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PLAINTIFF'S EXHIBIT

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Dear Hilton,

I am enclosing a copy of a further draft of the morbidity study. This is a copy which I have submitted to the Medical Working Group of the Asbestos Advisory Committee. Since I last wrote to you ~~that~~ various difficulties on the publication of the paper have been removed.

I have included some details of lung function and radiology as you suggested, but have limited this to men first employed after 1950 in view of the uncertainty of the earlier dust concentration which were not measured.

The priority now is to have a paper published. I have been discussing this with Dr. Gilson and there are a number of places where he thinks expansion is necessary. One of these is that a fuller description of the family of dose measures is needed but so that this does not detract from the main results the details should go into an appendix. Another point is that he thinks we should draw attention to a number of certified men in Tables 2 and 3, where it is not at all clear why they have been certified; the criteria of McVittie which we quote appear not to be satisfied.

I hope that you would like to be an author of the paper, and I don't think that management at T.B.A. would stand in your way. Perhaps you would let me know together with any comments you have.

With best wishes.

Yours sincerely,

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HEALTH AND DUST EXPOSURE IN A GROUP OF ASBESTOS WORKERS

The study described in this paper was carried out with considerable contributions of data and expertise from Drs. J.C. Gilson, S. Holmes, H.C. Lewinsohn and S.A. Roach. However it must not be assumed that any of these contributors accept all the points put forward; the paper will be revised for publication after consideration of their criticisms.

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INTRODUCTION

In 1968 the British Occupational Hygiene Society published hygiene standards for chrysotile asbestos dust (BOHS, 1968). One of the features was that risk was related to accumulated exposure, that is the sum of concentration x period of exposure to that concentration over the whole period of exposure. With an accumulated exposure of 100 fibre-years/cm^3 it was concluded that it was probable that the risk of contracting asbestosis would be less than 1%, where asbestosis was defined as the earliest demonstrable effects on the lung due to asbestos and in practice on the presence of basal rales. The recommendations were made with two main notes of caution. First, it was pointed out that few data were available and apart from the early study in the United States (Dreessen et al., 1938) the only relevant data came from an asbestos textile factory in England and consisted of 290 men, 16 of whom had basal rales. Secondly, it was observed that the conclusions could be biased because the data were obtained on men working at the factory at a particular time, and so were subject to selection as men left the factory possibly as a result of asbestosis. These two criticisms were repeated by Holmes (1973) and Berry (1973). Another possible bias was that exposures were considered from 1933 onwards but dust figures were only available from 1951. The early dust levels were estimated as at least 1½ times those in 1952 to give a lower limit to the exposure for workers with the longest durations.

In this paper we give the results of a later study at the asbestos textile factory considered previously (BOHS, 1968). In this revision both the medical data and the information about exposures have been improved. This has been possible for a number of reasons. First,

the time over which observations have been made has been extended by 6½ years so that the number of man-years of observation is greater. Secondly, the system of medical surveillance has been made more systematic and comprehensive by the regular use of lung function tests; also technically improved chest radiography with independent multiple readings using the ILO U/C 1971 classification (ILO, 1972) has been introduced. Thirdly, a high proportion of ex-workers co-operated by returning to the factory for a medical examination and chest radiograph. Fourthly, detailed job histories of all the men have been obtained by examining personnel records and departmental information in the factory.

The revised study was undertaken for the purpose of reviewing the British Occupational Hygiene Society's Hygiene Standard for chrysotile (BOHS, 1968; BOHS, 1973), but in this paper we are concerned with presenting the data and not with recommending standards.

METHODS

The group studied

Men who had worked at the asbestos textile factory for 10 years or more with all their exposure after 1st January 1933, and were still employed at that factory on 30th June 1966, were reported on in 1968 (BOHS, 1968).

The present study consists of 285 of the 290 studied previously with the addition of 107 men who completed 10 years' service between 30th June 1966 and 31st December 1972. Men who had left the factory after 30th June 1966 were included.

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When the detailed job histories were being compiled, it was impossible to produce an unambiguous job history for one man, and therefore he was excluded. Also 12 men had worked for several years (at least 7, average 17) in a subsidiary asbestos textile factory, where they were mainly employed in opening bags of asbestos. Dust conditions at this factory are unknown for the period in question, but were probably markedly different from the main factory. Therefore these 12 men were also excluded leaving 379.

Medical information

For all the men the following were extracted from the records in the factory's medical department:-

(i) the most recent chest radiograph

(ii) the date of the most recent medical examination and whether basal crepitations (rales) that did not clear on coughing had been heard, and if so, the date they were first heard and of the previous medical examination.

(iii) whether the factory medical officer thought that the man possibly had asbestosis, and if so, the date of first suspicion and of the previous medical examination.

(iv) details of the most recent lung function data, consisting of forced expiratory volume (FEV_1), forced vital capacity (FVC), functional residual capacity (FRC), total lung capacity (TLC), residual volume (RV), transfer factor (TL) by the single 'breath' technique and pulmonary arterial pressure of carbon dioxide ($PaCO_2$), together with height, weight, and smoking habits. Since lung function

testing was only introduced in 1967, data were available on only 311, or 82% of the men.

The factory medical officer wrote to all the men who had left after 30th June 1966 inviting them to attend for a chest radiograph and medical examination. Out of the 113 not known to be dead, 68 (60%) accepted this invitation, 13 (12%) refused or failed to attend, and the remaining 32 (28%) either did not reply or did not receive the letter. The most recent chest radiograph was taken in 1970 or more recently for 88% of the men in the cohort.

The men working in scheduled occupations have periodic medical examinations by the Pneumoconiosis Medical Panel under the Prescribed Diseases Regulations of the National Insurance (Industrial Injuries) Act, 1946. Also some men applied to the Panel for certification as asbestotics. We were allowed access to the records at the Pneumoconiosis Medical Panel for the men in the study and noted whether crepitations had been recorded at the periodic examinations and which men had been certified as asbestotics, together with the date of certification and degree of disability. Information on certification is complete up to 1975 on all men, including those who had left the factory.

The diagnosis of asbestosis is based upon the presence of physical signs of pulmonary fibrosis, radiological appearances and lung function defects. McVittie (1965) indicated that the Pneumoconiosis Medical Boards diagnosed asbestosis in the presence of an adequate exposure history, on the finding of end-inspiratory basal

rales, finger clubbing, radiological appearances and alterations of lung functions, i.e. gas transfer defect and restriction of ventilation. An adequate exposure history plus two of the other relevant criteria listed above is adequate for diagnostic purposes for certification. The Board, before diagnosing asbestosis, must be satisfied that there is disablement of the individual.

It has been the practice of the factory medical officer to examine all asbestos workers routinely on employment and then every two years and to advise them to change to less dusty jobs if he thinks they are developing symptoms or signs of early asbestosis. The company has supported this policy by paying possible asbestosis cases who change jobs a guaranteed basic wage plus an ex-gratia payment.

