

REPORT OF THE SUB-COMMITTEE ON ASBESTOS ON

A STUDY OF THE HEALTH EXPERIENCE IN TWO UK ASBESTOS FACTORIES

1. Introduction

The UK 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 in 1968, describing a study on a cohort of men in an asbestos textile factory (Factory A), first employed since 1st January 1933 and still employed on 30th June 1966, with at least 10 years' 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 years) considered to carry a one per cent risk of a worker exhibiting the earliest signs of the possible effect of asbestos exposure. The figure arrived at was 100 fibre-years/ml, giving an exposure of 2 fibre-years/ml over a working life of 50 years, 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 years' service since 1933, were not included if their exposure had ceased prior to 30th June 1966 as a result of leaving asbestos areas or death.
- b) Similarly, persons reaching 10 years' service after 30th 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 rates, but this is not always so. There are other early signs which might well precede rates 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.

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Since 1968, a good deal of extra information has become available on the adverse effects of exposure to asbestos. Diagnostic methods have improved, in particular the introduction of lung function measurements and the adoption of an agreed classification for the assessment of asbestos workers X-ray films (the ILO U/C 1971 Classification). In addition, considerably more experience has been gained in dust sampling and analysis for the measurement of exposure and some data have become available from a second factory (Factory B). In this factory also, however, while the fibre used was principally chrysotile, some crocidolite-based yarn was processed at one stage during the study.

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 years' service between 30th June 1966 and 31st December 1972. Men who had left the factory between those dates were also included.

The work of the BOHS Sub-Committee was to some degree overtaken by events. An Advisory Committee on Asbestos was set up by the Health & Safety Commission in 1976, and a Medical Working Group of this Committee was given the task of reviewing all the available information on asbestos and health and making appropriate recommendations. Although the BOHS Sub-Committee's study was still at an early stage, it provided for the Medical Working Group 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 Medical Working Group when submitting its report to the 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. They state 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 person should be occupationally exposed".

2. The Work of the Present Sub-Committee

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

- a) In addition to the cohort from Factory A (all 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 1st January 1951, because no dust exposure information was available prior to that date, and who had at least 10 years accumulated exposure by 31st 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.

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- c) Efforts were made to calculate the dust exposure for each individual in both cohorts, 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 year period of the study.
- d) At the outset, the objective of the Sub-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 other factor is cigarette smoking. There is a wealth of epidemiological evidence that smoking has a profound effect on the incidence of lung cancer in asbestos exposed workers, multiplying by many times the risk run by smokers in the general population.) In the cohorts studied by the Sub-Committee detailed mortality records were not generally available.
- e) The Sub-Committee was therefore obliged 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.

3. The Medical Data

Medical information which was made available to the Sub-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, who were asked to classify them independently in accordance with the ILO U/C (1971) International Classification of Radiographs of Pneumoconioses.
- b) All available information on medical examinations and lung function measurements carried out over the period of the study was provided by the medical officers of the respective companies. At Factory A, workers had been given chest radiographs every three years from 1951 to 1967 and every two years thereafter. Lung function tests were introduced in 1967 and had been carried out every two years. At Factory B, chest radiographs had been carried out every two years from 1951 (unless there was an indication to X-ray more often) and lung function tests had been carried out every two years since 1960.

In order to arrive at an agreed interpretation of these data, the medical members of the Sub-Committee were asked to meet as a Working Group under the chairmanship of Dr. W.J. Sulther "to determine the first medical indication or indicators of adverse effect of exposure to asbestos dust inhalation". A full report of their deliberations is given in Appendix 1.

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4. Dust Concentrations

a) Factory A

The Casella Thermal Precipitator (T.P.) was used from 1951 to 1960 and all monitoring was static, i.e. the sampling was conducted with a free-standing sampling instrument having the air inlet at head height and the instrument placed 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 x) under dark ground reflected light using a 4 mm objective. Fibres were not specifically looked for and all particles judged to have an equivalent diameter of 0.5 μ m and above were included in the count. Between 1960 and 1964, the Long Running Thermal Precipitator (L RTP) was used and again monitoring was static. With this instrument it was possible to count fibres at about 500 x magnification and the results were expressed in fibres/ml using the convention that only fibres greater than 5 μ m long and having an aspect ratio greater than 3 to 1 were counted. Later (circa 1970) when guidance notes on counting were published for outside bodies, a further convention limiting the count to fibres less than 3 μ m in diameter, was recommended. This 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 (set to give similar numerical results). The membrane filter samples were counted at about 500 x magnification under phase contrast conditions and the results were again expressed in fibres/ml. 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 (B.S. 1625 - 1963) mounted in the microscope eyepiece, instead of covering whole microscope fields of view. This had the effect of increasing the number 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 1960's (used in the 1968 BOHS study) would need to be multiplied by 2 to compare them with counts taken today. In an attempt to understand the early figures and relate them to 1977 membrane filter counts, an investigation was carried out running all instruments side by side. The samples obtained from the older instruments were counted using identical techniques to those employed in the factory when those instruments were in use. Bearing in mind that considerable extrapolation was necessary because conditions and processes in the factory are to-day very different, the following approximate relationships were derived:-

1977 Membrane Filter = 0.07 TP
 1977 Membrane Filter = 2.2 L RTP
 1977 Membrane Filter = 2 x 1964-74 Membrane Filter.

b) Factory B

The Owens Jet Impinger was in use in 1951 and continued to be used routinely until 1959. Up to 1956, the "ashed" coverslips were counted at a magnification of 900 - 1000 x and no differentiation was made between fibres and particles. After this date, the count

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was limited to particles of size greater than 1.0 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 count was observed as compared with counting full microscope fields.

