reader 3 classified 18% of these films into category 0/1 or higher, compared with 6% of the controls.

(b) *Radiological changes and dust exposure*

(i) *Factory A.* An effort was made to relate profusion of combined small opacities with cumulated dust exposure, and for this purpose four measures of exposure were examined for each individual. The first (E_a) was the cumulative exposure from commencing work in asbestos areas up to the time of the earlier of the two films and the second (E_b) was the exposure incurred between films. The third measure (E_c) was the cumulative exposure from commencement up to the later film, i.e. $E_a + E_b$. The fourth measure (E_d) was an attempt to approximate the exposure up to the point when the observed change occurred and was taken to be $E_a + \frac{1}{2}(E_b)$. No association could be found between radiological change and E_a or E_b separately. Both E_c and E_d were associated with increasing profusion of small opacities on the radiographs studied.

(ii) *Factory B.* As noted in Paragraph 8(b), the variety of methods by which the dust measurements had been made at Factory B, together with the number of changes in materials, conditions and processes at the factory which had occurred over the period of the study, ruled out any attempt to estimate cumulative dust exposures for individuals. However, reliable information on time worked over the period of the study was available for 187 persons who had definitely worked previously in occupations with potential exposure to dust other than asbestos and for 128 persons with no such prior exposure. An assessment was made of changes in profusion of combined small opacities for both of these sub-groups, related to time in years spent working with asbestos. Readers 1 and 3 recorded more radiological change between pairs of films for persons with longer periods of exposure to asbestos, but Reader 2 did not show this trend.

(c) *Lung function changes and dust exposure*

(i) *Factory A.* Of the 295 men in the group, one set of lung function measurements was available for 239 and two sets or more for 184 of them. An attempt was made to correlate the latest measurement recorded with the cumulative dust exposure up to that time, using a linear multiple regression model to take account of age, height, weight and smoking habits. The lung function criteria considered were FEV_1, FVC, TICO and the ratio FEV_1/FVC. Only for FEV_1 and FVC did the dust exposures correlate significantly at the 6% level; neither with TICO nor with FEV_1/FVC was any correlation observed.

(ii) *Factory B.* Despite the difficulty associated with the dust data, the information from Factory B was examined further in the hope that it might be possible to proceed to a case-control study. This analysis had to be abandoned, unfortunately, because the sub-set of data that might be suitable for detailed study was biased epidemiologically, as explained earlier [Paragraph 5(b)].

10. THE CRITERIA FOR 'ADVERSE EFFECT'

Further analyses were made in response to advice from medical members of the Sub-committee on what should constitute the earliest medical indication of adverse effects on the lungs whether through exposure to asbestos dust or otherwise (Appendix 1). Despite certain difficulties in applying these recommendations, seven statistical criteria were defined. Six of them reflect approximately some of the suggestions from the Medical Working Group. The seventh (rate of reduction in FEV_1) was included, because earlier analyses indicated that this measure of lung function was more closely related to the dust exposure data than the other indices of function under consideration. The seven criteria included two radiological criteria (parenchymal changes and pleural shadowing), four lung function criteria and one of basal rales (as used in the 1968 study). It must be remembered that none of these criteria is specific to asbestos exposure.

11. THE OCCURRENCE OF ADVERSE EFFECTS

The criteria employed were as follows:

A At least two readers agreed that there were two or more steps of change on the profusion scale for combined small opacities over the interval between films.

B At least two readers agreed that a pleural abnormality was present on the later but not on the earlier film of a pair (where 'pleural abnormality' means at least one of pleural thickening, pleural calcification, or costophrenic angle obliteration).

C Unusual* rate of change in FEV_1.

D Unusual* rate of change in FVC.

E Unusual* rate of change in TICO.

F Any one measurement of $FEV_1/FVC < 0.70$.

G Chest sounds which did not clear on coughing or on any subsequent examinations.

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* 'Unusual' defined in terms of distribution of residuals; see Appendix 3, Paragraphs 54–56.

For effects A–E the relevant exposures were assumed to be those accumulated halfway between the 'early' and 'late' examinations.

Effect F accounted for 40% of all effect-occurrences in Factory A and 34% of all effect-occurrences in Factory B. It did not correlate with exposure (in Factory A) and this bears out the latest thinking that $FEV_1/FVC < 0.70$ is an inappropriate criterion of an adverse effect of asbestos. It is well known, for example, that smokers develop a reduced FEV_1/FVC (COTES, 1975; PARKES, 1982) and there were many smokers in the populations studied.

(a) *Factory A*

Of the 295 men in the group, the results from 163 of them met one or more of the seven criteria. The total number of occurrences was 274. The most frequently occurring effect was F ($FEV_1/FVC < 0.70$), being present in 111 men, and in 52 of them it was accompanied by at least one of the other categories of adverse effect. Among the 163 men who met at least one of the criteria the distribution of those with one, with two and with three or more effects was 58, 26 and 16% respectively.

(b) *Factory B*

Of the 351 persons in the group, the results from 163 (154 men, 9 women) met one or more of the seven criteria. The total number of occurrences was 257. As in Factory A, the most frequently occurring effect was F, being present in 88 members of the group. Because there were fewer radiological changes recorded for Factory B, there was a smaller number with effects A and B, but among persons with at least one recording of an adverse effect the distribution of those with one, with two and with three or more was similar to that from Factory A, being 66, 19 and 15% respectively.

12. INTERPRETATION OF THE DATA ON ADVERSE EFFECTS

This was possible only for Factory A, for which cumulative dust exposures were available. The probability of the occurrence of an adverse effect before the corresponding dust exposure had been accumulated was estimated using the 'Product-Limit' (or 'Life-Table') method.

The probability–exposure results were plotted on logistic–log scales and the patterns for adverse effects A, B, D, E, F and G are shown in Figs. 4, 6–10 of Appendix 3. The results are summarised in Fig. 11 in the form of a plot of estimated probabilities that at least one of the seven adverse effects may occur by the exposure shown. When more than one effect was present in the same man, that occurring earliest was used. It will be seen that five persons showed an adverse effect at exposures less than 25 fibre-yr/ml. In two cases the effect concerned was E (unusual rate of change in Gas Transfer Factor) with one each for C (unusual rate of change in FEV_1), F ($FEV_1/FVC < 0.70$) and G (chest sounds). At first sight, the graphs suggest that it might be appropriate to fit straight lines to the individual observations, thus postulating a logistic model for the various adverse effect–exposure relationships, but the deviations below about 100 fibre-yr/ml (50 fibre-yr/ml by 1968 standards) argue against this. It would therefore be unwise to use such fitted lines to make predictions where exposures have been below this level.

13. CONCLUSIONS

(i) As far as Factory A is concerned, it appears unlikely that the criteria for admission to the study (not less than 10 yr exposure) excluded many who had suffered serious health effects arising from their exposure.

(ii) The data from Factory B must be regarded as biased for epidemiological purposes, because the medical care policy was to remove persons from exposure whenever examination indicated early signs of lung function abnormality. These persons were not included in the study of Factory B, yet some of them may have developed the signs as a result of their exposure to asbestos.

(iii) The radiological results for Factory A showed an association between the occurrence of parenchymal changes and estimates of cumulative exposure to asbestos dust up to the approximate point in time at which the changes were likely to have occurred. Although it was not possible to estimate cumulative dust exposures for most persons from Factory B, there was some evidence that longer periods of exposure were associated with higher chances of developing small opacities on chest radiographs.

(iv) Small opacities were detected more frequently among smokers and ex-smokers, but the parenchymal changes observed in the group could not be attributed wholly to smoking habits.

(v) Overall, the three readers judged 5.3% of films from Factory A and 3.8% of those from Factory B as showing obliteration of the costophrenic angle, results which were not significantly different from observations on the 160 radiographs of persons who had not been exposed to asbestos. The same was true of other pleural abnormalities which were recorded even less frequently.

(vi) Standardized levels of FEV_1 and FVC among men who had accumulated relatively high exposures in Factory A were lower than the levels among those who had received only low exposures and the correlations with dust exposure were statistically significant at the 6% level. Any such apparent correlations with Gas Transfer Factor and with FEV_1/FVC could easily have arisen by chance in view of the residual variability in the data.

(vii) The study period was limited to the years over which it was believed consistent estimates could be made of dust exposure when assessed by static monitoring. Technical investigations were undertaken which clarified the relationships between the various methods employed for sampling and counting, even though much uncertainty remains. The analysis was limited to estimates of grouped time-weighted average exposures over the period of study. It was not possible to allow for the variation in exposure between one worker and another doing the same job nor for the inevitable fluctuations in exposure between one day and the next. Finally, it should be noted that the Committee concluded it was not feasible to convert the estimates from static monitoring into measurements that would have been obtained by personal monitoring.

(viii) The results from Factory A suggest that, for cumulative exposures based on static sampling [see Paragraph 4(c)] up to about 25 fibre-yr/ml, the probability that *any one* of the seven defined events occurred is less than 2%. For exposures less than 50 fibre-yr/ml, the estimated probability is less than 7% and for exposures up to 100 fibre-yr/ml the probability increases to 17–20%. It must be recognised, however, that the statistical definitions of the events concerned are based broadly on guidelines suggested

by the Committee's Medical Working Group regarding 'the earliest index that the chest of a worker was adversely affected, whether through exposure to asbestos dust or otherwise'; they do not constitute clinical diagnoses of asbestos-related disease. Furthermore, these probabilities are based on the assumption that the adverse effects A–E occurred at exposures accumulated half-way between the earliest and latest medical examinations.

(ix) One of the criteria of adverse effect, namely $FEV_1/FVC < 0.70$, accounted for 40% of all effect-occurrences in Factory A and 34% of all effect-occurrences in Factory B. It did not correlate with exposure and this bears out the latest thinking that $FEV_1/FVC < 0.70$ is an inappropriate criterion of an adverse effect of asbestos.

Acknowledgements—The Committee wishes to record its thanks to those who assisted in the compilation of this Report as follows:

(a) The Asbestos industry for providing the medical and dust exposure data;
(b) Mr R. Clayton and Mr J. R Hoyes for providing Appendix 2;
(c) Dr L. H. Capel, Dr J. A. Dick and Dr J. C. Gilson for classifying the chest radiographs;
(d) Dr M. Jacobsen for carrying out the analysis of the data as detailed in Appendix 3, and the Director of the Institute of Occupational Medicine, Edinburgh, for providing the facilities.

The Chairman wishes to record his special thanks to all the members of the Committee who, over several years and under very trying circumstances, freely gave their time. Thanks go also to the officers of the Society and its Council members for their advice and help in the final stages. In particular, the Editor-in-Chief played an important part in smoothing the passage of this report through its pre-publication stage. Finally, thanks go to the ordinary members of the Society for their understanding and patience.

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APPENDIX 1

REPORT OF THE MEDICAL WORKING GROUP

MEMBERS

Dr W. J. Smither, Dr L. H. Capel, Dr W. H. A. Beverley, Dr J. G. Morris

TERMS OF REFERENCE

The medical working group was asked to advise on the first medical indication or indications of adverse effects on the lungs and to make recommendations.

DELIBERATIONS

The group re-emphasized the importance of the principle of using the records of each employee in such a way that he may act as his own biological monitor, to detect the earliest signs of adverse effects of asbestos dust exposure. This principle involves comparing a worker's clinical, radiological, and pulmonary functional findings at the time of examination with those obtained at previous examinations, especially at the initial or pre-employment examination. Deviations from the man's own norm determined by previous examinations and tests are more significant than deviations from the 'average' or 'general population' normal. Any such deviations that cannot be attributed to secular changes require careful consideration even in the absence of recognisable disease, disorder or disability.

It is impossible to use a simple test to detect the adverse effects of inhalation of asbestos dust such as the Mantoux test for tuberculosis. No such test exists.

In considering the role of 'crackles, crepitations or rales' the working party agreed that these had been inadequately defined or described in the past [See Conclusions, Paragraph (ix), Section 1].

Many other conditions can cause added sounds such as crackles at the lung bases, and even those crackles characteristic of interstitial pulmonary fibrosis in timing and persistence are not unique to asbestosis. For those reasons their significance may have been over-emphasized in past surveys. Just as the presence of crackles is not diagnostic of asbestosis, so radiological changes in themselves are not necessarily caused by asbestos dust exposure.

The working group discussed fully the value of lung function tests. Assessment of Forced Expiratory Volume (*FEV*) as a proportion of Forced Vital Capacity (*FVC*) or Vital Capacity (*VC*) can help in the recognition of airways narrowing from whatever cause.

If pulmonary asbestosis is the only lung disorder to be considered in any one case, the Gas Transfer Factor of the lung (*T*lco) does not necessarily give more information than serially recorded changes in *VC*. Moreover, *T*lco is more variable. If other lung disorders are present, such as emphysema, then the Gas Transfer Factor per unit of lung volume (*K*co) may help in differential diagnosis. For example, *K*co will drop in emphysema.

The working group felt that the change and the rate of change in *VC* are probably the most practically useful measurements in assessing the development of lung function change due to exposure to asbestos dust. The degree and rate of change depend for their determination on comparison with the worker's initial assessment.

In all these matters the working party concerned itself with the diagnostic and epidemiological importance of early detection of an adverse effect rather than medico-legal or prognostic aspects. They recognised the difference between evidence of the earliest signs of adverse effect *possibly* due to asbestos dust exposure and evidence supporting a diagnosis of asbestosis.

The presence of any physical, physiological or radiological finding which could be due to asbestos exposure requires further investigation before a diagnosis of early asbestosis can be made. The diagnosis of early asbestosis rests on experienced clinical judgement. There are no standardized criteria for the diagnosis of asbestosis.

CONCLUSIONS

(i) Adverse effects of asbestos dust inhalation arise from any structural, functional or serological change caused by it. Such change is not necessarily recognisable as of clinical or functional importance at the time of examination and is not likely to be the same in various affected persons.

(ii) It is unlikely that any single criterion would uniquely provide the earliest warning of adverse effects in all individuals.

(iii) The Sub-committee is concerned with the medical and epidemiological importance of detecting adverse effects, not with the medico-legal or statutory aspects of asbestos-related disease.