Workers had chest radiographs taken every 3 years from 1951 until 1967 and since then annually. Lung function tests were introduced in May 1967 and are carried out every two years.

The Medical Officer based his suspicions upon basal rales (crepitations), radiological changes of varying degree, altered lung function as indicated by a falling gas transfer factor, restrictive changes in lung volumes or ventilatory capacity.

Possible asbestosis is a diagnosis based upon minimal signs which may not be sufficient for the Pneumoconiosis Medical Board to award Disablement Benefit, but sufficient to alert the Medical Offier to the possiblility.

The radiographs were read in random order and without any knowledge of the identity of the man or of his job history by four readers (Drs J.C. Gilson, P.G. Harries, H.C. Lewinsohn and V.H. Springe independently using the ILO/UC 1971 classification (ILO, 1972).

The medical information for each man was brought together and examined by a clinician (Dr. J.C. Gilson), independently of the factory medical officer (Dr. H.C. Lewinsohn), and a list was made of cases where there was a possibility of conflict between the factory medical officer's assessment of whether or not a man might have asbestosis and the available evidence. This list contained 12 men whom the factory medical officer had placed in the possible asbestosis category and 37 men whom he had not put in this category. The clinician and the medical officer examined the medical files of these 49 men together and 7 men out of the 12 were removed from the possible category and 5 out of the 37 were added to it. The 7 men were removed because the signs were due to other disease, e.g. heart disease, bronchitis, or in 3 cases the man had died and asbestosis had not been recorded at post-mortem.

Dust exposure

A detailed job history was produced for each man by an independent industrial hygienist (Dr. S.A. Roach) who visited the factory and examined the employment records. A total of 222 job descriptions was used. This was supplemented by a finer breakdown for men working in the carding area during 1961-72, adding another 14 job descriptions. For each job description a dust level was calculated by taking the average of the levels measured at the dust

sampling locations appropriate to the job. In all 64 sampling locations had been used over the period 1961-72 and the results were calculated for each year.

For 1951-60 fibre counts were not available but thermal precipitator particle counts were available for 1952 and 1960. The fibre counts for 1951-55 were taken as those of 1961 multiplied by a constant representing the difference 1952/1960 determined by the thermal precipitator. This constant was dependent on job, ranging from 1.4 to 3.4 (BOHS, 1968). The counts for 1956-60 were taken as the same as 1961-65. There were no dust measurements before 1950. For 1933-45 the concentrations were taken as 1.5 times those in 1951 and for 1946-50 as 1.25 times the 1951 values. These concentrations, particularly for the early years, are probably underestimates of the actual concentrations (BOHS, 1968).

Some men were coded as doing more than one job at the same time; the dust level has been taken as the mean of the jobs. When a man was away from the factory, or at the factory but working in a job away from the production area, it was assumed that there was no exposure to asbestos.

As an indication of the dust conditions within the factory Table 1 gives the mean dust level and the percentages of men in the study in the ranges, 0-2 fibres/cm^3, 2-5 fibres/cm^3, and greater than 5 fibres/cm^3 for certain years, for those men in the study who were working in production areas on 31st December of the year concerned.

The type of asbestos imported to the factory since 1933 has been almost exclusively chrysotile. However, because of the possible special risks from crocidolite, a search has been made of company records to ascertain how much crocidolite has been imported. For those years with traced records the import of crocidolite was of the order of 10 tons compared with several thousand tons of chrysotile.

RESULTS

Numbers with conditions

82 men were recorded as having crepitations, 58 possible asbestosis and 34 were certified as having asbestosis. There was considerable overlap between these 3 conditions and 89 had one or more of them. The numbers with different combinations of the three conditions are shown in figure 1, both for the whole group and for those first employed at the factory after 1950.

One man was certified on post-mortem findings, and in addition out of 19 non-certified cases who had died, there were 3 where asbestos exposure was considered contributory to death, who would probably have been certified if an application had been made. In contrast out of 8 cases certified during life who had since died, there were 3 in whom no asbestosis was found at post-mortem.

The information on crepitations and possible asbestosis is complete up to the medical previous to 31st December 1972, or in the case of those ex-employees who agreed to come back for a medical up to December 1973. The information on certification is complete up to 1975.

Some information on the 89 men recorded as having one or more of the three conditions, and the 3 men who would probably have been certified if a claim had been made, are given in Tables 2 and 3. This information includes a summary of the radiological and lung function data, and within each table the men are given in order of increasing cumulative exposure to asbestos on first diagnosis. In Table 4 exposure at the factory is summarised. In the lowest part of this table the cumulative exposures for those with signs (crepitations, possible or certified asbestosis) have been calculated up to the first occurrence of the signs. This means that within exposure categories the data cannot be directly interpreted as prevalences; e.g. for those first employed after 1950 although 4 out of 36 of those with less than 50 f-yrs/cm^3 had signs, the other 161 men are known to have reached 50 f-yrs/cm^3 without signs. The analysis given later takes account of this.

Comparison of record of crepitations by factory medical officer and at Pneumoconiosis Medical Panel (PMP)

All except 2 of the men in the study had been seen at some time at the PMP. The factory medical officer recorded crepitations at the most recent medical for 82 men and crepitations were recorded consistently or at the most recent visit to the PMP for 78 men, 51 of whom were also recorded as positive by the factory medical officer. Thus there were 31 men recorded as positive by the factory M.O. but negative by the PMP, and 27 negative by the factory M.O. but positive by the PMP. Some of these discrepancies were due to the time of the examination, e.g. 7 of the men read as positive by the factory M.O. and negative by the PMP had been seen more recently by the former.

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Other discrepancies were probably due to the transient nature of the sign in some men and in others there were no doubt genuine observer differences. Although there is agreement in the level of recording of crepitations by the factory medical officer and independent medical officers, the discrepancies are of importance and will be discussed later.

Relation between possible asbestosis and certification

Except for the one man who was certified on death, and had not been seen in the factory medical department within the previous 10 years, all the certified cases were also in the possible category. An analysis, using life-table techniques, has been carried out on the interval between suspicion and certification or on the follow-up since suspicion during which certification has not occurred. The results of this analysis are given in Figure 2, which shows the cumulative percentage certified plotted again time since suspicion; 25% became certified within 15 months of suspicion and 50% within 3½ years. 19 men remained uncertified after 5 years' follow-up since first suspicion; only one of them was subsequently certified in, on average, a further two years' follow-up.

The influence of smoking

Smoking habits were available for all except 3 of the men. The associations between the most recent smoking habits and crepitations, possible and certified asbestosis, are given in Table 5. There are clear associations with non-smokers and light smokers less likely to develop any of › conditions.