In addition to membrane filters, the Royco Instrument was widely used from 1963 onwards. It is claimed that by careful calibration of the instrument against membranes, the Royco was more reliable than microscope counting.

c) The Effect of Personal Sampling

Towards the end of the period covered by the study, from about 1974 onwards, personal sampling was being increasingly used for biological monitoring. As experience was gained, it became apparent that the results of personal samples did not generally relate numerically to the results of static samples in the same working area, even for samples taken simultaneously. The Sub-Committee therefore made a study of the information available in this field as detailed in Appendix 2 and accepted the following conclusions:-

- (i) When identical sampling methods and simultaneous sampling is undertaken and the distances between the static and personal sampling points are reasonably small, most of the personal sampling results obtained in a given working location are higher than those obtained from static tests.
- (ii) The differences between the two types of results tend to be greater when the static sampling points are relatively remote from the dust emission points (e.g. when background static sampling is adopted).
- (iii) In certain cases results from static sampling may be higher than those from personal sampling, due to factors such as the positioning of the static sampling point with respect to air extraction systems.

5. The Groups Studied

a) Factory A

300 men met the criteria for inclusion in the study, but no medical records were available for 5 of them. The present study is therefore concerned with 295 men. It was recognised that the 10 year restriction might have resulted in bias if

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many persons with less than 10 years exposure had suffered adverse medical 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 years 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, 13 of whom had worked for more than 10 years. 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 one year's exposure up to the end of 1976 and only about 6% had worked for between 5 and 10 years. Of 16 men who had left the factory for medical reasons, one had worked with asbestos for 3 years and the remaining 15 had less than one year's 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 already suffered serious health effects arising from their exposure.

b) Factory B

Although at least 499 persons met the criteria for inclusion in the study, some had to be excluded because of incomplete medical and radiological data. In the end, only 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 years. The pattern of exposure in this group was different from that of Factory A, 22% having been exposed for less than one year, as against 71%, and 72% for 1 to 5 years, as against 22%. 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 been exposed for from 1 to 5 years. One reason for this difference was that a number of people were advised to leave asbestos areas in the early 1960s on the appearance of early signs of lung function abnormality. These persons were lost to the study, although some may have developed these abnormalities as a result of their exposure. It was also possible that some had completed more than 10 years' 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.

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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 293 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 the 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

An estimate of exposure to asbestos dust year by year was provided for each man, without knowledge of his medical history. Using the conversion factors given in Paragraph 4 (a), these exposures were expressed as fibre-years per cubic centimetre, assuming static sampling by membrane filter and counting to the 1977 standard method. No attempt was made to convert to personal sampling, because of the uncertainties attending such conversion (see Paragraph 4 (c) and Appendix 2).

b) Factory B

Information was given on the time worked by the persons concerned at the various factory locations and measurements of dust concentrations at some of these locations were provided. There were, however, many gaps in the records and 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

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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 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 important to note that the differences between readers were larger than the differences between factories.

(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 on 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

In an effort to relate profusion of combined small opacities with cumulated dust exposure, four measures of exposure were examined for each individual. The first (E_1) 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_2) was the exposure incurred between films. The third measure (E_3) was the cumulative exposure from commencement up to the later film i.e. $E_1 + E_2$. The fourth measure (E_4) was an

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attempt to approximate the exposure up to the point when the observed change occurred and was taken to be $E_a + 1/2E_b$. No association could be found between radiological change and E_a or E_b separately. There was a weak association with E_a , but the strongest was with E_b and it was this measure of exposure which was finally adopted.

(ii) Factory B

As referred to in Paragraph 5 (d) (ii), the way in which the dust data had been collected for Factory B, together with the number of changes which had been made over the period of the study, precluded any attempt to estimate cumulative dust exposures for individuals. Reliable information on time worked, however, 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 FEV₁, FVC, CTF and the ratio FEV₁/FVC. Only for FEV₁ and FVC did the dust exposure correlate significantly at the 6% level; neither with CTF nor with FEV₁/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. Unfortunately, this analysis had to be abandoned because the sub-set of data suitable for detailed study was seriously biased epidemiologically (see also 5 (a) (ii) above).

10. The Criteria for Adverse Effect

Further analyses were made in response to advice from the medical members of the sub-committee on what constitutes the earliest

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medical indication of adverse effects of exposure to asbestos dust (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 FEV₁) 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.

11. The Occurrence of Adverse Effects

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 (FEV₁/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. The distribution of men with one, two and with three or more effects was 58, 26 and 16 per cent 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 the distribution of persons with one, two and with three or more effects was not dissimilar from Factory A, being 66, 19 and 15 per cent respectively.

12. Interpretation of the Data on Adverse Effects

This was only possible 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, C, D, E, F and G are shown in Figures 4, 6, 7, 8, 9 and 10 of Appendix 3. The results are summarised in Figure 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-years/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 FEV₁), F (FEV₁/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-years/ml (50 fibre-years/ml by 1968 standards) preclude this. It would therefore be unwise to use such fitted lines to make predictions where exposures have been below this level.

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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 years 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 1.8% 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) Standardised levels of FEV₁ and FVC among men who had accumulated relatively 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 FEV₁/FVC could easily have arisen by chance in view of the residual variability in the data.
- (vii) The results suggest that for cumulative exposures, based on static tests, (see Paragraph 4 (c)) up to about 25 fibre-years/ml, the probability that any one of the seven defined events occurs is less than 2%. For exposures less than 50 fibre-years/ml, the estimated probability is less than 7% and for exposures up to 100 fibre-years/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 Sub-Committee's 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 asbestos-related disease.

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