(iv) Examination of the pattern of serial trends in the records of an employee's physical, functional, radiological and serological findings is likely to provide the earliest warning of adverse effects of exposure to inhalation of asbestos dust.

(v) Any pattern of changes which cannot be attributed to ageing or to co-existing disorder should provisionally be attributed to the results of asbestos dust inhalation in exposed workers.

(vi) An individual employee may belong to any one of the following:

Group (a) Unaffected by asbestos dust exposure but ageing normally.

Group (b) Unaffected by asbestos dust exposure but affected by other disorders.

Group (c) Affected by asbestos dust exposure but not affected by other disorders.

Group (d) Affected by both asbestos dust exposure and other disorders.

(vii) For epidemiological purposes the distribution of these groups among all employees and the probability that an individual belongs to any particular group would best be determined by comparison with matched controls.

(viii) In the absence of such matched controls the groups and any individual assigned to a particular group might be identified as follows:

Group (a) Having no clinical abnormality, and with functional and radiological findings within the normal range (and serological findings unchanged).*

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* Serological examinations have not been regularly recorded in factories in the past; in future this may become a more widespread practice.

Group (b) Having a pattern of clinical, radiological and functional changes (with serological findings taken into account) recognized as occurring in conditions other than those arising from asbestos dust exposure.*

Group (c) Having a pattern of clinical, radiological and functional changes (with serological findings taken into account) showing one or more abnormalities in any one or more of these parameters.

Group (d) Having a pattern of changes as defined in both (b) and (c) above.*

(ix) The important criteria for recognition of the adverse effects of exposure to asbestos dust can include the following:

(1) *Clinical findings.* The development of end-inspiratory crackles. These are interrupted sounds occurring towards the end of a long, slow inspiration following a complete expiration. They do not clear with coughing or on any subsequent examination and are likely to persist throughout life.

The possibility that wheeze is also important is not excluded, particularly when wheeze and crackles occur together. Clubbing of the fingers, breathlessness and cyanosis are very late findings and by no means unique to the adverse effects of asbestos dust inhalation.

(2) *Radiological features.* Any parenchymal or pleural change, excluding those due to conditions other than exposure to asbestos dust.

(3) *Lung function changes.* (a) A fall in the Vital Capacity greater than that to be expected from ageing.

(b) A fall in the Single Breath Gas Transfer Factor greater than expected from ageing. It is considered that any such fall would parallel a fall in the Vital Capacity. The Gas Transfer Coefficient (KCO) may prove helpful in differential diagnosis, especially in the recognition of alveolar damage from inflation and loss of alveolar walls (as in emphysema) when the value of both Coefficient and Factor will fall.

(4) *Serological investigations.* Antinuclear, rheumatoid and HLA factors should be taken into account. It seems probable that changes in the first two of these will parallel changes in other features. Any other diagnostic use and the importance of any other serological changes remain to be discovered.

(x) If there were a control population matched for age, sex, cigarette smoking and climatic exposure in which occupational exposure to asbestos dust has been excluded, then the incidence and prevalence of the adverse effects of asbestos dust inhalation in a test population could be assessed and used in the judgement of any dust exposure standard.

(xi) In the individual case, recognition of the presence of adverse effects of exposure to asbestos dust inhalation is a judgement of probability.

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* The evaluation of these changes would need to be based on the opinion of a group of observers of wide clinical experience able to judge the balance of probabilities.

RECOMMENDATIONS

The members of the Working Group agreed that, *solely for the purpose of this study*, the earliest index that the lungs of a worker were adversely affected, whether through exposure to asbestos dust or otherwise, excluding early tuberculosis, would include the first appearance of one or more of the following:

(i) Late inspiratory crackles in the lower third of the thorax which do not clear on coughing or on any subsequent examination.

(ii) Radiological pleural shadowing (with or without calcification).

(iii) Radiological parenchymal changes in the lower half of the lung fields.

(iv) Vital Capacity more than 20% below the predicted value, with the FEV_1/FVC remaining over 0.70.

(v) Vital Capacity falling faster than predicted by 20% or more without concomitant increases in the Functional Residual Capacity.

(vi) Single Breath Gas Transfer Factor 20% or more below the predicted value.

(vii) Gas Transfer Factor falling faster than predicted by 20% or more.

(viii) FEV_1/FVC less than 0.70.

It is recognised that the commonest cause of obstructive lung disease as measured by diminution in FEV_1/FVC is cigarette smoking (PARKES, 1982).

It is possible that there are adverse effects of asbestos dust inhalation if one of the above eight adverse affects is present; the possibility increases with the presence of additional factors and with increasing magnitude of the abnormality in each factor. A scoring of probability should be taken into account when other conditions which might cause the abnormalities are deemed to be present in addition.

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APPENDIX 2

DUST MEASUREMENTS

SECTION A. WORK CARRIED OUT TO PRODUCE A CUMULATIVE EXPOSURE HISTORY FOR THE COHORT AT FACTORY A

INTRODUCTION

Owing to developments in instrumentation and methods of measurement, allied with a better understanding of occupational hygiene practices, present-day air sampling and sample evaluation techniques differ considerably from those used during the period from 1951 to 1964.

In order to obtain a better understanding of the cumulative asbestos dust exposure of the members of the Factory A cohort by static sampling, taking into consideration the various changes in methodology, a re-appraisal has been made of the available past dust data. Comparisons have been made between the results obtained from the different sampling and measuring methods used in the past with the present-day methods. Personal sampling is discussed in Section B below.

The historical development of these techniques at Factory A is summarized below and further illustrated by the calendar of events in Fig. 1.

(a) *Casella Thermal Precipitator* 1952–1960

The first quantitative measurements were carried out from 1952 to 1960, using the Casella Thermal Precipitator (TP) as a static monitoring device. Samples were obtained on glass slides which, after incineration, were examined under dark-ground illumination at 800–1000 × magnification. All particles >0.5 μm were counted, not just fibres. The results were expressed as particles/ml.

(b) *Long Running Thermal Precipitator* 1960–1964

The Long Running Thermal Precipitator was used between 1960 and 1964, with static monitoring. The sample was collected over a 0.5 in. square on a glass slide and fibres were counted using 500 × total magnification and light-ground microscopy. Results were expressed as fibres/ml but with no detailed knowledge of the standard error, which can be assumed to have been high.

(c) *Static membrane filter and Royco* 1964–1974

Between 1964 and 1974 static sampling was carried out with membrane filter techniques and by means of a Royco particle counter calibrated to give equivalent membrane filter results. Membrane filter samples were evaluated at about 500 × magnification under phase contrast conditions, utilizing the full field of view. Results were expressed as fibres/ml. Although no proper understanding of the standard error was established at the time, the standard error for this form of estimation must have been greater than the ±40% experienced with the modern procedure.

(d) *Personal membrane filter* 1974 *to present day*

The samples after collection are analysed by a team specially trained to carry out

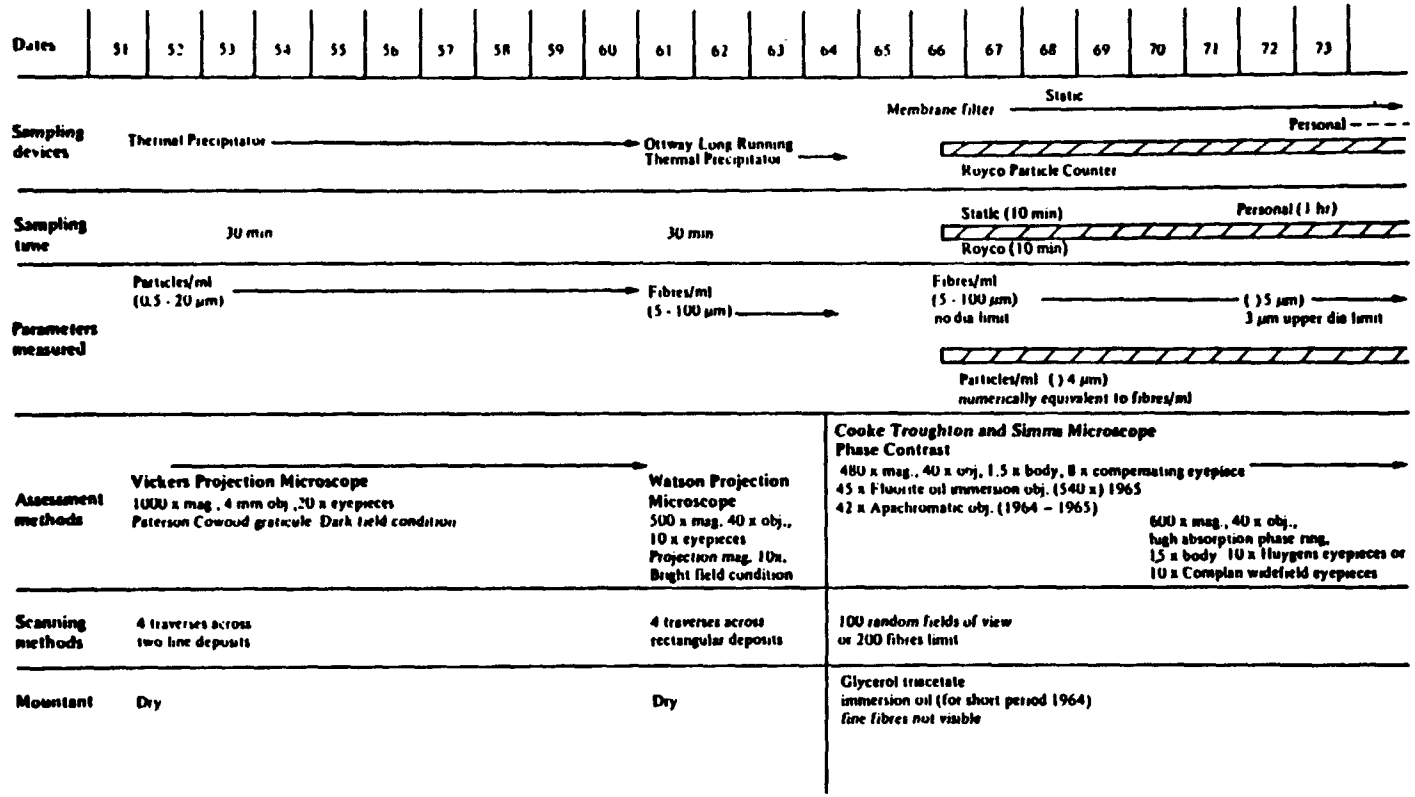


FIG. 1. Historical development of measurement techniques at Factory A.

the microscopy fibre counting procedure described in the ASBESTOSIS RESEARCH COUNCIL Technical Note 1 (1971). This procedure requires that a statistically meaningful number of fibres greater than 5 μm in length and less than 3 μm dia. are observed through a phase contrast light microscope using a 40 × objective giving an overall magnification of 600 ×. Present-day fibre counting is carried out using a standard eyepiece graticule (BS 3625, 1963) in contrast to earlier fibre counting procedures which related to full field of view observations. Results from this type of analysis are recorded as fibres/ml and are known to have a standard error of $\pm 40\%$ of the mean from monthly observations of performance of the counting team.

CORRELATION EXERCISE 1977

It is clear from the preceding history that some way of interrelating the data from the different measurement procedures was needed if cumulative exposure histories were to be constructed. Fortunately, it was possible to assemble the various pieces of equipment used during the past and to obtain the direct involvement of a person who was involved in the past monitoring programmes. Consequently, correlations have been studied between the different measuring procedures.

In all instances, conversion factors have been derived to relate past data to modern membrane filter procedures, expressed as fibres/ml. It is important, however, to appreciate that standard errors cannot be quoted for the conversion of past data without a full knowledge of all the errors associated with the original data.

Static membrane filter method

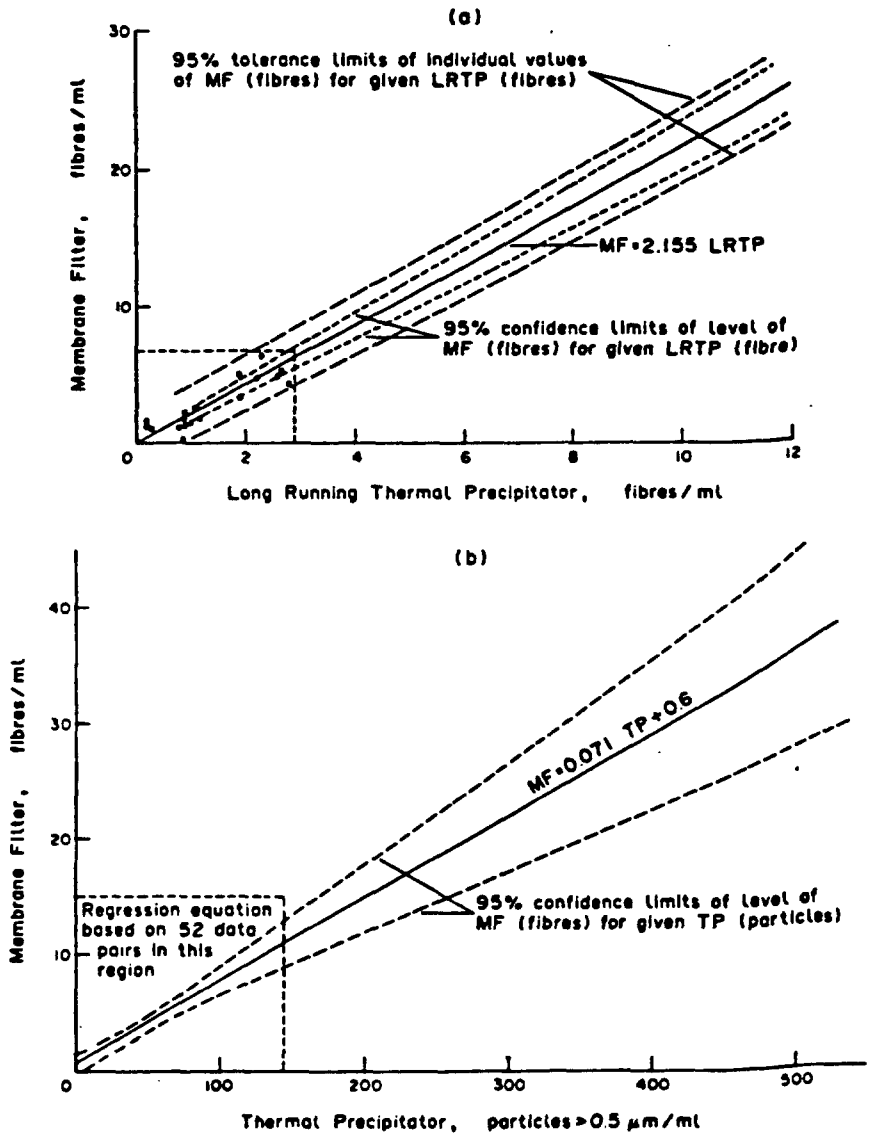
In order to convert the 'old' membrane filter and Royco results to present day values a conversion factor of times 2.0 as derived by BECKETT *et al.* (1976) has been used to allow for the 'graticule effect'.