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Radiological findings, lung function and exposure

The radiological findings and lung function have been related to cumulative dust exposure restricting attention to those first employed after 1950 because of the lack of dust measurements in earlier years. The profusion of small opacities and bilateral pleural thickening are given in Table 6. There is little evidence of a relationship of these radiological features and cumulative exposure.

The lung function measurements have been expressed as percentages of predicted where the reference values have been calculated taking account of age and height from the reference relationships used at the factory; these relationships have been calculated on men not exposed to asbestos for FEV, FVC, TLC and TL. The analysis was carried out on 141 Caucasian men and the mean lung function values within exposure categories are shown in Figure 3. The regression coefficients on cumulative exposure are given in Table 7. FEV and FVC were significantly related to exposure, there was no evidence of a relationship for TLC whilst the relationship for TL, although it could have arisen by chance, cannot be considered unimportant

Analysis of medical evidence and dust exposure

If the factory medical officer suspected that a man had asbestosis then he would recommend transfer to a less dusty job. Any modification to a man's dust exposure based on medical signs is of relevance to the methods used to relate these signs to dust exposure.

An unbiased analysis can be constructed using the time at which each man with a positive sign first reached this stage.

Relationship of signs with cumulative dust exposure

The simplest measure of total exposure is the integrated dust concentration over the period of exposure. This measure, which is the one used previously (BOHS, 1968) gives equal weight to a given concentration independently of when the exposure occurred. The data are first presented in terms of this measure of dust exposure, and for all the men in the study. However for reasons which will be discussed later, this is not the most informative way of looking at the data.

The dose response relationship used previously (BOHS, 1968) was based on the assumption that the distribution of exposure at which a sign occurred was log-normal. A similar approach has been followed except that to simplify the calculations, a logit transformation has been used instead of a probit transformation. This modification makes only negligible differences to the fitted dose response relationships. The functional form of the relationship is

$$\ell n\{P/(1-P)\} = a + b\ \ell n(D)$$

where P is the proportion of men developing the sign before dose D. This relationship was fitted to the signs, crepitations, possible asbestosis, and certified asbestosis.

In the 1968 analysis, it was estimated that the 1% risk of crepitations was at a dose of 112 fibre-years/cm^3 with 90% confidence limits of 51 and 153 f-yrs/cm^3. In the present analysis

the response at a given dose is higher; e.g. at 112 f-yrs/cm³, there would be a 9.7% risk of crepitations, and the 1% risk would be at 43 f-yrs/cm³ (90% confidence limits, 34 and 52). For possible and certified asbestosis the 1% risks are at 55 and 72 f-yrs/cm³ respectively. The exposures estimated to give 1% risks are given as illustrations and not as suggested standards; other points have to be taken into account in setting standards.

There are three reasons for the differences in the dose relationships for crepitations between 1966 and 1972. First the dust exposures are now known more accurately and in particular it is known now that some men spent part of their time in less dusty jobs than the job category defined in 1966. It has not been possible to match exactly the 1966 group with the present group, but for those men in the present cohort who satisfied the criteria for inclusion in the 1966 cohort, the revised average cumulative dust exposure up to 30.6.66 was 131 f-yrs/cm³. In 1966 the average cumulative dust exposure was taken as 199 f-yrs/cm³. Thus with the more detailed job histories the figure of 112 f-yrs/cm³ calculated previously would be adjusted to 74 f-yrs/cm³. Secondly more crepitations were recorded than previously (82/379 = 22% compared with 16/290 = 6% in 1966). This is due both to the longer follow-up and to a difference between observers; the factory medical officer changed in 1967. Thirdly the 1966 data consisted entirely of men still working at the factory whereas in the present data, this selective effect, although still present, has been diluted by not excluding men who left the factory between the studies. As an indication of the difference this makes, if the analysis had been carried out only on those still employed at the end of 1972 then the prevalence of crepitations would have been 17% (42/241) compared with

22% in the whole group. This selective leaving appeared not to be caused by crepitations as such but was due to certification which was correlated with crepitations; 29 out of the 34 certified asbestotics were not employed at the factory at the end of 1972.

Date of first employment

Dust conditions in the factory are only known from 1951 onwards. The above analysis depends on the assumptions of what the dust conditions were in the period 1933-50, but an analysis restricted to men first employed from 1951 onwards would not. In addition such an analysis largely eliminates the bias due to the 1966 group consisting only of current employees. Therefore the analyses have been repeated for the group of men starting at the factory after 1950 (Figure 1). Figure 4 shows the observed and fitted relationships between the three signs and cumulative dose for men first employed after 1950. The exposures giving 1% risks were 37,46 and 63 f-yrs/cm^3 for crepitations, possible asbestosis and certified asbestosis respectively; again these figures are given only as illustrations.

Limitations of cumulative exposure

Comparing risk with the dust concentrations weighted by duration of exposure to them is unsatisfactory in the sense that the possibility of developing disease in the absence of dust exposure is assumed to be zero. There is evidence that this occurs in that 5 men changed from negative to positive crepitations and 2 from negative to positive for possible asbestosis, during a period when they were considered not to be exposed to asbestos.

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One possibility is to use a measure which weights the dust concentration in terms of the time since exposure. Such a measure would attach more importance to exposure a long time ago relative to more recent exposure, and would continue to increase after exposure had ended. The simplest way of doing this is to weight by this time, i.e. to weight the average concentrations in each year by the time the dust has been in the lung ignoring elimination (Jahr, 1974). This has been done for men first exposed after 1950 and gives quite different interpretations from Figure 4; e.g. 1% crepitations occur at a dose of 163 fibre/years^2/cm^3, i.e. at the end of 50 years' uniform exposure to a concentration of 0.13 fibres/cm^3 (using the unweighted cumulative exposure the same risk occurs after 50 years' exposure to 0.74 fibres/cm^3). For possible asbestosis and certification to concentrations of 0.19 and 0.37 fibres/cm^3 respectively.

Thus the choice of a suitable measure to compare against risk is highly critical, and it is not known what measure is most appropriate. In a sense both measures discussed earlier are extremes; the cumulative dose takes no account of when the exposure took place, and weighting by time since exposure takes no account of elimination of dust. If we suppose that, over a long period, dust is eliminated from the lungs at a rate proportional to the amount present, and that risk is caused by cumulative dose weighted by residence time of each contribution, then a family of measures of risk is produced (BTTA, 1975) This family is indexed by the rate of exponential decay, or half-life time, and as extreme cases contains the cumulative dose (half-time zero) and the cumulative dose weighted by time since exposure (half-time infinity).

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This family of curves has been fitted to crepitations and possible asbestosis for a number of half-life times for men first employed after 1950. It was found that it was not possible to estimate the half-life time giving the best fit to the data with any precision. In fact any value in excess of 3 years was adequate. Failure to estimate the half-life time is not surprising since the critical data would be observations on men who had left the factory many years previously.

