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Evidence of Dose-response Relation in Pneumoconiosis (1)

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Summary

Although a quantitative scale exists for dose of dust, a true scale for severity of simple pneumoconiosis is unknown. Severity is often graded in terms of profusion of small opacities using the ILO classification. A technique has been developed for approximating a true scale based on the number of readings of each category in the classification in groups of workers.

Using this technique, a good relation has been found for coalworkers between the response of radiographic change and the dose of dust retained in the lungs. Progression following further exposure may also be closely related just to that exposure. Asbestos is a more biologically active dust and dose-response relations are much less strong, probably because the different radiographic changes reflect not dose of dust in the lungs but the resulting pathological changes.

The differences between the biological activities of the dusts inhaled by coalworkers and asbestos workers are seen in the relatively poor relations to mortality, pathology and lung function in the former and the better relations for the latter.

One of the uses of the chest radiograph is to provide a measure of response to dust exposure, particularly for control purposes and at a stage before disease can be confidently diagnosed. A main problem in assessing quantitatively a relation of dose to response in the radiograph is that of the scales to be used. For dose, scales such as amount of dust or years of exposure are obviously appropriate, as they are relevant and a unit change is the same at all points on the scales. For the response of radiographic change, however, no scale is known such that a unit change is the same at all points on the scale, nor is it necessarily true that scales exist which are relevant in that they reflect the effect of dose alone.

Assessment of Response

The radiographic change being considered is the profusion of small round opacities seen on the radiograph. This profusion is assessed on the scale defined by the National Coal Board's elaboration of the ILO classification (Liddell and Lindars, 1969), in which the four ILO categories are subdivided into 12 (Figure 1).

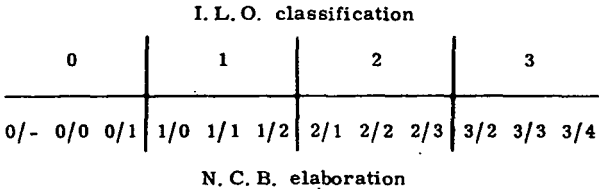

FIG. 1

National Coal Board's elaboration of the ILO classification of simple pneumoconoisis.

This scale is a continuous one, the boundary points between the categories being defined by the standard films and the reading rules. However, this implies only that a reading for example of category 1/0 places the film at some point between the upper and lower limits for category 1/0. It does not imply that all films read as 1/0 have the same amount of radiographic change, and there is no suggestion that the sizes of the categories are equal or even known.

The statistical problem is to relate readings on this scale, with largely unknown properties, to exposure levels and patterns. An analogous situation exists in the grading of dyspnoea. Grade 2 is worse than grade 1, but it is not reasonable to assume that there are equal steps of disability from grade to grade (Fletcher 1952).

If the readings of profusion of round opacities for a population of dust exposed workers are available, then the number of readings of each category should provide a guide to the size of that category in terms of dust exposure. In 1960, Wise suggested that category 2 was nearly 40 per cent larger than category 1, and he proposed a transformation of the scale of ILO categories to compensate for this (Rivers *et al*, 1960). Recently, Oldham (1971) has reviewed the problem of scoring simple pneumoconiosis categories and showed that Wise's proposal was applicable in a wide range of studies.

I shall consider some examples of this approach to the scoring of simple pneumoconiosis, first for coalworkers and then for other dust-exposed groups.

Coalworkers: Simple Pneumoconiosis and Dust Content of the Lungs

The most basic measure of dose against which to assess the response of simple pneumoconiosis is the amount of dust retained in the lungs. In a collaborative study of 233 coalminers (Rossiter, 1972), changes seen in radiographs usually taken shortly before death were related to the content and composition of the dust in one lung.

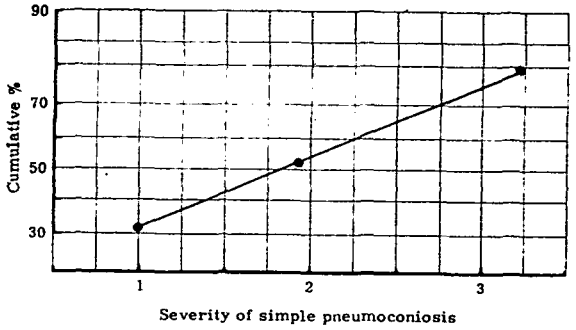

FIG. 2

Cumulative distribution of readings of categories of simple pneumoconiosis.

Each radiograph was read by eleven readers and the cumulative distribution of all the readings is shown in Figure 2. The scale for the severity of pneumoconiosis is that suggested by Wise in which category 2 is 37 per cent larger than category 1. The proportions with category 0, category 1 or less and category 2 or less are plotted against the appropriate severity scale values, forming a straight line. Using this line, scores were derived for each category and average scores calculated for each radiograph.