Ottway Long Running Thermal Precipitator (LRTP)

A series of samples from the LRTP has been obtained and the results compared with data obtained from membrane filter samples obtained at the same time and from the same location. The LRTP values were obtained, as originally, in fibres/ml. There are many reservations about the precision of the comparison, not least of which is that factory conditions during 1977 are quite different from those of the past. The levels of fibres observed in 1977 were much lower than those recorded in the 1950s and 1960s, resulting in an extrapolation of the fitted line well beyond the range of the current experimental observations. Bearing this aspect in mind along with the approximate nature of the actual experimental data, the regression line has been used to derive an approximate conversion of LRTP data to modern membrane filter values. The correlation plot along with the mean line and its extrapolation are illustrated in Fig. 2(a). The derived conversion factor was such that 2.2 times the LRTP value is roughly equivalent to a modern membrane filter result in fibres/ml.

Casella Thermal Precipitator (TP)

A comparison similar to that for the LRTP has been carried out for the TP. Similar reservations about the subsequent correlation must be made and several other factors must also be considered. It is of prime importance to remember that TP results were



FIGS. 2(a) and (b). Relationships between membrane filter (fibres/ml) and (a) Long Running Thermal Precipitator (fibres/ml), (b) Thermal Precipitator (particles/ml). The boxes near the origin indicate the ranges of concentrations measured in the comparison trials, while the full figures indicate the ranges of extrapolation to earlier concentration levels.

expressed as particles/ml and not fibres/ml. ENTERLINE (1976) draws attention to the uncertainties of obtaining correlation between particle counts obtained by the impinger sample collection device and membrane filter fibre counts, which further substantiates the need for caution in interpreting these early data.

A further minor confusion was introduced by some of the TP samples being 'contaminated' by a bloom forming on glass collecting slides. This bloom gave rise to exaggerated particle counts. However, subsequent repeat samples at the same locations

gave lower values than those first obtained, partly confirming the bloom effect. The interference of TP samples by bloom was a well-known feature of this instrument when it was in use.

The fitted line for the TP data is given in Fig. 2(b). Again, extrapolation has been necessary well beyond the range of the experimental data. The conversion factor derived from the graph is that a modern membrane filter value is approximately 0.07 times the result from the TP sample. This is, of course, different from the conversion factors employed in the 1968 BOHS study which referred to membrane filter counting as conducted in 1961.

CUMULATIVE DUST DATA

By using the approximate relationships described above, the records of measured dust levels in the factory have been converted to modern membrane filter values for the various job locations. Using these relationships the job histories of the individuals in the cohort have been related to dust exposures. Personal histories have been constructed with a 'static' dust exposure value for each separate year employed within the specified period of the cohort, resulting in a cumulative exposure.

Clearly, the estimated exposure is not precise. Apart from the reservations about TP, LRTP and membrane filter correlations the number of approximations is large, not least of which is that annual average values from static measurements are assessed to be the actual individual exposures. The relationship between static and personal monitoring results is discussed in Section B. Also, some of the job histories were not quite complete and further assumptions had to be made to fill in the gaps.

SECTION B. A COMPARISON OF FIBRE CONCENTRATIONS DETERMINED FROM PERSONAL SAMPLING AND STATIC SAMPLING

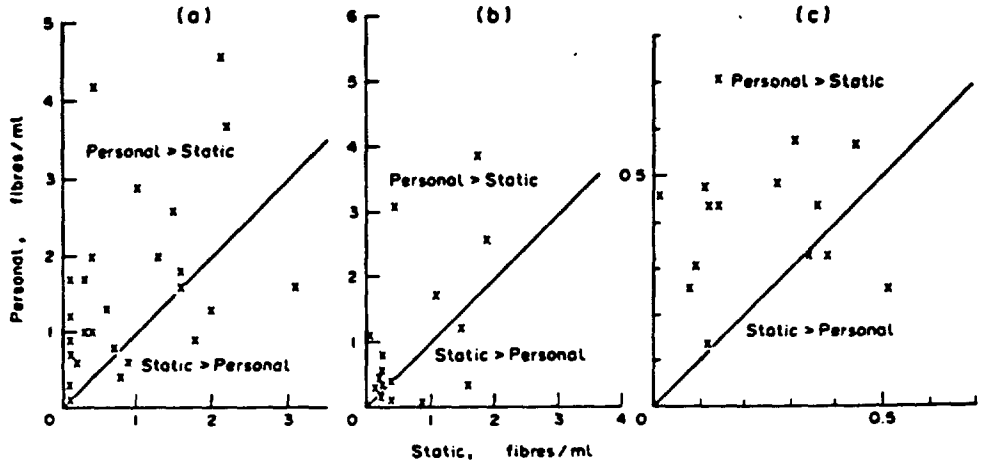
INTRODUCTION

Personal sampling involves attaching a membrane filter sampling head to the lapel of the person under test. Before the advent of personal sampling, asbestos dust concentrations were determined with static sampling techniques. Consequently, much of the historical information about asbestos dust concentrations, including that considered by previous BOHS Sub-Committees, refers to static sampling. In order to translate static sampling into values that would have been obtained had personal sampling been adopted, a knowledge of the relationship, if any, between personal and static sampling is required. In this section results from personal and static sampling surveys submitted by Committee members are presented in graphical form and some tentative conclusions are drawn about the relationship between the two types of data.

SOURCES OF DATA

(a) *Factory A*

Three sets of data from Factory A were presented. The first was from personal and static samples in the same work areas although they were not obtained simultaneously



FIGS. 3(a), (b) and (c). Personal vs static sampling results from Factory A. (a) First set of data. Samples not obtained simultaneously. (b) Second set. Each point represents mean of five 20 min static samples covering 3 hr personal sample on operative nearest (1–3 m) to static site. (c) Third set. Simultaneous static samples and operatives' personal samples at various machines. Each personal and static result is the mean from two samples (4 in one case).

[Fig. 3(a)]. The pump flow rate for the static sampling was twice that for the personal sampling. The second set, shown in Fig. 3(b), refers to simultaneous personal and static results over a representative range of operations. For this second set, five 20 min static samples were taken over the 3 hr period during which personal samples were being collected in the vicinity. The distance from the static sampling position to the nearest personal sampler depended upon the nature of the work but was generally between 1 and 3 m. The pump flow rate for the static sampling was four times that for the personal sampling.

The third set of data was obtained at Factory A during an investigation by the HSE into sampling and measurement errors. Personal samples were obtained from operatives tending certain machines and static samples were collected simultaneously at those machines. Some personal results were also obtained when sampling during shifts other than the ones during which the static samples were obtained. All the results are shown in Fig. 3(c).

(b) *Factory B*

An extensive set of results from textile processes at Factory B is shown in Fig. 4. They are values obtained from 4 hr personal samples and 15 min static sampling Royco counts taken on the same day. The Royco readings are in terms of particles/ml, the machine being set to give results equivalent to fibres/ml for textile processes at the factory.

(c) *Factory C*

These data consist of 32 pairs of results from simultaneous personal and static sampling undertaken during the sawing of Marinite board. The distance between the personal sampling head and the static sampling location was between 1 and 2 m. The data are shown in Fig. 5.

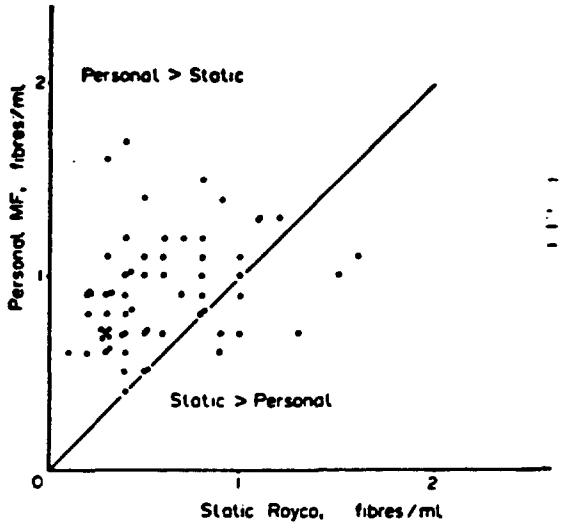


Fig. 4. Personal vs static sampling results from textile processes at Factory B. Personal, 4 hr MF samples. Static, 15 min Royco counts taken on same day as personal samples.

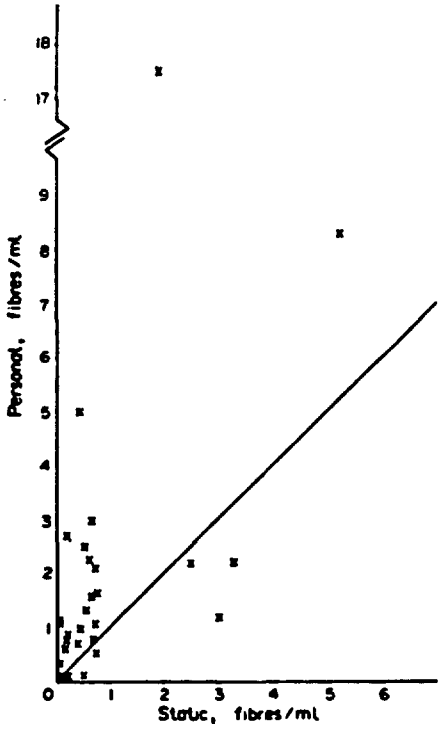


Fig. 5. Personal vs static sampling results from Factory C. Simultaneous sampling during sawing of Marinite board. Distance between instruments 1–2 m.

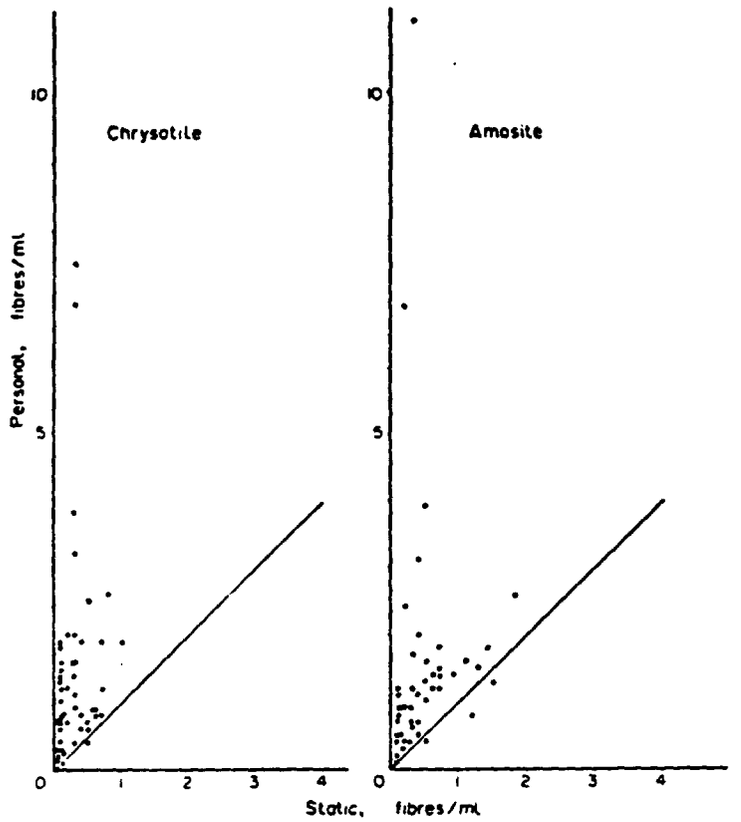


FIG. 6. Personal vs static sampling results from Factory D classified by asbestos type. Various operations; mostly overlapping sampling periods; distances between instruments mostly in range 6–15 m.

(d) *Factory D*

This set refers to both chrysotile and amosite and many different operations. There was generally some overlap of the sampling periods, although they were not strictly simultaneous. The distances between personal and static sampling locations were mostly in the range 6–15 m, the most extreme distance being 30 m. The results are shown in Fig. 6.

DISCUSSION

Figures 3–6 are plots of personal against static sampling results for data from different sources. On each graph a demarcation line has been drawn between the 'personal greater than static' and the 'personal less than static' regions. In every case there is a tendency for the personal sample results to be greater than the static results.

The relationship between personal and static sampling results obtained in a particular work area depends on:

(i) the spatial distribution of dust concentrations in the area, which in turn depends on the nature of the dust emission sources, the work practices and ventilation arrangements;

(ii) the location of the static sampling point within the area;

(iii) the operative's position relative to the static point and his personal working practices;

(iv) time factors, including the duration of sampling with the two types of measurement, the frequency of sampling over a given time period and whether or not the sampling is simultaneous;

(v) inherent sampling and counting errors.

In the limit, where the operative wearing a personal sampler is stationary and standing next to a static sampling point, the two results obtained might be expected to differ least. However, where there are large distances between the personal and static sampling points and/or when there are large gradients in concentration and when the measurements are not simultaneous, the situation becomes increasingly more complex.

The second and third set of results from Factory A, Figs 3(b) and (c), and the results from Factory C (Fig. 5) provide data on simultaneous sampling where the distances between the personal and static sampling sites were reasonably small. It can be seen that, although there is a great deal of variation in the personal sampling results corresponding to a given static sampling result, there is a marked tendency for the personal sampling results to be greater than those obtained from static sampling (49 out of 64).