Another way in which the risk measure may be inappropriate is that a given dose is assumed to be effective immediately. This could be amended by introducing a lag period for the developing of an observed effect, i.e. to assume that however severe the exposure disease will not be observed until some minimum time has elapsed since the start of exposure. There are insufficient data to estimate this lag period and the model has been fitted for a lag of 5 years.

Alternative dose-response model

The dose-response model used, i.e. that the logit of the prevalence is linearly related to the logarithm of the dose is arbitrary and, although it fits the data, other models may be appropriate. An alternative model is that the incidence of diagnosis of an adverse effect is proportional to the amount of dust in the lungs The alternative model may be written in the form,

$$\ell n\ (1-P) = -cD$$

The analyses have been repeated with this model and, after allowing for it containing one less parameter, it fitted as well as the logit model for the case with a 5 year lag provided that the half-life was at least 5 years.

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Implications for modern conditions

The disease pattern observed in this study has occurred as a result of higher dust levels than those which occur. now observed (Table 1). It is therefore of interest to estimate the likely disease pattern with current standards and the concentrations estimated to result in a given percentage of men developing disease. This has been done for continuous lengths of exposure of 30, 40 or 50 years. First the percentage of men estimated to have reached the possible asbestosis category by the end of a period of exposure to 2f/cm³ and secondly the estimated concentration necessary to limit this percentage to 1% have been calculated. These calculations have been based on the parameter estimates from the post-1950 group for both models for a range of values of the half-life time of dust elimination. The results are given in Table 8.

The choice of dust index is critical. This is mainly because of the large effect of varying the half-life time of dust elimination but there is also an effect due to assuming a lag period before the dust produces an effect. The choice of the functional form of the dose-response relationship is of little importance as long as the one used fits the data, since the two models gave similar results.

It is impossible with the data in the present study to discriminate between any of the possibilities listed in Table 8, except that those based on cumulative dose (half-life time = zero) may be relatively unsatisfactory.

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One reason for the wide range of values in Table 8 is that only 6 men have average exposures of less than 2 f/cm^3 (Figure 5) but all of the figures in Table 8 are below this value. Another reason is that the maximum follow-up in the data is only 23 years but longer exposures are considered. Therefore the figures in Table 8 are all estimates derived from extrapolations and are presented only to illustrate the difficulties of drawing any firm conclusions on the safety of present standards from the data of the more dusty conditions which existed until recently.

DISCUSSION

By restricting the main analysis to men first employed after 1950 two important sources of bias have been removed. First estimated dust concentrations for earlier years were not used. Secondly the selective effect of men leaving the factory for health reasons was largely eliminated. Men leaving between 1961 and 1966 were excluded but it is unlikely that this resulted in much bias. Certainly in agreement with other studies (e.g. Newhouse, 1973; Selikoff et al., 1973) there was little evidence of an excess lung cancer incidence in this factory until more than 15 years after entry (Peto et al., 1977). Of men starting in 1956 or later and working for at least 10 years, only 2 left within 15 years of first exposure with a possible health effect due to this exposure. Both of these men had crepitations but not more serious condition.

There are errors in both the response and dose in the data analysed. Evidence of error in response is provided by asbestosis not

being found at post-mortem in 3 out of 9 men with certified asbestosis. Also the differences in the recording of crepitations by the factory medical officer and the Pneumoconiosis Medical Panel indicated another source of error. Crepitations were not recorded at the PMP in those men with the lowest exposures who had crepitations recorded at the factory (Tables 2 and 3). The dust concentrations used were obtained from static sampling sites and therefore took no account of the work-style of individual men. The effect of these errors, even if it was valid to regard them as purely random, would be to give lower dust levels associated with low prevalences of signs than would have been the case if it had been possible to collect the data without error. Thus, for example, the dust concentrations given in Table 8 would require to be increased before being applied to a situation in which the dust was measured by personal samplers. We have no data on the likely size of this increase.

The data were analysed in terms of a family of risk measures assuming exponential decline of the amount of active material. This could be a result of both elimination of dust and a reduction in activity of the dust remaining. Beattie and Knox (1961) determined the mineral content in post-mortem lungs in workers from the factory and found no evidence of a decline in the first 8 years after exposure had stopped. However they took no account of changes in dust level and those who had survived for a period after leaving the factory were on average probably first exposed about 15 years earlier than those who died whilst still employed, and 70% of the men in the study had been employed before 1932. There is evidence that trace metals are leached from chrysotile asbestos in vivo (Morgan, Holmes & Gold, 1971; Morgan, Lally & Holmes, 1973). This leaching, and other changes within

the lungs, may decrease the hazard of the remaining material. The range of risk measures was introduced because it was felt that the simplest measure, that of cumulative exposure, was not completely satisfactory because it did not allow for development of disease after exposure had ended. The extent to which asbestosis develops after the end of exposure determines the most appropriate member of the family of risk measure. If cases continued to develop many years after the end of exposure, then a long half-life time would be necessary; otherwise a short half-life time would be necessary and use of cumulative dose would be approximately valid. Crepitations occurred in 5 men while they were not exposed but in 2 of these the change could have been due to the change in the medical officer. The ~~other~~ in the other 3 men changes could have been due to the transient nature of the sign or because crepitations occur for reasons other than asbestos exposure. Therefore the assumption that the changes were all associated with previous asbestos exposure is an oversimplification, and the study provides little evidence for rejecting cumulative dose and the predictions based on it in favour of the other measures. It must be emphasised that the range of risk measures is considered appropriate only for asbestosis, and not for lung cancer which continues to occur in severely exposed apart in excess of expectation many years after exposure had ended. The fact that it proved impossible to estimate the value of the half-life from the data was due to the inadequacy of the data and not of the family of risk measures.

A dose-response relationship between morbidity and asbestos exposure has been considered in two other studies. McDonald et al. (1974) considered several facets of disease, death, radiological changes pulmonary function changes and respiratory symptoms and related these to the cumulative exposure measured as millions of particles per cubic

foot times years (mpcf-yr). They concluded that there was a 1% risk of acquiring clinical significant disease for an exposure between 100 and 200 mpcf-yr. Some of their observations were based on a complete cohort but others only on current employees. Weill et al. (1975) considered lung function measurements and irregular small opacities on the chest radiographs and found little evidence of a dose-response relationship below 100 mpcf-yr. Using the results of simultaneous sampling with the impinger and fibre counting method they equated this dose with 200 f-yr/cm^3. Their observations were based on current employees only.