Figure 3 shows that the average lung coal and other mineral contents rise with increasing average category of simple pneumoconiosis for the 145 miners with simple pneumoconiosis alone. A clear dose-radiographic appearance relation exists. However as the graphs show some inverse relation-

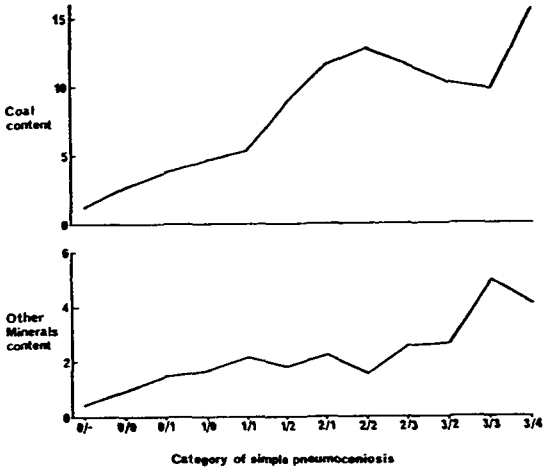

FIG. 3

Average content of one lung (grams). 145 miners without PMF.

ships between coal and other minerals some combination of the two would be a better measure of dose than either separately.

Exploration of the dose-response relation showed that films with the largest size of small opacity (type 'n') were over-read, suggesting that there was some response to dust as well as simple accumulation; that technically poor films tended to be read in categories 1 or 2 irrespective of lung dust content; and that radiographs of Scottish miners were also over-read. Bentley and Bergman (1970) have shown that this was probably due to the soot in their lungs from working in "naked light" pits.

For the remaining group of 98 miners there was a marked dose-response relation, but it was not quite linear, emphasizing the point that the precise scale for radiographic change is unknown. However, the use of a scale based on the proportions of readings in each category was quite effective in approximating to the desired linear scale. After correcting the radiographic scale for this non-linearity, 80 per cent of the scatter of radiographic scores was accounted for in terms of the dose of dust in the lungs (Figure 4). The other minerals contributed weight for weight 3.8 times as much as the coal in the lung dust, which accords with the 3.3 to 1 ratio of their X-ray mass absorption coefficients (S.M.R.E. 1963).

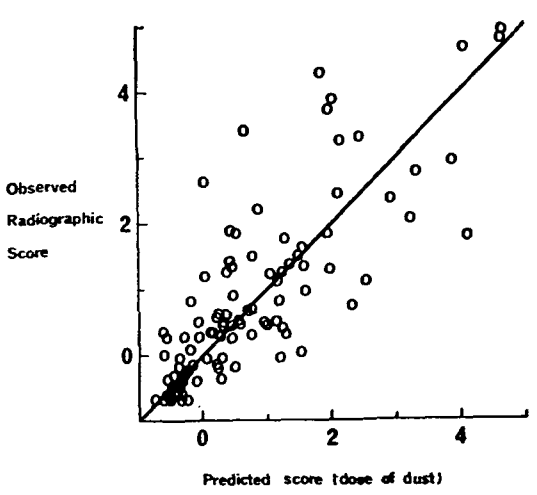

FIG. 4

Relation between radiographic score and that predicted from the coal and other mineral contents of one lung. 98 miners without progressive massive fibrosis.

The implications of this differential effect are shown in Table 1. The higher the proportion of coal in the lung dust, the more total dust is needed to produce any given radiographic change. For South Wales miners, for example, the coal proportion is about 90 per cent. Thus to produce a mid-category 1 film would require almost as much dust as is needed to produce a mid-category 2 film in the East Midlands, where only about half the lung dust is coal. Another implication is in relation to the hypothesis that the risk of attack of progressive massive fibrosis is dependent principally on the total amount of dust in the lungs. From this hypothesis it would be deduced that the attack rate for category 2 miners in South Wales would be much higher than for category 2 miners in the East Midlands coalfield, and this is what has been observed (McLintock *et al*, 1971).

TABLE I

TOTAL AMOUNT OF DUST ACCUMULATED IN BOTH LUNGS WHICH WOULD BE EXPECTED TO PRODUCE CERTAIN RADIOGRAPHIC CHANGES

Radiographic Change	*Total Dust (Grams)* 90% *Coal*	70% *Coal*	50% *Coal*
Mid-category 1 ..	22·1	15·3	11·7
Mid-category 2 ..	44·3	30·7	23·5

Coalworkers: Dust Exposure and Progression of Simple Pneumoconiosis

In the National Coal Board's Pneumoconiosis Field Research, a study has been made of 4,122 coalface workers over a period of ten years (Jacobsen *et al*, 1971). For each miner, radiographs at the beginning and end of the period were read by each of eight film readers and dust exposure assessments made. Figure 5 shows the distribution of the average radiographic readings for the two surveys, using the scale suggested by Wise. The lines for the two surveys are both linear and parallel to each other within their standard errors.

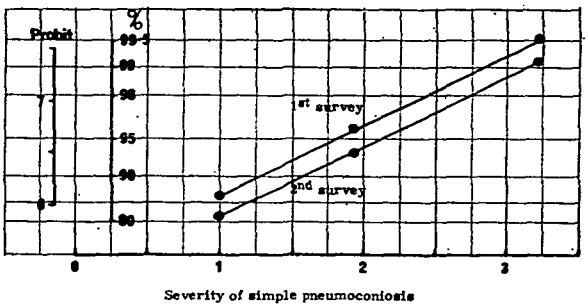

FIG. 5

Cumulative distribution of categories. NCB Pneumoconiosis Field Research. Two surveys approximately 10 years apart of 4,122 coalface miners. Average of 8 readings of each film.