The sets of data for which the results are not strictly simultaneous, but for which the same type of sampling instrument was used for both variables, support the conclusion that there is a tendency for personal sampling results to be greater than those from static sampling. Indeed, in the data from Factory D (Fig. 6) nearly all the personal sampling results are higher than those obtained from static sampling. It is possible that this is due to this set of data including a higher proportion of static sampling results that were obtained in more remote positions than those obtained at Factory A. (In some working locations, it is impractical to position a static sampler close to a typical operative.) Discussions on past static sampling strategies between the staff concerned tend to support this possibility.

The results from Factory B strongly support these findings, even though different types of instrument were employed for the personal and static sampling.

CONCLUSIONS

The relationship between static and personal sampling results varies according to the characteristics of the dust emission sources and the general and individual work practices adopted in a particular work area.

The present study indicates that:

(i) When identical sampling instruments are deployed simultaneously at personal and static sampling points and the distances between them are reasonably small, at least two-thirds of the personal sampling results obtained in a given working location are higher than those obtained from static sampling.

(ii) The differences found between the two types of result tend to be particularly great where the static sampling points are relatively remote from dust emission points, as, for example, when 'background' static testing is adopted.

(iii) In certain cases, results from personal sampling may be lower than those from

static sampling, owing to factors such as the positioning of the sampling point with respect to air extraction systems.

(iv) The correlation coefficient between the personal and static measurements is statistically significant, but, even so, no consistent relationship of great practical utility could be found in the limited data available.

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APPENDIX 3

AN ANALYSIS OF MEDICAL AND DUST EXPOSURE DATA FROM TWO ASBESTOS FACTORIES

A REPORT TO THE BOHS COMMITTEE ON ASBESTOS FROM DR M. JACOBSEN

CONTENTS

INTRODUCTION

(1) This report describes results from statistical analyses of material considered by the BOHS Committee on Asbestos during the period 1977–1979. The data are from two factories, A and B.

(2) Earlier studies by the previous Sub-committee were based on related, but different, information from Factory A. The first report (BOHS, 1968) referred to a group of men who had worked at Factory A for 10 yr or more, whose exposures to asbestos had occurred only after 1 January 1933 and who were still employed at the factory on 30 June 1966. BERRY *et al.* (1979) have described later results from the same factory, based on an extended group of men which included also those who completed 10 yr service between 30 June 1966 and 31 December 1972.

DEFINITION OF STUDY GROUPS

Factory A

(3) The specification for inclusion in the study was, for Factory A: all men* who began work in 'asbestos areas' in the factory after 31 December 1950, who had no known previous exposure to asbestos dust and who had completed at least 10 yr (not

* Men only, following the pattern of earlier studies at this factory.

necessarily continuous) work with asbestos by 31 December 1976. This definition was designed to provide an administratively manageable number of persons for medical follow-up who had been exposed to asbestos only during a period when records of dust concentrations at the factories were preserved. In this way it was hoped to reduce the uncertainties in estimating retrospectively cumulative exposures to dust. It was recognised, however, that the imposition of these criteria could lead to bias in the results if persons with less than 10 yr exposure (but who otherwise meet the definition) included many who had suffered adverse medical effects as a result of their exposure. An investigation was made therefore to assess approximately whether it is likely that such exclusions have influenced the findings. The results are reported below (Paragraphs 5–10).

Factory B

(4) Similar criteria were applied in an effort to arrange medical follow-up examinations for employees at Factory B. In this case women workers were also included. However, the data made available to the Sub-committee did not include records from persons at Factory B who had been removed from exposure when clinical examinations indicated early signs of lung function abnormalities. In some cases such persons had been exposed for more than 10 yr.

EFFECT OF EXCLUDING PERSONS WITH LESS THAN 10 YR EXPOSURE AT THE FACTORIES

Factory A

(5) An inspection of the Personnel Department's numbering system indicated that a total of 17 073 persons had joined the factory and might have worked with asbestos during the 26 yr period considered. It was not feasible to examine all these records individually and thus determine how many had been exposed to asbestos. A 5% random sample of the identification numbers was therefore selected. The relevant records were extracted from the files and summarized by staff in the company's Medical Department.

(6) No records could be traced for 10 of the 850 numbers sampled. Seven men had worked with asbestos before 1951 and a further 150 had never worked with asbestos up to 31 December 1976. Of the numbers sampled, 196 referred to women employees. Thus the total number of men who had worked with asbestos in Factory A for the first time during the 26 yr is estimated to be of the order of 10 000.

(7) Table 1 shows the distribution of exposure times for the corresponding fraction of men sampled (487/850). Of 15 men who had been exposed for more than 10 yr, 14 are in the study-group; one had been omitted inadvertently when records were searched originally by factory medical staff to identify men meeting the criteria.

(8) The sample results also indicated that 71% of the men who were not included in the study because they had worked less than 10 yr with asbestos had experienced less than 1 yr of exposure up to the end of 1976. About 6% had worked between 5 and 10 yr with asbestos. If the arbitrary 10 yr exposure period qualification for inclusion had been relaxed to, say, 8 yr, then this might have increased the number involved by about 200–400 (depending on how many of the 10 untraced records referred to men with at least 8 yr work with asbestos).

TABLE 1. FACTORY A; ANALYSIS OF A RANDOM SAMPLE OF RECORDS OF MEN WHO HAD SOME EXPOSURE TO ASBESTOS

	Duration of exposure to asbestos (yr)								
	<1	1–5	5–	6–	7–	8–	9–	10 or more	Total
In study group								14	14
Still working with asbestos	10	15	3		2	3	1	1	35
Ceased work at factory for medical reasons	15	1							16
Other leavers	313	90	8	5	1	3	2		422
All men sampled with history of exposure to asbestos	338	106	11	5	3	6	3	15	487

(9) One of the men sampled who left the factory for medical reasons had worked with asbestos for 3 yr; the other 15 had less than 1 yr exposure. It seems unlikely, therefore, that the criteria for admission to the study excluded many who had already suffered serious health effects arising from their exposure. However, BERRY *et al.* (1979) have reported that when the medical officer at Factory A considered that men were starting to develop symptoms or signs of early asbestosis then they were advised to change to less dusty jobs. It is possible, therefore, that some of the men not eligible for study, because they had worked for less than 10 yr in asbestos areas, had demonstrated an early adverse effect of exposure.

(10) Nearly 90% of the men sampled had left the factory before 1977 and most of these had experienced less than 5 yr exposure. (One of these men had died while still working with asbestos.) A rigorous medical follow-up of all such men from Factory A would have been impractical.

Factory B

(11) Table 2 shows the distribution of time worked with asbestos in Factory B for 3361 persons who were first exposed there after 1 January 1951 but who had not completed 10 yr exposure by 31 December 1976. The information was extracted by company staff from their files.

(12) Of those excluded from the study because of failure to complete the 10 yr exposure period, 22% had worked with asbestos for less than 1 yr; 72% had been exposed for periods ranging from 1–5 yr; 6% had been exposed for at least 8 yr. This

TABLE 2. FACTORY B; DURATION OF EXPOSURE TO ASBESTOS (yr) FOR 3361 PERSONS NOT QUALIFYING FOR INCLUSION IN THE STUDY

	Duration of exposure to asbestos (yr)							
	<1	1–5	5–	6–	7–	8–	9–10	Total
Still working with asbestos	64	393	44	53	94	74	27	749
Ceased work at factory for medical reasons	46	106	9	3	4		3	171
Other leavers	636	1399	137	97	71	54	47	2441
All groups	746	1898	190	153	169	128	77	3361

indicates a different pattern from that in Factory A: the corresponding estimated figures there were 71, 22 and 6%, respectively.

(13) The contrast between the factories in this respect is particularly noticeable for the sub-groups who had left the factory on medical advice. Of the 171 such persons in Factory B, 106 (62%) had been exposed for at least one but less than 5 yr. A further 16 had been exposed for at least 5 yr; three of them for more than 9 yr.

(14) Of those excluded from the Factory B study-group, 78% were no longer working there at the end of 1976. Some medical follow-up examinations have taken place in this sub-group, but this information has not been considered for the present study.

(15) Of the 2441 persons no longer at Factory B on 31 December 1976, 150 had died by that date.

THE GROUPS STUDIED

Factory A

(16) From Factory A, 300 men met the criteria for inclusion in the study. No medical records were available for five of them. The remainder of this report is concerned therefore with 295 men. Of these, 137 were still employed at the factory on 31 December 1976; 130 had left; and 28 had died before that date. (All 295 men are included in the continuing mortality follow-up study by PETO *et al.*, 1977.)

(17) Records of employment prior to joining the factory were examined for all 295 men. In 152 cases, there were references to jobs or industries which might have involved exposure to dusts or fumes, e.g. coal-mining, iron-mining, quarrying, foundry work, welding and cotton textiles. Complete previous employment records with no such references were available for only 6 men. The records for the other 137 men were incomplete in this respect and it is possible, therefore, that some of them may have been exposed to dust or fumes during periods not accounted for in their job histories. The age distributions of the two groups are shown in Table 3.

TABLE 3. PERCENTAGE AGE DISTRIBUTIONS NEAR MIDDLE OF STUDY PERIOD, ACCORDING TO AVAILABLE INFORMATION ON OCCUPATIONAL HISTORY BEFORE START OF STUDY PERIOD

Exposure to dust or fumes before 1.1.51	Age at 1 January 1965 (yr) ⩽19	20-	25-	30-	35-	40-	45-	50-	55-	60-	65–70	No. of persons in group
Factory A												
Yes	0.7	2.6	12.5	11.2	17.1	16.4	9.9	17.1	8.6	3.3	0.7	152
Possibly some	3.5*	5.6	13.3	11.9	10.5	13.3	17.5	9.8	9.8	4.2	0.7	143*
All	2.0	4.1	12.9	11.5	13.9	14.9	13.6	13.6	9.2	3.7	0.7	295
Factory B												
Yes	3.1	9.9	11.5	12.0	12.6	23.6	11.0	10.5	4.2	1.6	0	191
No	6.7	11.2	13.4	11.2	9.7	13.4	14.9	14.2	4.5	0.7	0	134
Possibly some	11.5	34.6	7.7	3.8	7.7	3.8	7.7	15.4	7.7	0	0	26
All	7.7	10.3	11.7	11.4	10.8	18.5	11.7	12.3	4.0	1.1	0	351

* Includes six men with no exposure before 1 January 1951.

Factory B

(18) At least 499 persons from Factory B met the criteria for inclusion in the study. The analyses reported here refer to 351 of them, for whom two serial chest radiographs were available. Of the 48 persons excluded because of incomplete medical data, 32 had died before 31 December 1976.

(19) Of the 351 persons considered, 28 were women workers. There were 19 deaths among the 351 persons before 31 December 1976. At least 191 (54%) of the study group had worked in jobs with potential exposure to dust or fumes prior to joining the factory. Complete occupational history records (i.e. with no time-gaps) for 134 others (38%) showed no jobs in a dusty environment. Records for the remaining 26 were incomplete. These workers may have been exposed to some dust. The age distributions for the sub-groups are also shown in Table 3. Those with some known prior exposure included a greater proportion in the middle age-groups and in this respect the age distributions from the two factories are similar.

AVAILABLE DATA

Radiological data

(20) A large number of chest radiographs were potentially available for study, since periodic medical examinations had taken place for exposed employees at both factories for many years. It was not possible to arrange for an epidemiologically valid re-examination of all this material at the time (January 1978) when the Committee was endeavouring to supply to the HSC Advisory Committee on Asbestos a summary of the information which was then available to it. The Committee decided, therefore, to arrange for a controlled study of a limited number of the radiographs potentially available.

(21) The earliest (post-1950) and latest (pre-1977) available chest radiographs for 295 men from Factory A and 351 persons from Factory B were considered. Individual films from the 646 pairs were pooled and arranged in random order. Additionally, 160 chest radiographs from 160 persons employed at the factories, but with no known exposure to asbestos dust, were inserted randomly among the 1292 radiographs. (Each factory provided 80 of these films.) The total of 1452 films were presented in turn to three physicians in February 1978. They were asked to classify them according to the ILO U/C (1971) International Classification of Radiographs of Pneumoconioses. None of the three readers was aware of the inclusion of the 160 'control' films. This work was carried out over a period of 7 weeks early in 1978. An interim report on the results was communicated to the Medical Working Group of the HSC Advisory Committee on Asbestos in April 1978.

Clinical data

(22) *Factory A*. During the latter half of 1978, lung function and anthropometric measurements, information on smoking habits, and records of whether or not chest sounds had been heard were extracted from records of medical examinations by the medical staff at Factory A and made available to the sub-committee. The lung function measurements considered were Forced Expiratory Volume in 1 s (FEV_1), Forced Vital Capacity (FVC) and Gas Transfer Factor (T_{LCO}). There were no lung function data for 56 men from Factory A, but all had attended for medical examination at least once

during the study period. At least two sets of lung function measurements had been recorded during the 26 yr for 184 men.

(23) *Factory B.* Similar information had been made available earlier for the 351 persons from Factory B. There were no lung function data for 38 of them. The presence or absence of post-tussive chest sounds at the latest medical examinations was recorded, but results from earlier assessments of whether this condition had occurred were not studied by the Sub-committee.

Exposure to asbestos

(24) *Factory A.* Manuscript sheets describing occupation, work area in the factory and relevant calendar dates were compiled by Factory A occupational hygiene staff for each man included in the study. Also shown were the corresponding annual averages of concentrations of asbestos dust at those work places during the calendar years concerned. The concentrations were expressed as fibres/ml of sampled air as determined from fibre counts on membrane filter samples by the counting method used at the factory since 1977 (Appendix 2).

(25) Exposures to dust for portions of time in each work area were recorded on the same sheets, which were made available for the statistical analysis. The exposures were calculated as the sum of the time-weighted average fibre concentrations for years and fractions of years in the work area concerned. Cumulative exposures, expressed as fibre-yr/ml sampled air, were calculated as the sums of these work-area and time specific exposures. (The distributions of various elements in these exposures are included in Table 11.)

(26) *Factory B.* Information was obtained on time worked during the 26 yr period at various factory locations involving exposure to asbestos at Factory B. Measurements of dust concentrations at some of these locations were also provided. However, there were many gaps in these records. A detailed study of the data showed that the material available might provide reasonably reliable estimates of cumulative dust exposures for only 55 (16%) of the 351 persons in the Factory B study group. The analysis of radiological results from Factory B therefore relates only to time periods during which persons were exposed, rather than to estimates of cumulative dust exposures.