Comparing the present results with those given earlier (BOHS, 1968) shows that there is a higher prevalence of crepitations at any given dose than was observed previously. The amount of significant disease which would occur in those employed for a lifetime under the present standard is not known, if significant disease is defined as disability or shortening of life. The presence of crepitations would not be considered as disease in that sense. Peto (1977) has considered mortality within the same factory and concluded that 50 years exposure to 1 f/cm^3 might increase lung cancer mortality by a factor of 1.25 after retirement. This is equivalent to approximately 3% of those exposed to 2 f/cm^3 dying of lung cancer in excess of the number expected to die from this cause.

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A00704

Table 1

Dust exposure of men employed in certain years

Year	Mean dust level (f/cc)	Percentage of men exposed to ≤ 2 f/cc	2-5 f/cc	> 5 f/cc
1936*	13·3	0	0	100
1941*	14·5	4	0	96
1946*	13·2	2	2	96
1951	10·8	3	8	89
1956	5·3	2	40	58
1961	5·2	6	35	59
1966	5·4	23	22	55
1972	2·9	32	65	3

*there were no dust measurements in these years and the dust levels given are considered to be lower limits.

A00705

TABLE 2 - Information on men first employed at factory before 1951 with one or more of crepitations, possible Asbestosis or Certified Asbestosis.

Year started	Max. conc.	Crepitations Yr	Crepitations CUMD	Crepitations PMP	Poss. Asb. Yr	Poss. Asb. CUMD	Cert. Yr.	Cert. CUMD	Cert. %	Small opac.	Pleural thick.	Lung function FEV	Lung function FVC	Lung function TLC	Lung function TL	Died.
1946	7	70	47		70	47				1/0		50	60	110	90	
1944	18	68	60							1/0	3	80	80	120	90	
1947	7				64	70	65	72	10	1/1	4	70	80	100	90	
1947	6	67	74		67	74	70	86	10	1/2	4	70	80	110	70	
1945	8	70	84		70	83				1/2	4	80	120	150	80	
1946	8	69	93							0/0	1	100	110	100	100	
1948	9	72	99		70	92				0/1	1	110	100	120	90	
1947	10	67	101	✓	71	124				0/1						
1939	8	68	116	✓	59	115	59	116	10	3/3	2	80	80	90	80	1968 aged 60. Cancer Lung + asbestosi
1941	18	67	121	✓	67	121				1/1	2	110	100	110	80	
1946	23	71	124	✓	71	124	71	124	10	0/0		80	90	110	80	1974 aged 60. Retroperitoneal tumour, asbestosis
1937	28	67	124	✓	67	124	68	125	10	1/1		100	90	100	80	
1945	28	67	129							0/0		100	110	130	90	1969 aged 63. Cancer lung.
1940	8	73	138							0/0		30	50	70	60	
1939	18	67	138							0/1	2	60	80	100	80	1974 aged 71. cancer lung - no asbest
1939	23	65	139	✓						0/0		90	100	130	130	
1946	23	70	140	✓	70	140	71	146	10	1/0		100	120	110	60	
1933	11	68	142	✓	66	140				1/1	4	90	90	100	100	
1937	18	68	146							0/0		60	70	100	110	
1949	16	66	151	✓	66	151	67	153	30	1/1		90	90	110	40	
1937	8	65	152	✓	67	153	69	156	10	0/1		90	90	100	80	
1946	11	66	152	✓	66	159	69	174	10	3/2	1	60	60	90	70	
1937	23	65	159	✓	66	163	66	163	10	0/1	1					1968 aged 57. Coronary + asbestosis.
1941	18				70	159				1/0	1	60	80	100	50	
1948	16	67	162							0/0	2					

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[illegible] : page 2.

Year started	Max. conc.	Crepitations Yr	Crepitations CUMD	Crepitations PMP	Poss. Asb. Yr	Poss. Asb. CUMD	Cert. Yr	Cert. CUMD	Cert. %	Small opac.	Pleural thick.	Lung function FEV	Lung function FVC	Lung function TLC	Lung function TL	Died.
1937	28				73	168				1/0	4					
1945	28	65	168	✓	65	168	67	176	30	0/0		40	60	100	80	
1937	14	66	169	✓	66	169	65	169	50	0/1						
1949	23	69	185		67	171				0/1	3	110	100	110	70	
1939	14	68	179	✓	68	179				0/0		60	80	100	110	
1948	16	67	182	✓						0/0		20	50			1974 aged 66. Bronchitis, emphysema, nc asbestosis.
1939	13	70	183		70	183				0/0	1	90	90	100	70	
1948	23	67	192	✓	68	202	71	219	30	1/1	4	80	70	80	60	
1946	16	67	197		72	223				1/1	4	90	90	100	80	
1934	10	72	199	✓						0/0	1	80	100	120	90	
1941	18						(68	200)†		0/0	3					1968 aged 62. Mesothelioma.
1937	28	64	206	✓	64	206				1/2	3	80	80	90	90	1973 aged 68. Cancer lung.
1939	20	58	208	✓	63	211				2/2	3	90	110	140	90	
1939	14				69	211				1/0	2	100	100	130	120	
1946	16	73	212							1/0	4					
1946	23	66	216	✓	72	240	75	243	10	0/1	2	80	70	90	80	
1936	21	68	220	✓	68	220				0/0		100	90	100	70	
1948	23	67	228	✓	67	226				1/2	1	110	110	140		
1948	21	70	234	✓						0/1		80	100	130	90	
1935	13	66	235	✓	68	246	71	265	10	2/1	3	90	70	110	70	1973 aged 62. Cancer lung + asbestosis
1947	23	67	242		70	258	71	262	-*	2/2		80	60	70	40	1971 aged 62. Mesothelioma + asbestosis
1946	16	72	245	✓	69	232	72	249	10	1/0	2	90	80	100	60	
1945	28	67	251		70	270	74	277	30	0/0	1	70	70	90	100	
1933	50	71	259	✓	71	259	71	259	10	2/2		90	80	110	60	1975 aged 63. Cancer stomach and lungs, r asbestosis
1939	24	67	267		67	267				1/0	2	80	90	110	110	
1942	19	66	273	✓	66	273				1/0		110	110	150	110	

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ear rted	Max. conc.	Crepitations Yr	CUMD	PMP	Poss. Asb. Yr	CUMD	Cert. Yr.	CUMD	%	Small opac.	Pleural thick.	Lung function FEV	FVC	TLC	TL	Died.
[illegible]	23	69	275							0/0		80	90	90	90	
[illegible]	29	70	282							1/0		80	100	140	100	
[illegible]	21	70	282	✓	70	282				0/1	1	80	90	120	100	
[illegible]	21	65	289		68	313				1/0		80	70	120	70	1970 aged 67. Cancer G.I. tract.
[illegible]	23	66	315	✓	66	315	68	328	10	1/2	3	80	70	100	60	
[illegible]	20	61	321	✓	66	352	69	377	20	2/1		100	100	80	60	
[illegible]	29			✓			75	324	30	no recent film						
[illegible]	28	69	330	✓						0/0	1					
[illegible]	28	68	365	✓	69	369	72	382	10	1/1	3	90	80	80	80	
[illegible]	20	69	405		69	405				1/1	1	90	80	100	100	
[illegible]	20	67	436	✓	67	436	68	445	10	0/1	4	90	80	100	70	

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FOOTNOTE: Fuller details of the column headings are:- (i) maximum annual time-weighted average concentration is given in f/cm^3; (ii) all years of diagnosis are in the 1900s; (iii) CUMD, the cumulative exposure is in units of f-yrs/cm^3; (iv) if crepitations were recorded at the Pneumoconiosis Medical Panel, a ✓ is given under PMP; (v) for certification the % disability at first certification is shown; (vi) small opacities is the average over the four readers of the maximum of rounded and irregular opacities; (vii) the number of readers out of 4 recording pleural thickening is shown; (viii) lung function measurements are given as % of predicted normal.