RADIOLOGICAL RESULTS

Parenchymal abnormalities

(27) Table 4 shows the distributions of film classifications to pneumoconiosis categories, by factory, reader, type of opacity and whether the films concerned were the earlier or later of the pairs examined. Similar distributions are shown for the 160 non-exposed controls. The mean interval between the 295 serial pairs of radiographs from Factory A was 16.9 yr (SD 5.1 yr). The mean interval between 351 serial pairs from Factory B was 10.8 yr (SD 7.1 yr).

(28) A systematic difference between readers is evident in their interpretations of the distinction between small rounded and small irregular opacities. Readers' assessments of radiological abnormality in terms of 'combined profusion' of small

Table 4. Distributions of film classifications

		Factory A					Factory B					Controls (A and B)				
	Category	0/- and 0/0	0/1	1/0	1/1+	*N*	0/- and 0/0	0/1	1/0	1/1+	*N*	0/- and 0/0	0/1	1/0	1/1+	*N*
Small opacities (Earlier films)	Reader															
Rounded	1	284	4	3	2	293	329	15	4	2	350	155	3	2	0	160
	2	287	6	0	0	293	348	3	0	0	351	158	1	0	1	160
	3	294	0	0	0	294	351	0	0	0	351	159	1	0	0	160
Irregular	1	292	1	0	0	293	347	0	1	2	350	157	2	1	0	160
	2	286	6	1	0	293	338	11	2	0	351	154	3	3	0	160
	3	283	4	7	0	294	325	12	10	4	351	153	6	2	1	160
Combined	1	283	5	3	2	293	326	15	5	4	350	152	5	3	0	160
	2	280	12	1	0	293	335	14	2	0	351	152	4	3	1	160
	3	283	4	7	0	294	325	12	10	4	351	150	7	2	1	160
(Later films)																
Rounded	1	231	37	11	12	291	322	15	7	5	349					
	2	279	9	4	2	294	339	9	3	0	351					
	3	282	0	0	1	283	336	5	2	2	345					
Irregular	1	281	1	1	7	290	345	1	0	1	347					
	2	250	26	9	9	294	325	18	6	2	351					
	3	231	21	14	23	289	296	26	18	11	351					
Combined	1	224	38	11	18	291	321	15	7	6	349					
	2	241	28	13	12	294	318	22	7	4	351					
	3	230	21	14	24	289	287	31	20	13	351					

N = number of films not judged 'unreadable' and for which data sheets were completed according to protocol.

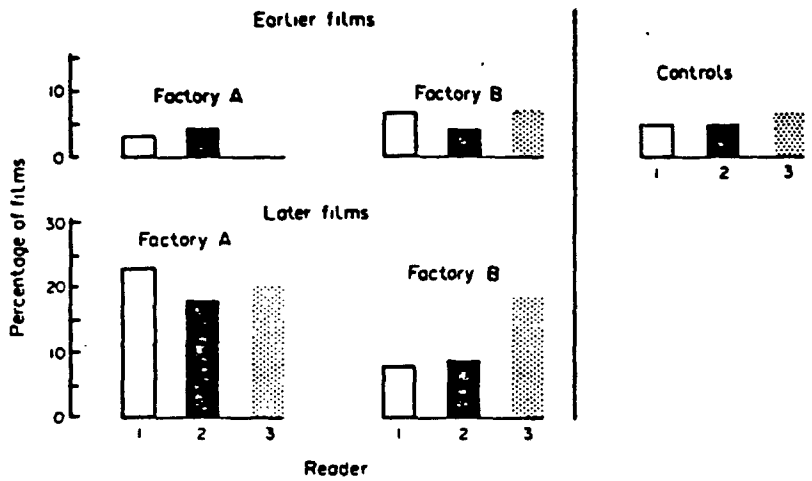

FIG. 1. Combined opacities: percentages of films classified as higher than category 0/0.

opacities are less variable, as is illustrated in Fig. 1. The only conspicuous deviation from the general pattern there is the relatively frequent assessment of abnormality by Reader 3 among the later films from Factory B.

(29) Table 5 compares readers' classifications in terms of a coefficient of consistency. This is a simple measure of the degree to which pairs of readers agree in their classifications of individual films (as distinct from an overall comparison of the proportions they judged to be other than category 0/– or 0/0). The index ranges from high consistency (97%) for earlier films with relatively little abnormality, down to 72% for later films from Factory A where the occurrence of radiological abnormalities was

TABLE 5. CONSISTENCY (%) BETWEEN PAIRS OF READERS IN THEIR CLASSIFICATIONS OF INDIVIDUAL FILMS

			Readers		
		Opacities	1 and 2	1 and 3	2 and 3
Factory A	Earlier	Rounded	94	92	94
	Films	Irregular	96	92	94
		Combined	92	89	90
	Later	Rounded	79	78	94
	Films	Irregular	85	79	74
		Combined	73	72	73
Factory B	Earlier	Rounded	93	91	97
	Films	Irregular	95	89	88
		Combined	89	87	87
	Later	Rounded	92	90	94
	Films	Irregular	93	83	83
		Combined	87	79	80
	Controls	Rounded	96	94	96
		Irregular	94	90	88
		Combined	91	88	88

The figures shown are the numbers of concordant classifications on the 12-point scale, by two readers, expressed as a percentage of all validly recorded classifications by both the readers.

most frequent. The generally lower consistency for profusion of combined opacities is a reflection of the higher frequency with which these signs were recorded by Reader 2.

(30) Table 6 records the numbers of men showing changes in profusion of small opacities in the intervals between films, by factory, reader and type of opacity. (Recall that individual films from a pair were not presented to readers at the same time, but were mixed with all other films and were arranged in random order.)

(31) The difference between readers (Paragraph 28) in the way they classified the type of small opacities seen (round or irregular) affects the frequency with which changes are possible. Again, results with respect to combined opacities are less variable for Factory A, but there remains a substantial difference between Readers 1 and 3 in their recordings of positive changes at Factory B.

(32) The columns headed 'net change' in Table 6 do not reflect the *amount* of change recorded by a reader on the radiological scale. However, the net number of men found with positive radiological changes provides a simple index for comparing readers and factories. Note that the difference between Readers 1 and 3 in their assessments of combined opacity profusion in Factory B is reflected by a nearly six-fold difference in this index.

Pleural abnormalities

(33) On average, 4.4% of the films were noted as showing obliteration of the costrophrenic angle; 2.1% showed pleural thickening; and 0.4% were classified as showing pleural calcification. In each case, rather more abnormalities were seen on films from Factory A as compared with Factory B, but there were bigger differences between readers than there were between factories, and there was no important difference between results from Factory B and the control films. These results are summarized in Table 7. One reader (3) noted pleural plaques on three radiographs from Factory A.

Technical quality of radiographs

(34) Readers were asked to record whether the technical quality of each film seen was acceptable. There were large differences between readers in these judgements. Reader 1 faulted 25% of the radiographs that he classified; Reader 2 faulted 12% and Reader 3 53%. All three readers were less satisfied with films from Factory A than from Factory B; the average proportions faulted were 34 and 26%, respectively. Two of the independent film-readers (1 and 3) believed that on the basis of their familiarity with industrial chest radiography they were able to distinguish between films from Factories A and B. Reader 2 noticed differences in radiographic technique, but he was not aware that they were associated with one or the other factory.

(35) Table 8 indicates how this factor might have affected readers' judgements of whether there had been a change in profusion of small opacities in the intervals separating films in a pair. Where both films were judged as acceptable, the net proportion with at least one (positive) step of change (combined small opacities) was 17% for Factory A and 5.5% for Factory B. This result (for a sub-set of 'good' quality radiographs) is similar to that reported above for all the films (Table 6). It confirms that the difference between the factories, as judged by readers' assessments of film quality, is not the sole reason for the apparently more frequent radiological changes among men from Factory A.

TABLE 6. RADIOLOGICAL CHANGES OVER 10-26 YR INTERVALS

Small opacities	Reader	Factory A				Factory B			
		N	Number of film-pairs* showing radiological change†		Net change (%)	N	Number of film-pairs* showing radiological change†		Net change (%)
			+ ve (a)	− ve (b)	100(a−b)/N		+ ve (a)	− ve (b)	100(a−b)/N
Rounded	1	289	58	4	18.7	348	26	17	2.6
	2	293	14	6	2.7	351	12	2	2.8
	3	282	1	0	0.4	345	9	0	2.6
Irregular	1	288	9	1	2.8	346	2	1	0.3
	2	292	44	5	13.4	351	24	10	4.0
	3	288	56	3	18.4	351	50	19	8.8
Combined	1	289	64	3	21.1	348	27	20	2.0
	2	297	50	7	14.5	351	31	12	5.4
	3	288	57	3	18.8	351	58	17	11.7

N = number of film-pairs whose classifications were recorded validly by the reader concerned.
* Note that any two films from a pair were classified independently by any one reader.
† 'Radiological change' defined as change of one or more sub-categories on the ILO scale, ignoring changes between categories 0/− and 0/0.

Table 7. Pleural abnormalities

	No. of films:	Factory A 590		Factory B 702		Control 160		All films 1452	
		x	%	x	%	x	%	x	%
	Reader								
Costophrenic angle obliteration	1	41	6.9	35	5.0	9	5.6	85	5.9
	2	22	3.7	17	2.4	3	1.9	42	2.9
	3	31	5.3	28	4.0	6	3.8	65	4.5
	Average		5.3		3.8		3.8		4.4
Pleural thickening	1	20	3.4	15	2.1	5	3.1	40	2.8
	2	1	0.2	0	0	0	0	1	0.1
	3	29	4.9	14	2.0	6	3.8	49	3.4
	Average		2.8		1.4		2.3		2.1
Pleural calcification	1	2	0.3	2	0.3	0	0	4	0.3
	2	0	0	0	0	0	0	0	0
	3	7	1.2	5	0.7	0	0	12	0.8
	Average		0.5		0.3		0		0.4

x = number of films where abnormalities were recorded. The percentages tabulated are 100x/(number of films classified).

Table 8. Radiological changes (combined small opacities) between film-pairs in relation to readers' assessments of technical quality of films in a pair

1st film:	Film quality: Acceptable			Acceptable			Faulted			Faulted		
2nd film:	Acceptable			Faulted			Acceptable			Faulted		
	N	x+	x−	N	x+	x−	N	x+	x−	N	x+	x−
Factory A												
Reader												
1	141	24	3	37	5	0	74	9	0	40	12	4
2	221	46	0	40	11	0	22	6	2	5	1	1
3	55	4	0	56	6	1	11	13	2	106	34	0
Average over all readers (%)		17.7	0.7		16.5	0.8		16.8	2.4		31.1	3.3
Factory B												
1	231	22	5	47	5	4	57	3	2	16	1	1
2	269	19	13	43	2	3	29	5	3	5	1	0
3	95	15	5	48	5	0	128	26	9	80	12	3
Average over all readers (%)		9.4	3.9		8.7	5.1		15.9	6.5		13.9	4.0

N = number of film-pairs.
$x+$ = number with positive radiological change, (one or more sub-category).
$x-$ = number with negative radiological change (regression, one or more sub-category).

(36) Nevertheless, it is clear from Table 8 that the higher proportion of film-pairs in Factory A where both were faulted (19% on average, compared with 10% in pairs from Factory B) was associated with more frequent judgements of positive radiological change. The fortuitous lack of bias in the overall results recorded in Table 6 is due to the relatively few changes seen on film-pairs from Factory B where the earlier film was judged acceptable and the later film was faulted.

TABLE 9. FILM QUALITY AND PLEURAL ABNORMALITIES

Pleural abnormality	Film quality	Factory A No.	A %	B No.	B %	Control No.	Control %	All films No.	All films %
Costophrenic angle obliteration	Acceptable	65	5.7	61	3.9	16	4.1	142	4.6
	Less than acceptable	29	4.7	19	3.4	2	2.2	50	4.0
Pleural thickening	Acceptable	30	2.6	19	1.2	9	2.3	58	1.9
	Less than acceptable	20	3.3	10	1.8	2	2.2	32	2.5
Pleural calcification	Acceptable	5	0.4	2	0.1	0	0	7	0.2
	Less than acceptable	4	0.7	5	0.9	0	0	9	0.7

The numbers tabulated are the total number of classifications with the pleural abnormality indicated. The percentages are:

$$100 \times \frac{\text{(number of classifications with pleural abnormality)}}{\text{(number of classifications in film quality category)}}.$$

(37) Table 9 demonstrates that variations in film quality assessments did not affect the pattern of pleural abnormality assessments described in Table 7.

Small opacities and smoking habits

(38) *Factory A.* Table 10 shows that all readers detected small opacities more frequently among smokers (and ex-smokers) than among non-smokers. BERRY *et al.* (1979) have reported a similar finding from related data. The magnitude of the effect in terms of combined small opacity profusion is similar for the three readers, averaging nearly twice as many (combined) small opacity classifications among men who had smoked or who were still smokers at time of X-ray as compared with non-smokers.

TABLE 10. FACTORY A; PERCENTAGES OF LATER FILMS CLASSIFIED AS CATEGORY 0/1 OR HIGHER, IN RELATION TO SMOKING HABITS AT TIME OF LATER FILM

Reader		N	Percentage of films with opacity profusion greater than category 0/0: Small rounded	Irregular	Combined
1.	NS	63	1.6	7.9	9.4
	S	185	7.0	16.2	20.5
	Ex-S	46	2.2	19.6	19.6
2.	NS	64	15.6	0	15.6
	S	182	23.1	4.4	26.4
	Ex-S	45	17.8	2.2	20.0
3.	NS	61	0	11.1	11.1
	S	179	0.6	22.6	23.2
	Ex-S	43	0	22.2	22.2

NS. non smoker; S. smoker; Ex-S. ex-smoker; *N*, number of men (whose films were classified) in smoking category.