* certified at death

† would probably have been certified at death if a claim had been made

TABLE 3: Information of men first employed at factory after 1950 with one or more of crepitations, possible Asbestosis o Certified Asbestosis.

Year started	Max. conc.	Crepitations Yr	Crepitations CUMD	Crepitations PMP	Poss. Asb. Yr	Poss. Asb. CUMD	Cert. Yr.	Cert. CUMD	Cert. %	Small opac.	Pleural thick.	Lung function FEV	Lung function FVC	Lung function TLC	Lung function TL	Died.
1961	6	72	33							0/1	1	90	90	90	100	
1957	7	71	33							1/0	2	80	110	130	100	
1955	5	71	34							0/0		110	110	120	100	
1962	8				70	36				1/0	4	90	100	100	90	
1957	5	70	52							0/0		60	70	100	50	
1951	6	67	53	✓						0/1	2	100	90	110	120	
1954	18	66	59	✓	65	55	66	59	10	0/0						1966 aged 57. LV failure, no asbestos
1955	13	67	56	✓	67	56	72	75	10	1/0	1	80	110	130	70	
1951	6			✓	68	58				1/0	4	110	100	110	90	
1956	7	69	58	✓	69	58	71	64	10	1/1	1	80	90	90	60	
1955	13	69	71	✓	69	71	69	71	30	1/1	3	50	80	110	70	
1960	8	71	74							0/1	3					
1952	11	68	87	✓	66	79	69	94	20	3/3	1	100	100	120	40	1975 aged 63. Ca. bronchitis + asbes
1956	8	70	87	✓						0/1	3	100	110	120	90	
1956	14	67	92	✓	67	92	67	92	20	2/1		60	80	110	40	1974 aged 59. Ca. lung + asbestosis.
1954	13	66	92	✓						1/1	4					
1955	13	70	102							1/0	1	100	120	100	80	
1952	36	67	104	✓						1/0		90	90	120	90	
1954	13	72	110							0/0		100	120	120	70	1974 aged 63. Coronary, no asbestosis
1951	21	66	112	✓	70	112	73	112	40	1/0	3	70	110	140	50	
1952	13	68	112	✓	68	112	70	124	10	2/3		100	100	100	50	
1952	13						(71	114)†		0/0						1971 aged 60 Ca. lung + asbestosis
1951	13	71	116	✓						0/0		100	120	140	90	
1953	14	66	121	✓						0/1		110	100	100	90	
1953	13	69	125	✓	69	125	70	131	10	0/1		80	70	90	70	

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TABLE 3: page 2.

Year started	Max. conc.	Crepitations Yr	Crepitations CUMD	Crepitations PMP	Poss. Asb. Yr	Poss. Asb. CUMD	Cert. Yr	Cert. CUMD	Cert. %	Small opac.	Pleural thick.	Lung function FEV	Lung function FVC	Lung function TLC	Lung function TL	Died.
1953	13						(74	129)†		0/1		100	110	140	90	1974 aged 49. Ca. lung + asbestosis
1951	13	67	133		71	154				1/0		80	70	90	80	
1951	18	66	137	✓						1/1		90	100	110	60	
1952	18	68	145							0/0		90	100	120	150	
1951	18	70	167	✓	73	171	74	171	30	1/1	2	60	60	70	50	

FOOTNOTE: See footnotes to Table 2.

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TABLE 4 - SUMMARY OF EXPOSURE AT FACTORY

	First employed before 1951		First employed after 1950	
	Total	With signs	Total	With signs
Year started at factory				
1933-35	11	7	-	-
1936-40	50	21	-	-
1941-45	28	11	-	-
1946-50	93	23	-	-
1951-55	-	-	109	22
1956-60	-	-	75	6
1961-65	-	-	13	2
Maximum concentration (f/cm^3)				
<5	1	0	11	1
5-10	38	9	82	9
≥10	143	53	104	20
Cumulative exposure ($f\text{-}yrs/cm^3$)				
<50	5	1	36	4
50-99	25	6	95	12
100-149	36	12	52	13
150-199	44	17	14	1
200-249	39	11	-	-
≥250	33	15	-	-
Total	182	62	197	30

A00711

First employed before 1951

	Total	Crepitations	Possible Asbestosis	Certified Asbestosis
Never smoked	22	4	3	2
1-4 cigarettes/day	7	3	3	1
5-14 " "	62	22	15	7
15+ " "	62	20	18	9
Ex-smokers	28	7	6	5

First employed after 1950

Never smoked	42	0	0	0
1-4 cigarettes/day	13	0	0	0
5-14 " "	48	11	6	5
15+ " "	68	11	4	3
Ex-smokers	24	4	3	2

A00712

TABLE 6 - Radiological findings and exposure in MEK first employed after 1950

Cumulative exposure (f-yrs/cm³)	Total	Profusion of small opacities* 0/1	1/0	1/1	1/2 or more	Bilateral pleural thickening †
<25	5	1	0	0	0	1
25-49	31	10	2	0	1 (1/2)	2
50-74	59	9	5	3	1 (1/2)	2
75-99	37	14	1	1	1 (3/3)	3
100-124	26	2	5	0	1 (2/1)	0
125-149	22	6	3	0	1 (2/2)	1
≥150	17	4	2	2	0	0
Total	197	46	18	6	5	9

*average of 4 readers; if the average is halfway between two adjacent categories the reading is rounded downwards (there were 12 such cases between 0/0 and 0/1).

† at least 2 of the 4 readers recording bilateral pleural thickening.