(39) Nevertheless, small opacities were also detected on about 12% of the non-smokers' radiographs. This indicates that the radiological signs seen on the later films from Factory A (Fig. 1) are not wholly attributable to smoking. But the corresponding classifications of later films from Factory B, as judged by Readers 1 and 2, showed only a marginally higher proportion with combined small opacities than was recorded for the control films. Note, however, that Reader 3 classified 18% of these films from Factory B into category 0/1 or higher, as compared with 6% of the control films.

Radiological changes and dust exposure

(40) *Factory A.* Table 11 refers to men from Factory A whose film-pairs showed evidence of increasing profusion of combined small opacities over the 10–26 yr intervals considered. The numbers concerned are expressed as percentages of men in sub-groups defined according to convenient but arbitrary ranges of four measures of dust exposure. The first of these measures, E_a, is the cumulative exposure from start of work in asbestos areas up to the time of the earlier film. The second, E_b, is the exposure during the interval between films. These quantities were estimated by direct proportion, using the detailed records of exposure up to the point nearest to the time when the films were made. The third measure, E_c, is the cumulative exposure up to the

TABLE 11. POSITIVE RADIOLOGICAL CHANGES IN FACTORY A, IN RELATION TO FOUR MEASURES OF DUST EXPOSURE

	Ranges of dust exposure (fibre-yr/ml)	Reader 1		Reader 2		Reader 3	
		N	%	*N*	%	*N*	%
E_a	0–4	116	12.1	113	21.2	115	19.1
	5–9	70	22.9	68	27.9	65	20.0
	10–19	48	16.7	49	16.3	49	16.3
	20+	50	24.0	51	21.6	51	27.4
E_b	0–69	43	11.6	44	25.0	43	18.6
	70–109	44	4.6	44	11.4	44	11.4
	110–149	60	20.0	58	17.2	58	20.7
	150–199	46	17.4	44	25.0	44	18.2
	200–299	63	22.2	63	28.6	63	19.0
	300+	28	32.1	28	25.0	28	42.9
E_c	0–89	50	8.0	50	20.0	49	16.3
	90–129	54	11.1	53	11.3	52	11.5
	130–169	52	19.2	50	24.0	50	20.0
	170–239	50	24.0	49	36.7	51	25.5
	240–329	49	18.4	50	20.0	49	16.3
	330+	29	31.0	29	20.7	29	41.4
E_d	0–44	48	8.3	48	18.8	47	17.0
	45–74	67	9.0	66	12.1	65	13.8
	75–104	56	28.6	53	28.3	54	20.4
	105–139	53	17.0	53	32.1	53	24.5
	140+	60	25.0	61	21.3	61	26.2

The percentages shown refer to men for whom positive changes in profusion of combined small opacities were recorded. N = number of film-pairs for which classifications were recorded by the reader concerned. The measures of exposure are: E_a, cumulative exposure to time of earlier film; E_b, exposure in the interval between films; E_c, cumulative exposure to later film ($E_a + E_b$); E_d, cumulative exposure up to a point approximately mid-way in the interval between films, estimated as ($E_a + \frac{1}{2}E_b$).

time of the later X-ray, that is, the sum $E_a + E_b$. The final set of figures, E_d, is an attempt to approximate to the exposure up to the point when the observed change occurred. The estimate used for this purpose for each man was $(E_a + \frac{1}{2}E_b)$.

(41) The low range of E_a confirms that the earlier radiographs obtained from Factory A did, in general, correspond approximately to the start of exposure to asbestos dust, and Table 11 shows no association between these early exposures and subsequent radiological changes. The mean exposure in the interval between films (E_b) was 163 fibre-yr/ml (SD 103 fibre-yr/ml), but, again, there is no obvious pattern of association between this measure of exposure and the grouped radiological results in Table 11. However, there is a positive correlation between percentages showing at least the earliest evidence of parenchymal changes and cumulative exposure up to the later film (E_c). A very similar pattern is evident in relation to E_d and, again, results from Readers 1 and 3 show a clearer correlation than those from Reader 2. These data are illustrated in Figs. 2(a) and (b). Readers 2 and 3 both recorded lower percentages of men with combined small opacities in the second exposure group than in the first. This apparent 'reduction' in response in the exposure group adjacent to the lowest may be attributable in part to removal from workplaces with relatively high dust concentrations of men who showed early signs of disease after very low cumulative exposures (see

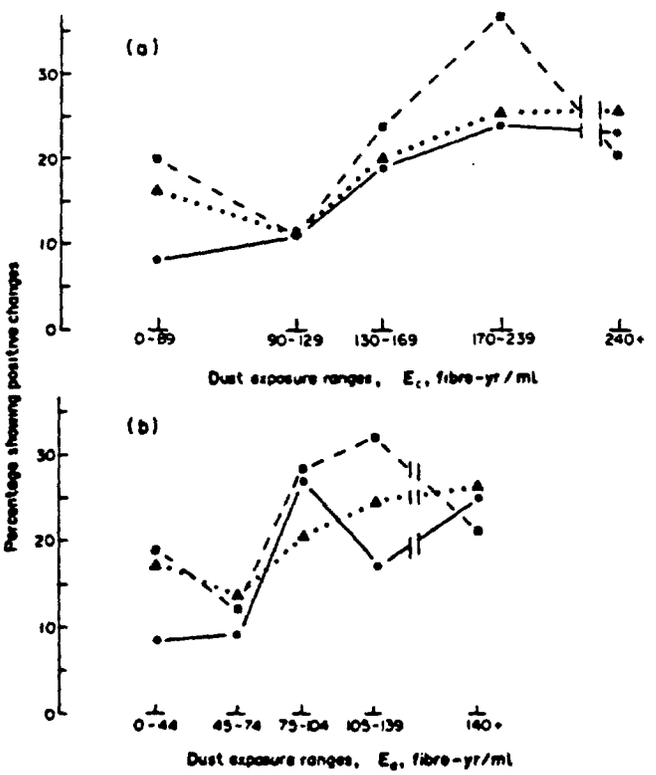

FIG. 2. Percentages of men from Factory A showing positive changes in profusion of combined small opacities over 10-26 yr intervals, in relation to two estimates of dust exposure: (a) E_c = cumulative exposure to later film, (b) E_d = cumulative exposure up to a point approximately mid-way in the interval between films. (Data from Table 11) Reader 1●, 2■, 3▲.

Paragraph 9). Similar selection effects may have distorted the real relationship between exposure and response at higher levels of exposure.

(42) *Factory B.* Information on time worked in jobs involving exposure to asbestos at Factory B was complete for 187 (98%) of those who had definitely worked in occupations with potential exposure to dust prior to 1951, and for 128 (96%) of those with no such prior exposure. Table 12 shows each reader's assessment of changes in profusion of combined small opacities for these two sub-groups in relation to three categories of time worked in asbestos jobs *after 1951* and up to 31 December 1976. The last column of this Table shows the amount of radiological change for each sub-group as the algebraic sum of the number of steps (positive and negative) on the 12-point scale of radiological abnormality per 100 men in the sub-group concerned. These results are summarized graphically in Fig. 3. Both Readers 1 and 3 recorded more radiological change between films in a pair among persons with longer periods of exposure to asbestos while at the factory; the trend is clearest in the sub-group of persons who had worked with dust or fumes before 1951.

Table 12. Factory B; steps of change on the radiological scale (combined small opacity profusion) over 10–26 yr intervals per 100 film-pairs classified in relation to time worked with asbestos

Exposure to dust or fumes before 1951	Exposure to asbestos after 1951	Reader	*N*	Steps of change (combined small opacities) +ve	−ve	Net change/100 film-pair classified 100(*a*-*b*)/*N*
Some	<5 yr	1	76	4	1	3.9
		2	76	10	3	9.2
		3	76	8	3	6.6
	5–10 yr	1	49	7	0	14.3
		2	49	8	10	−4.2
		3	48	11	7	6.2
	⩾10 yr	1	62	22	5	27.4
		2	62	11	2	14.5
		3	62	43	7	58.1
None	< 5 yr	1	10	0	0	0
		2	10	1	0	10.0
		3	10	0	0	0
	5–10 yr	1	20	3	0	15.0
		2	20	1	0	5.0
		3	20	4	0	20.0
	⩾ 10 yr	1	98	9	0	9.2
		2	97	8	9	−1.0
		3	98	27	4	23.5

N = number of film-pairs classified validly.

CORRELATION BETWEEN LUNG FUNCTION AND DUST EXPOSURE AT FACTORY A

(43) At least one set of lung function measurements was available from 239 men, and at least two for 184 men out of the total of 295 men in the Factory A group. The correlation between the latest measurement recorded and estimates of cumulative dust

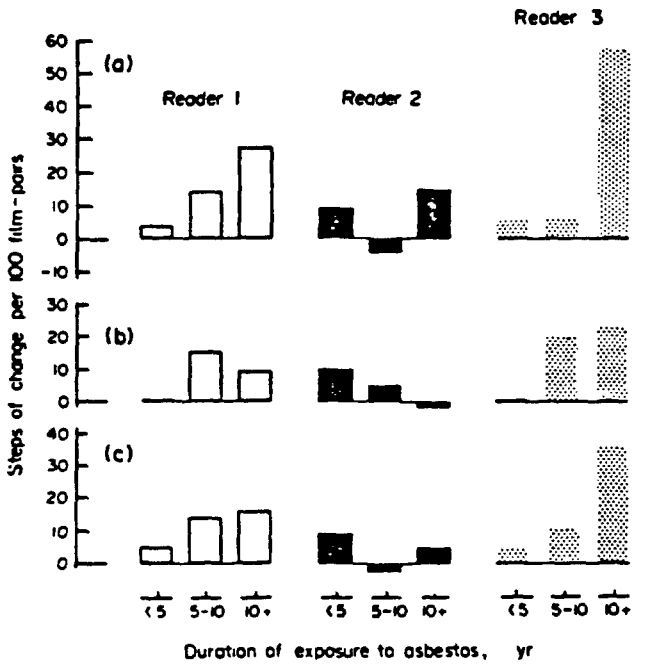

FIG. 3. Steps of change on the radiological scale (combined small opacities) over 10–26 yr intervals per 100 film-pairs classified from Factory B, in relation to time worked with asbestos at Factory B. (a) Some prior exposure to dust or fumes. (b) No prior exposure. (c) Results of (a) and (b) combined. (Data from Table 12.)

exposure up to the time of the test were examined. A linear multiple regression model was used to take account of age, height, weight and smoking habits at that time.* The measures of lung function considered were FEV_1, FVC, $TlCO$ and the ratio FEV_1/FVC.

(44) Results are summarized in Table 13. This shows that more than half of the total variability in the data remained unexplained by the variables included in the model.

(45) The bigger reductions in total variability were for the FEV_1 and FVC (44 and 38%, respectively). These were the two response variables where the estimates of dust exposure made contributions approaching statistical significance at the 5% level ($P \approx 0.06$). Neither the $TlCO$ nor the FEV_1/FVC ratio was correlated with the measure of dust exposure used.

'ADVERSE EFFECTS'

Preliminary remarks

(46) The Committee was advised that, solely for the purpose of this study, the earliest sign that the lungs of a worker were adversely affected 'whether through

* The exposures were estimates by direct proportion, using data relevant to points nearest to the time when the lung function measurements were made. Smoking habits were represented in the regression models by dummy variables corresponding to men who smoked cigarettes only, other smokers, ex-smokers, and non-smokers.

Table 13. Factory A; summary of results from multiple regression analyses of the latest lung function measurements available for 229 men

	Mean	Crude correlation with dust exposure (r)	Multiple regression coefficient for exposure (b_e)*	Standardized regression coefficient (t)	Percentage of total variance accounted for
FEV_1	2.85 (l)	−0.271	−0.075	−1.88	44
FVC	3.94 (l)	−0.241	−0.090	−1.93	38
$TIco$	26.2 (ml min^{-1} mmHg^{-1})	−0.085	0.133	0.35	26
FEV_1/FVC	0.72	−0.182	−0.005	−0.82	22

* The regression coefficient with dust exposure is expressed as the change in lung function per 100 fibre-yr/ml cumulative exposure.

Data for explanatory variables were incomplete for 10 of the 239 men with at least one measurement of lung function.

exposure to asbestos dust or otherwise' would be the first appearance of one or more of eight conditions (see Appendix 1). The phrase 'whether through exposure to asbestos dust or otherwise' reflects the difficulty in making an aetiological judgement based only on clinical examination of an individual. Application of these medical guidelines to an epidemiological study of the results presents a number of problems.

(47) The first difficulty resides in the use of the phrase 'whether through exposure to asbestos dust or otherwise' in the context of a study directed primarily at determining what level of exposure to asbestos dust is associated with the occurrence of the earliest sign of an adverse medical effect. The formulation implies that the occurrence of at least one of the nominated signs is to be regarded as a *necessary* but not as a *sufficient* condition for asserting that exposure to asbestos is responsible. Any attempt to estimate probabilities of the occurrence of these adverse effects as a function of exposure must therefore be qualified with the caveat that their occurrence may, in fact, be unrelated to asbestos exposure.

(48) Secondly, with the exception of the radiological classifications, none of the medical data available were obtained under the kind of controlled, standardized conditions normally required in epidemiology. The lung function measurements were made, and the records of chest sounds were noted, in a clinical context. Different medical staff conducted these examinations over the years, using various conventions. No data are available to estimate the variability associated with the application of the lung function tests.

(49) Thirdly, determination of what constitutes 'pleural shadowing' or 'parenchymal changes' requires definition in terms of a standard radiological classification system and bearing in mind the variability between physicians making the classifications.

(50) Fourthly, a decision on whether a particular value of lung function is 'more than 20 per cent below the predicted value' is not as clear-cut in epidemiology as it might be in a clinical setting. Whether or not such a discrepancy from the result predicted is statistically significant depends not only on the variability associated with the prediction but also on the variability of the data under examination. Moreover,

choice of a suitable prediction may not be simple, because of ethnic, demographic, social-class factors affecting lung function.

(51) Notwithstanding these and other difficulties, an attempt was made to apply the medical advice of the Sub-committee in an analysis of the available data. The statistical methods used are described below.

Statistical methods

(52) Seven criteria for determining the occurrence of an 'Adverse Effect' in an individual were defined. For brevity, they will be identified by the letters A–G and will be referred to collectively as Adverse Effects (with capital letters and no qualifying quotation marks).