A00713

TABLE 7 - Regression coefficients of lung function indices and exposure in MTI - first employed after 1950

Index	Regression coefficient ± standard error (% predicted/f-yrs/cm^3)
FEV	- 0.121 ± 0.039
FVC	- 0.106 ± 0.035
TLC	- 0.006 ± 0.037
TL	- 0.069 ± 0.046

A00714

TABLE 8 - Estimated prevalence of possible asbestosis after uniform exposure to 2f/cm³ and estimated concentration giving a prevalence of 1%

Half-life (years)	Estimated prevalence (%)-2f/cm³ Length of exposure (years)			Estimated concentration (f/cm³)-1% prevalence Length of exposure (years)		
	30	40	50	30	40	50
Logit model (no lag)						
0 = Cumulative dose	2	4	7	1.5	1.1	0.9
5	4	7	11	1.0	0.7	0.5
10	5	9	15	0.8	0.5	0.4
25	6	12	19	0.6	0.4	0.3
∞ = no elimination	7	14	24	0.5	0.3	0.2
Logit model (5 year lag)						
0	4	6	9	1.0	0.7	0.5
5	6	10	14	0.4	0.3	0.2
10	8	12	17	0.3	0.2	0.1
25	8	14	21	0.2	0.1	0.1
∞	9	16	24	0.2	0.1	0.1
Alternative model (5 year lag)						
0	-	-	-	-	-	-
5	7	10	13	0.3	0.2	0.1
10	8	12	17	0.3	0.2	0.1
25	8	14	21	0.2	0.1	0.1
∞	9	17	26	0.2	0.1	0.1

A00715

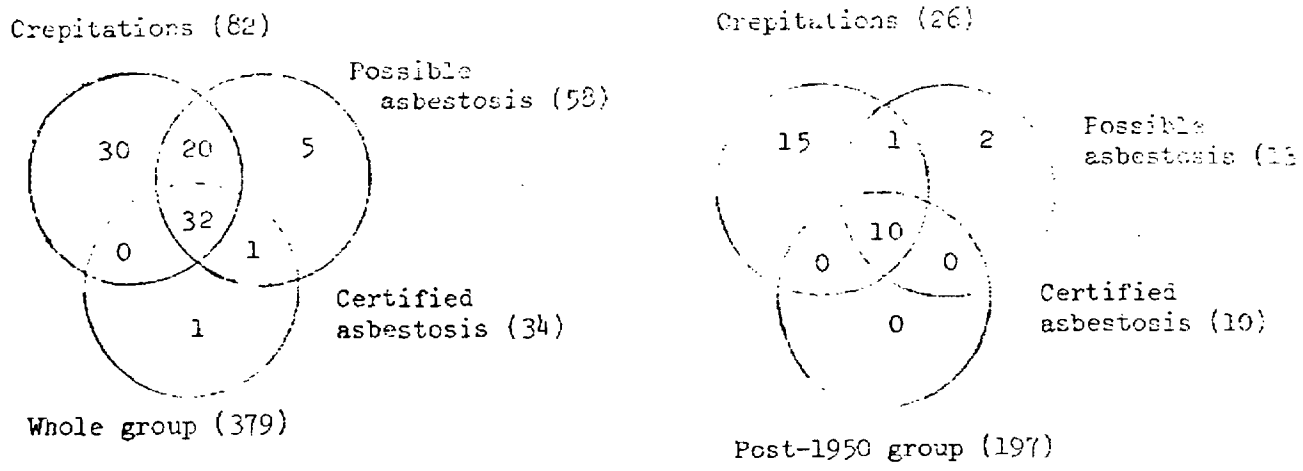


Figure 1 - Number of men with combinations of conditions, crepitations, possible asbestosis and certified asbestosis, for whole group and those first employed after 1950.

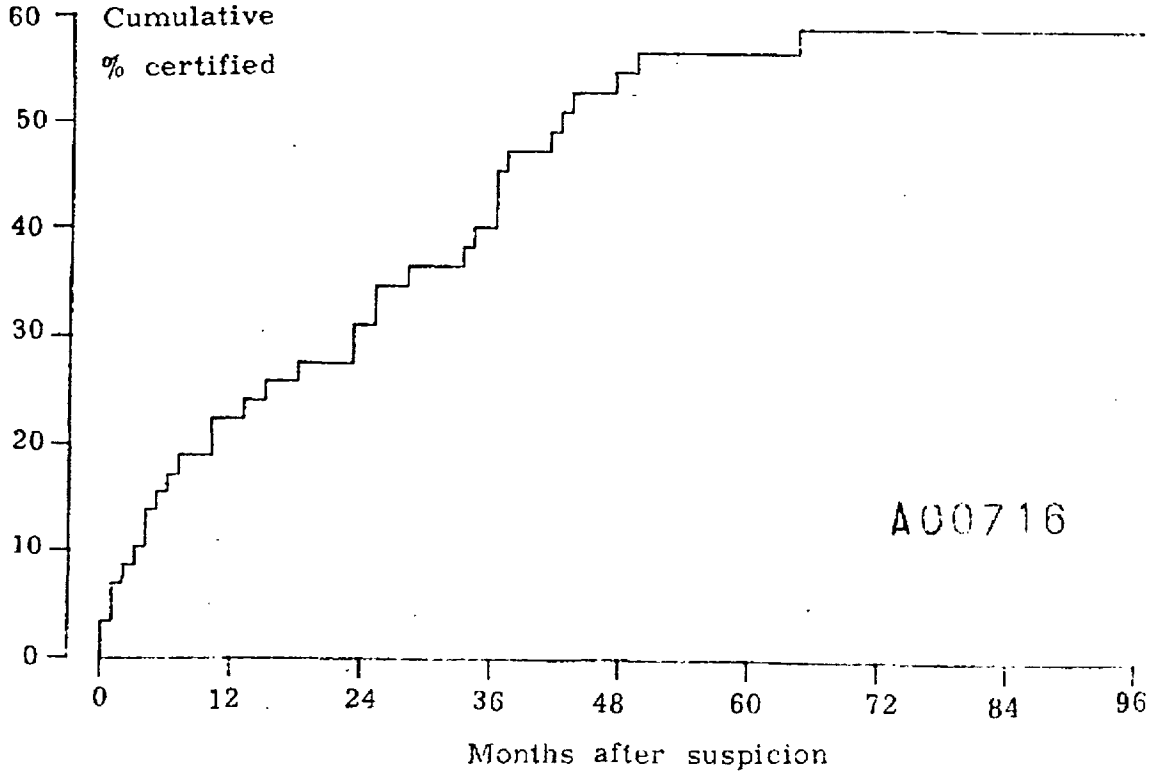
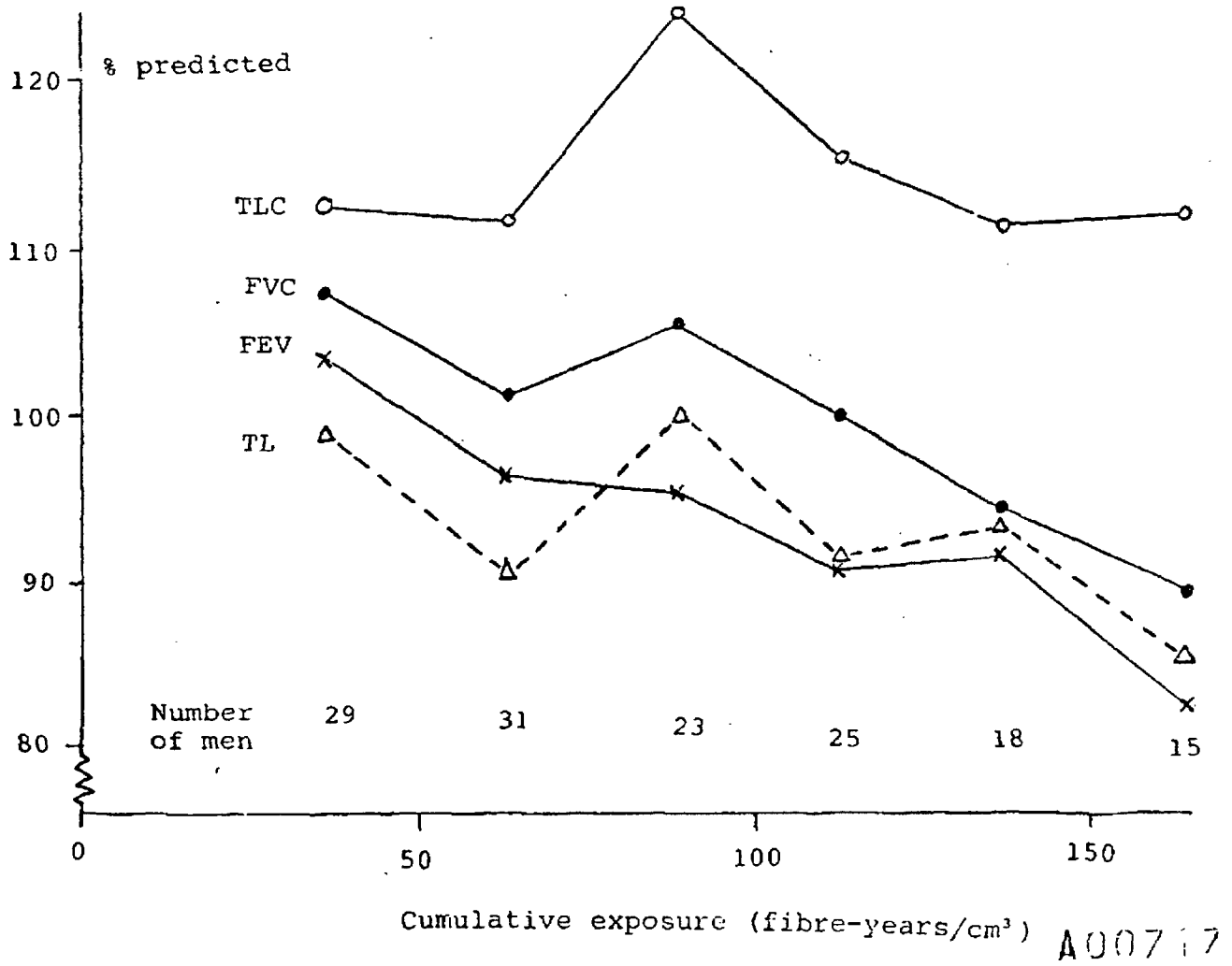