(53) The Adverse Effects considered are listed in Table 14. The first two of these conditions (A and B) are interpretations of the medical recommendations concerning radiological abnormalities in terms of the film classifications described above.

TABLE 14. LIST OF ADVERSE EFFECTS STUDIED

Notation	Adverse Effect
A	At least two readers agreed that there were two or more steps of change on the profusion scale for combined small opacities over the interval between films
B	At least two readers agreed that a pleural abnormality was present on the later but not on the earlier film of a pair (where 'pleural abnormality' means at least one of pleural thickening, pleural calcification, or costophrenic angle obliteration)
C	Unusual rate of change in FEV_1
D	Unusual rate of change in FVC
E	Unusual rate of change in $TlCO$
	'Unusual' defined in terms of distribution of residuals; see text, paras 54–58
F	Any one measurement of $FEV_1/FVC < 0.70$
G	Chest sounds which did not clear on coughing or on any subsequent examinations

Parenchymal changes were accepted as having occurred if at least two readers' independent assessments of serial radiographs from a person showed two or more steps of change on the 12-point profusion scale for small combined opacities, irrespective of which lung zone was involved. Pleural shadowing was judged as being present if at least two readers agreed that a pleural abnormality was present on the later but not on the earlier films.

(54) The letters C, D and E refer to *changes* in lung function. Thus, the procedures described below to determine the presence or absence of any of these Adverse Effects could be applied only to those persons for whom at least two serial measurements of lung function had been recorded. For each such individual, a Least Squares estimate was made of the *rate of change* in the lung function measurement of interest, with a simplifying assumption that lung function falls linearly with age. The individually estimated rates of change in lung function were then treated as the response variables in analyses which sought to relate the rate of change concerned to:

(a) the initial value of lung function observed;
(b) age at the time of the initial examination;
(c) height as measured at the initial examination;
(d) body weight as measured at the initial examination;
(e) smoking habits as recorded at the initial examination.

(55) A multiple linear regression model was used in which cigarette smokers, ex-smokers, other smokers (pipe, cigar or mixed), and non-smokers were differentiated by dummy variables. The predicted value of the rate of change in lung function for an individual (estimated from the fitted equation) was then subtracted from the rate of change as estimated from the measurements on the individual. The distributions of these differences ('residuals'), considered separately for Factories A and B, were then used to define C, D and E arbitrarily as any value of a residual in the lower 20-percentile of the distribution, assuming that the residuals are distributed normally with zero mean, and variance as estimated from the regression analysis.

(56) If the residuals are distributed exactly normally, then this definition ensures that about 20% of them would attract classification as indicating an Adverse Effect. On the other hand, deviations from normality in the observed distributions would result in more or fewer such classifications. Thus, C, D and E refer to relatively severe rates of reduction in lung function which are not explicable simply in terms of the initial level of the functional measure concerned, age, height, weight or smoking habits.

(57) D and E are approximations to the recommendations that Vital Capacity or Gas Transfer Factor measurements which fall faster than predicted by 20% could be regarded as an adverse effect; but note that D, referring to Vital Capacity changes, was attributed irrespective of concomitant changes in Functional Residual Capacity. 'Predicted' has been interpreted here as a prediction based on the internal evidence from the data, rather than on predicted 'Normal' values derived from other sources. In this way it was hoped to avoid some of the difficulties referred to in Paragraph 50.

(58) The definition of C (rate of reduction in FEV_1) was not based on any suggestion from the Sub-committee's medical advisers. It was included because of the relatively high correlation of FEV_1 with dust exposure which emerged from the cross-sectional analyses summarized in Table 13.

(59) The presence or absence of F was determined for all persons for whom FEV_1 and FVC were recorded at least once at the same time, strictly in accordance with the advice from the medical members of the Sub-committee (Appendix 1). If the ratio FEV_1/FVC was less than 0.70 then this was classified as F.

(60) For Factory A, attributions of G were made to conform as closely as possible to the recommendations from the medical members of the Sub-committee regarding the occurrence of chest sounds indicative of an Adverse Effect. All serial records of medical examinations from the same man were inspected. At least two notations, at different times, were required of the presence of either 'crepitations' or 'crackles' or 'rales' which did not clear on coughing on either occasion, and with no subsequent record of such sounds which did clear on coughing. Where the data (from Factory A) indicated the presence of one of these chest sounds and no entry was made in the record to indicate that it did clear on coughing, then it was assumed that the sound noted had *not* cleared on coughing. Dated entries recording a medical examination with no reference to chest sounds were treated as 'no chest sounds' on that occasion.

(61) The above definition of G was not applicable to the Factory B data, because the record cards provided to the Sub-committee contained references to the presence or absence of post-tussive chest sounds only on the occasion of the latest medical examinations (see Paragraph 23). The presence of these sounds in the Factory B group is therefore symbolized by G' rather than G.

(62) Collectively then, the seven Adverse Effects defined represent criteria, based

on the data, which reflect, approximately, six of the eight clinical signs mentioned by the medical members of the Sub-committee. No attempt was made to interpret the *absolute* levels of Vital Forced Capacity or Gas Transfer Factor as Adverse Effects because of the high level of residual variability found in the Factory A data when these measures were regressed on cumulative dust exposure, age, height, weight and smoking habits (Table 13). It was hoped that consideration of *rates of change* in lung function might show a clearer association with dust exposure. Implicit in this approach was the hope that, even if an early exposure-related functional disturbance is not detectable in the raw data, the associated more rapid rate of decline in function with age might be a more sensitive signal of possible severe respiratory dysfunction at a later date (FLETCHER *et al.*, 1976). In the event, however, graphical analyses of the residuals which were used to define Adverse Effects C, D and E did not show any trend suggesting that they were correlated with dust exposure.

Occurrence of Adverse Effects

(63) *Factory A.* Table 15 shows the distribution of Adverse Effects found in the Factory A data. Results from 163 men met one or more of the seven criteria. The most frequently occurring effect was F, that is, at least one measurement of the FEV_1/FVC less than 70%. This result was recorded for 111 of the 239 men for whom at least one set of lung measurements was available. For 52 of them it was accompanied by at least one of the other Adverse Effects, including 16 of 26 men who also had chest sounds as defined (G). The relatively high number of occurrences of F is consistent with the mean level of the ratio shown in Table 13 (72%).

(64) *Factory B.* Table 16 shows similar distributions of Adverse Effects from the Factory B data. Results from 154 men and from nine women met one or more of the seven criteria. The total number of occurrences was 257. As in Factory A, the most

TABLE 15. FACTORY A; DISTRIBUTIONS (a) OF ADVERSE EFFECTS; AND (b) OF MEN TO COMBINATIONS OF ADVERSE EFFECTS

(a) Number of Adverse Effects		(b) Numbers of men with combinations of Adverse Effects shown				
A 22	A 6	AB 2	ABF 1	ABDG 1	BCDEF 1	ACDEFG 2
B 25	B 8	AF 3	ADF 1	ABEG 1		
C 23	C 2	AG 1	BDF 1	ACEF 1		
D 33	D 6	BD 1	BEF 2	ACFG 1		
E 34	E 9	BF 7	CDF 6	AEFG 2		
F 111	F 59	CD 4	CFG 1	CDEF 2		
G 26	G 5	CE 1	DEG 1	DEFG 1		
		CF 2	EFG 1			
		DE 3				
		DF 3				
		EF 6				
		EG 1				
		FG 8				
Total 274	Total no. of men 95	42	14	9	1	2

No Adverse Effects were recorded for 132 men.

Table 16. Factory B; distributions (a) of Adverse Effects; and (b) of persons to combinations of Adverse Effects

(a) Number of Adverse Effects		(b) Numbers of persons with combinations of Adverse Effects shown				
A 5	A 3	AF 1	BCD 1	CDEF 6	ABCDF 1	
B 18	B 8	BE 1	BDF 1	CDFG' 1	BCDEF 2	
C 43	C 15	BF 4	CDE 1			
D 39	D 4	CD 8	CDF 4			
E 59	E 28	CE 2	CEF 1			
F 88	F 49	DE 3	CEG' 1			
G' 5	G' 0	DF 3	DEF 4			
		EF 8	EFG' 2			
		FG' 1				
	Total. no. of					
Total 257	persons 107	31	15	7	3	

No Adverse Effects were recorded for 188 people.

frequently noted single Effect was F; 88 of the 313 Factory B workers for whom lung function data were available had at least one examination where the FEV_1/FVC ratio was less than 70%. There were fewer radiological changes recorded for Factory B (Table 6) and consequently also a much smaller number with Effects A or B. Only five records of post-tussive chest sounds were recorded, all were in men, and all occurred in the presence of one or more of the other Adverse Effects. Among those individuals whose results attracted at least one designation as an Adverse Effect (163 in both Factory A and Factory B) the distributions of persons with only one, with two, and with three or more Effects were similar (58, 26 and 16%, respectively at Factory A; 66, 19 and 15% at Factory B).

Derivation of probabilities of the occurrence of Adverse Effects at Factory A

(65) Some of the analyses considered in Paragraphs 40–45 indicated correlations between the medical findings and the measures of dust exposure used; but there remains a high level of unexplained variability in the data. This implies that estimates of exposure-specific probabilities of the occurrence of Adverse Effects will be imprecise. If the exposures associated with the occurrence of particular Adverse Effects are known then these occurrences can be arranged in order of increasing exposure. In principle, the 'Life Table' method, commonly used in actuarial science, can then be used to estimate probabilities that *no* Adverse Effect occurs up to particular exposures. The complement of such a 'survival probability' is an estimate of the parameter of interest: the probability that an Adverse Effect occurs at an exposure less than a given value.

(66) Berry *et al.* (1979) used this idea in their study of earlier data from Factory A. These authors referred to the results from their calculations as 'observed relationships ... obtained by life-table methods'. But it is important to note that application of the method involves use of the product law of probability to generate *estimates* of cumulative probabilities. The results should not be confused with observed prevalences of the condition associated with increasing ranges of dust exposure (Table 11 in the present case).

(67) Application of the method to the results reported now presents difficulties, because, as noted by BERRY *et al.*, 'an unbiased analysis can be made only by using the times at which men with positive signs *first* reached this stage' (emphasis added). It is not enough to know that the exposure accumulated at that time was less than a particular value.

(68) For effects F and G (FEV_1/FVC ratio <0.7 and chest sounds), use of estimated exposures to time of examination will probably introduce a relatively small error, since both F and G are associated with clinical features which are likely to have been noted by the factory medical staff soon after they occurred.

(69) Changes in lung function, over several years, present a more difficult problem. The convention adopted for the analyses described below was to assume arbitrarily that the physiological disturbance which determined an abnormally severe rate of change began at a point in time mid-way between the initial and final measurement of lung function used. Estimates of the corresponding exposures were then made by direct proportion.

(70) A similar convention was applied to the Adverse Effects involving radiological changes (A and B). The corresponding exposures are the E_d defined in Paragraph 40. It has to be recognized that the radiologically defined events, A or B, may reflect the results of biological processes which began soon after the initial X-rays were taken. Or it may be that the changes occurred only a short while before the final radiographic examination. Use of an exposure corresponding approximately to that likely to have been accumulated in the middle of the interval concerned ensures that the (unavoidable) errors in estimating the true exposures of interest may occur on either side of the unknown true values. [Cumulative exposures *up to* the final examination (E_c), on the other hand, would certainly be biased; the errors involved could then be in one direction only—that of overestimating the required exposures.]

(71) Figure 4 shows 22 estimates of probabilities of the occurrence of A, in relation to exposures E_d. Figure 4 should be regarded as a convenient graphical representation of the range and distribution of the corresponding dust exposures. It should not be interpreted as graphical evidence of a real association between the Adverse Effect and dust exposure, because the increasing pattern of the plotted points is a consequence of the Product Limit method which generates a *cumulative* distribution of probabilities with respect to the time-dependent exposure levels under consideration.* This property of the method used for estimating the probabilities may be illustrated by an example: Figure 5 shows results from 22 calculations of the kind which were made to generate Fig. 4; but in this case the 22 individuals whose ordered exposures were used to make the calculations were not selected on the basis of the radiological results: they were selected *at random* from the whole group of (286) men considered.

(72) Figures 6–10 were calculated from the observed data. They show similar representations of estimated probabilities for other Adverse Effects and they indicate the ranges of exposure measures used in their derivation.

(73) Figure 11 summarizes the results in the form of a (cumulative) plot of estimated probabilities that at least one of the seven Adverse Effects may occur. In

* This is not to say that there is *no* real association, but only that the association is not to be inferred simply from the presentation in Fig. 4. In fact, Fig. 2 suggests strongly that the probability of finding radiological signs of parenchymal changes does increase with increasing exposure.

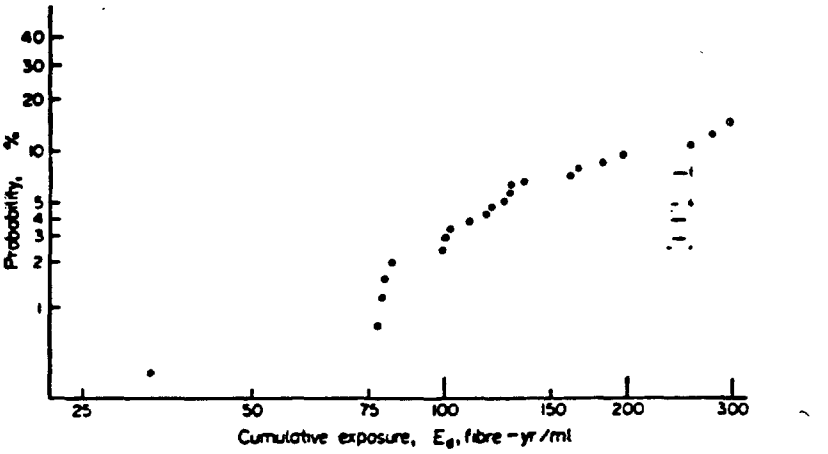

FIG. 4.