Figure 2 - Delay between suspicion of asbestosis



A00717

Figure 3 - The relationship between indices of lung function and cumulative exposure to asbestos, for

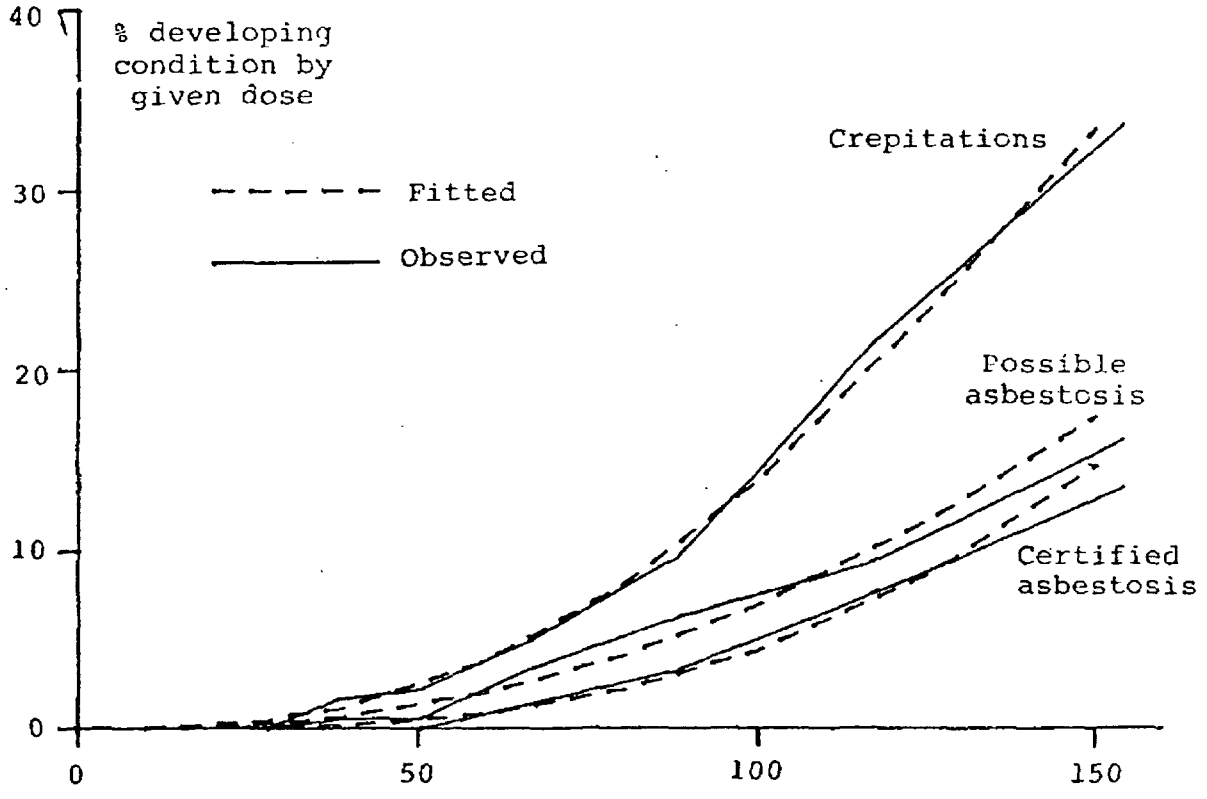


Figure 4 - The relationships between the percentage developing the conditions, crepitations, possible asbestosis and certified asbestosis, and cumulative exposure to asbestos, for men first employed after 1950.

A00718