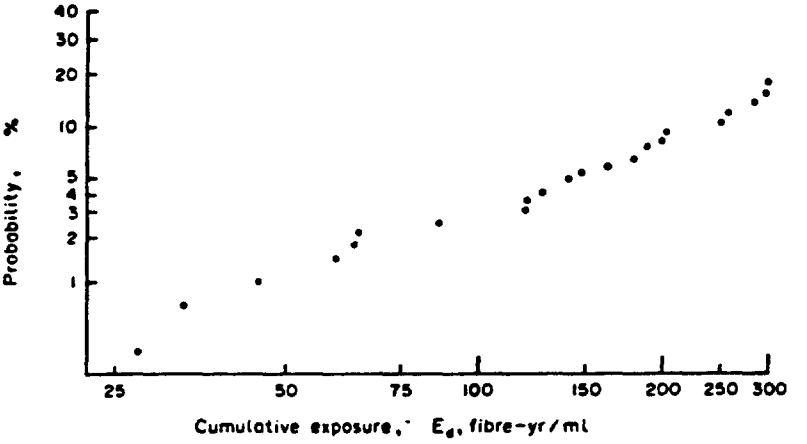

FIG. 5.

FIGS. 4 and 5. Product-limit estimates of probabilities of the occurrence of Adverse Effect A in 22 men (Fig. 4), and of 22 simulated events in the same group of 286 men from Factory A (Fig. 5). In both cases the cumulative probabilities, on a logistic scale, are plotted against exposures E_d, defined in Paragraph 40 of the text, on a log scale. The 22 men whose exposures are shown in Fig. 5 were selected at random from the 286 for whom the presence or absence of Adverse Effect A was assessed. Figure 5 illustrates that graphical representations of cumulative probabilities as in Figs. 4 and 6–11 are not to be interpreted as if they were scattergrams.

those cases where more than one Effect was noted in the same man, the measure used to order the event in relation to increasing exposure was that corresponding to the earliest occurrence. Again, it is assumed for this purpose that the observed radiological changes occurred at points in time corresponding approximately to the cumulation of exposure E_d. Figure 11 shows that five Adverse Effects occurred before exposures amounting to 25 fibre-yr/ml had been accumulated. Two of them, including the earliest, were unusually rapid rates of reduction in *TI*co (Effect E; see also Fig. 8). The other three refer to Effects F ($FEV_1/FVC < 0.7$), at 7 fibre-yr/ml; G (post-tussive chest sounds), at 8 fibre-yr/ml, and C (unusually rapid rate of reduction in FEV_1), at 24 fibre-yr/ml.

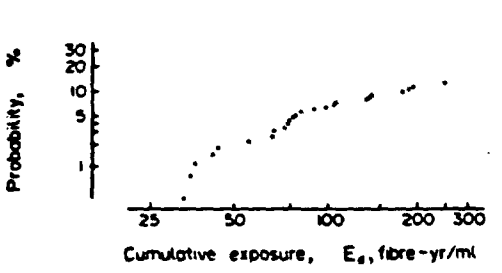

FIG. 6. Effect B.

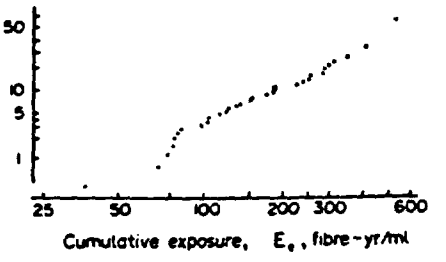

FIG. 7. Effect D.

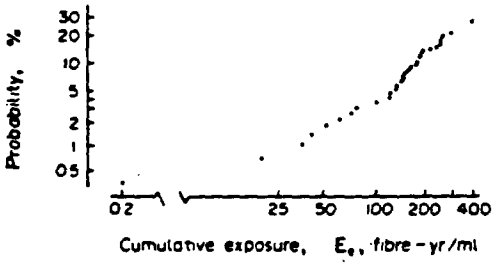

FIG. 8. Effect E.

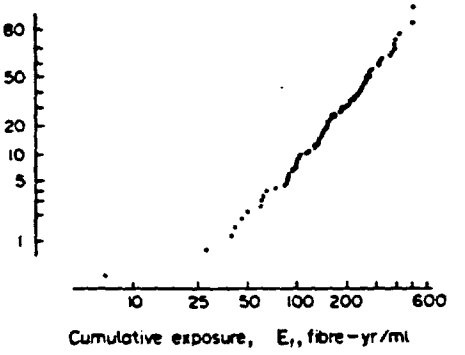

FIG. 9. Effect F.

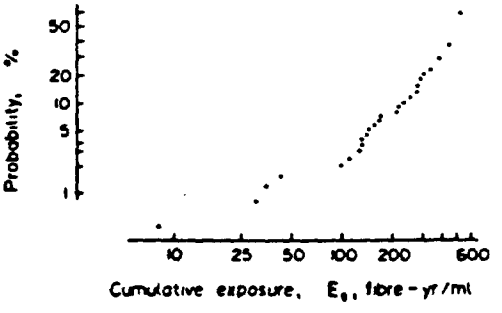

FIG. 10. Effect G.

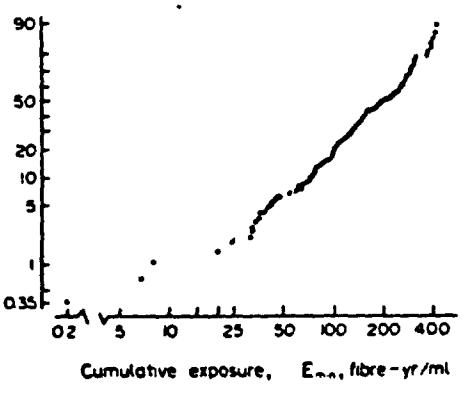

FIG. 11. Any Effect.

FIGS. 6–11. Product-limit estimates of probabilities of occurrence of Adverse Effects B, D, E, F, G, and (Fig. 11) of any one of the six Adverse Effects (A–G) before accumulation of the exposures indicated. N.B. (1) The Adverse Effects are defined in Table 14. (2) E_d is defined in Paragraph 40 of the text. (3) E_e is an estimate of the cumulative exposure up to the mid-point of the intervals over which the rates of reduction in lung function were determined. (4) E_f and E_g are estimates of cumulative exposures up to the points when the Effects F and G first occurred. (5) Where more than one Adverse Effect occurred in the same man, the exposure (E_{min}) shown in Fig. 11 corresponds to the occurrence of the earliest of these Effects. (6) The interpretation of graphs of this kind is discussed in the text (Paragraphs 47, 66, 71 and 74).

(74) The various graphical presentations of the occurrences of Adverse Effects in the Factory A data suggest that improved estimates of the corresponding probabilities might be obtained by fitting straight lines to the points shown. This would be equivalent to postulating a logistic model as appropriate. BERRY *et al.* (1979) and PETO (1978) discuss this and alternative mathematical formulations for data of the kind considered here. The graphs indicate that a logistic model would be plausible for cumulative exposures higher than about 100 fibre-yr/ml. But the scatter of points below about 100 fibre-yr/ml show deviations which are not consistent with a straight line on the logistic-log scale. It would therefore be unwise to use such fitted lines to estimate probabilities corresponding to exposures less than 100 fibre-yr/ml.

ADDITIONAL COMMENTS

(75) Paragraphs 27–42 of this Appendix describe results from a radiological study arranged by the Committee in January 1978. From an epidemiological point of view, these data are the most reliable of all those considered because they were obtained under controlled conditions. The Committee's interim statement, dated 25 April 1978, incorporated a large part of the radiological results, but it was noted that more data were being collected and that the statistical analysis was incomplete. Attention was drawn particularly to the need to document details of persons who had not completed exposure periods amounting to 10 yr or more in the interval 1 January 1951 to 31 December 1976 and who had been excluded from the study on those grounds although they had worked with asbestos for the first time after January 1951. The additional work on this matter was pursued during 1978 and 1979. The results are reported now in Paragraphs 5–15.

(76) The appendix to the Committee's interim statement included also an analysis of material describing the occurrence of Adverse Effects in the Factory A group. Those data are not reproduced here. They were based on a review by Factory A medical staff of their medical records. That review identified individuals who were considered to show evidence of having experienced an Adverse Effect, using clinical judgement and taking into consideration the views of the medical members of the Committee.

(77) The Committee resolved subsequently to study the individual lung function and clinical records from Factory A in relation to the corresponding exposure data. Results from this work are described in Paragraphs 43–45. There was no evidence that the *TlCO* measurements or the ratios FEV_1/FVC were related to the estimates of exposure to asbestos.

(78) Nevertheless, the Committee had decided that the available medical data from Factory A, and that from Factory B, should be used to try to determine the occurrence of Adverse Effects as defined in the recommendations from its medical members. Implementation of that decision presented technical and conceptual difficulties from a statistical point of view. These are discussed in Paragraphs 46–50.

(79) The way that these difficulties were tackled is described in Paragraphs 52–62. The methods adopted were arbitrary to some extent, of necessity, and they are therefore open to challenge. However, they represent an effort to translate the essence of the items incorporated in the recommendations from the medical members of the Committee into unambiguous decision rules that could be applied to the available data. The rules were applied and the results are reported in Paragraphs 63–64.

(80) The Committee was anxious to compare the implications of these results with those published previously (BOHS, 1968; BERRY *et al.*, 1979). With this in mind, the available data were subjected to an analysis similar to that adopted in earlier studies, despite reservations about the validity of such presentations (Paragraphs 67 and 74), the ambiguity of how to interpret the Adverse Effects identified (Paragraph 47), and the absence of evidence that the lung function changes considered or the FEV_1/FVC ratios were correlated with the available data on exposure to asbestos (Paragraphs 62 and 45).

(81) The results from this work are also reported above (Paragraphs 65–74), but it is appropriate at this point to reiterate two major qualifications that are attached to these findings:

(i) The Adverse Effects described do not constitute diagnoses of disease. They are statistical definitions of events that might be associated with exposure to asbestos or that may occur also in the absence of such exposure.

(ii) On their own the graphical representations of derived cumulative probabilities of the occurrence of these Adverse Effects cannot be interpreted as demonstrating necessarily that these Effects are correlated with cumulative exposure to asbestos dust.

SUMMARY AND CONCLUSIONS

(82) Radiological, physiological and clinical data from two asbestos factories have been examined in an effort to establish what cumulative exposure to asbestos dust is associated with the first signs of adverse pulmonary effects.

(83) Persons included in the study had all started work with asbestos after 1950 and had then been exposed to asbestos for at least 10 yr.

(84) An effort was made to assess approximately the extent to which criteria for inclusion in the study may have influenced results. As far as Factory A is concerned, it appears unlikely that the criteria for admission excluded many who had suffered serious health effects arising from their exposures (Table 1). Nevertheless, it is recognized that some of those who had worked for less than 10 yr with asbestos (and who therefore were not studied) may have shown early adverse respiratory signs.

(85) The data from Factory B cannot be regarded as a representative sample of possible adverse effects from exposure to asbestos. This is because the medical-care policy at this factory was to remove persons from exposure to asbestos whenever clinical examination indicated early signs of lung function abnormalities. Such persons were not included in the study, regardless of their exposure times, and some of them may have developed the functional abnormalities as a result of their work with asbestos.

(86) Three physicians made independent assessments of chest radiographs from 295 men who had worked at Factory A. Collectively, the results show an association between the occurrence of parenchymal changes during 10–26 yr intervals and estimates of cumulative exposures to asbestos dust up to approximate points in time when the changes are likely to have occurred (Table 11 and Fig. 2).

(87) It was not possible to estimate cumulative dust exposures for most persons in the Factory B study group, but there was some evidence that longer periods of exposure at Factory B were associated with higher chances of developing small opacities on chest radiographs (Table 12 and Fig. 3).

(88) Small opacities were detected more frequently among smokers and ex-smokers from Factory A than among non-smokers (Table 10), but the parenchymal changes observed in the Factory A group are not wholly attributable to smoking habits.

(89) Overall, readers judged 5.3% of films from Factory A and 3.8% of those from Factory B as showing obliteration of the costophrenic angle. Neither of these results differed significantly from observations of similar abnormalities in the 160 radiographs of persons who had not been exposed occupationally to asbestos. Other pleural abnormalities were recorded even less frequently and their prevalence among asbestos-exposed persons was not distinguishable statistically from the assessment of control films (Table 7).

(90) Standardized levels of FEV_1 and FVC among men who had accumulated relatively high exposures in Factory A were lower than results from men who had received low exposures (Table 13). The negative correlations with dust exposure were statistically significant at the 6% level. Gas Transfer Factor measurements also showed a negative correlation with dust, but the residual variability in the date was such that the apparent relationship could easily have arisen by chance ($P > 0.7$).

(91) The radiological, physiological and clinical data from Factory A were used to identify persons who exhibited one or more of seven statistically defined events possibly indicative of an early adverse medical effect of exposure to asbestos (Table 14). Estimates were made also of the cumulative exposures to asbestos up to the approximate times when these features were likely to have occurred. Cumulative probabilities of the occurrence of the defined events before the passage of these times were calculated and they are expressed graphically as a function of the corresponding estimated exposures (Figs. 4, and 6–11).

(92) The results suggest that for cumulative exposures up to about 25 fibre-yr/ml, the probability that *any one* of the seven defined events occurs is less than 2%. For exposures less than 50 fibre-yr/ml the estimated probability is less than 7%; for exposures up to 100 fibre-yr/ml the (cumulative) probability increases to about 17–20% (Fig. 11).

(93) The statistical definitions of the events concerned are based broadly on guidelines suggested by medical advisers regarding 'the earliest index that the chest of an asbestos worker was adversely affected from whatever cause'; they do not constitute clinical diagnoses of disease. The exposures refer, in the main, to dust clouds in the work areas where men are employed ('static' sampling), rather than to dust in the immediate vicinity of individuals' breathing zones. They approximate to time-weighted concentrations of fibres in sampled air determined by the membrane filter counting method used at Factory A since 1977.

(94) Much of the material used for this study originates from medical and environmental records that were not collected for epidemiological purposes. Every effort has been made in the data processing and statistical analysis to avoid pitfalls that can arise in this situation. However, a not easily quantifiable, but nonetheless important, residual uncertainty about the reliability of results is unavoidable in these circumstances. The above summary of findings reflects this uncertainty.

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