The simplest summary of the change between the two surveys is that there has been uniform progression. This is not entirely a reasonable assumption as there was fairly wide variation in dust exposure during the ten-year period. However, if there was no relation between initial category of simple pneumoconiosis and subsequent dust exposure, the same pattern of two parallel lines would be expected.

In Figure 6 the two distributions are plotted as normal distributions with the boundaries between the categories shown. The sizes of the categories from 1/0 to 2/1 are much the same as the average progression whereas 0/0 is much larger. Thus most of those in the central categories would be expected to have progressed compared to only a few of those in category 0/0. Figure 7 shows the progressors from one category to a higher category

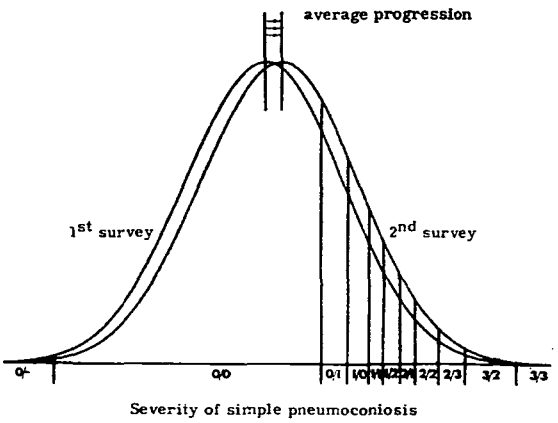

FIG. 6

NCB Pneumoconiosis Field Research. Distribution of readings from two surveys approximately 10 years apart—4,122 miners.

on the assumption of uniform progression. The expected proportion of progressors for those in categories 0/- or 0/0 is 8 per cent whereas for categories 0/1 or more, 67 per cent would be expected to be progressors. Allowing for variation in dust exposure levels, these rates would be less and could well agree with the observed progressor rates of 7 per cent and 44 per cent. This was proposed as an explanation of the different progressor rates during the discussion on the paper by Jacobsen *et al*, and they replied that they thought the difference was possible a true difference in biological response. It seems more likely that it arises just because of the non-equality of the sizes of the categories.

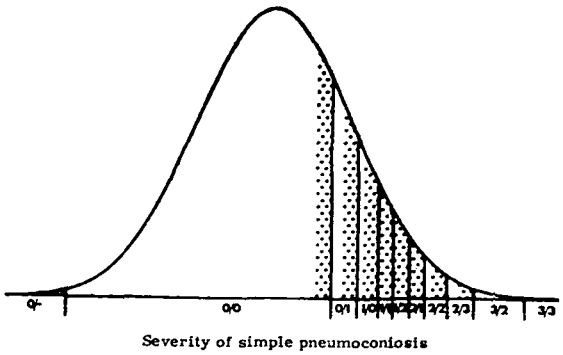

FIG. 7

NCB Pneumoconiosis Field Research. Distribution of readings from the first survey showing progressors, assuming uniform progression.

Dockyard Workers: Duration and Degree of Exposure to Asbestos

In an initial study of the effects of exposure to asbestos in the Royal Naval Dockyard at Devonport (Harries, 1971), the radiographs for 406 men were read by each of four readers. The small opacities recorded were of the irregular type, using the UICC/Cincinnati classification (UICC Committee, 1970), but again the cumulative distribution of readings was virtually linear on the transformed severity scale. Scores for each radiograph were calculated in the same manner and these scores related to the periods and degrees of exposure to asbestos.

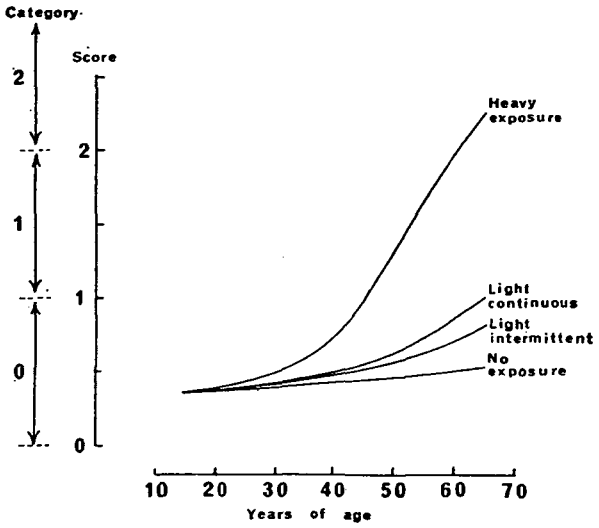

FIG. 8

Devonport Dockyard survey: regression of simple pneumoconiosis score on age, for different types of exposure beginning at age 15.

Figure 8 shows that the effect of heavy exposure to asbestos was much greater than the effects of light continuous or light intermittent exposure to asbestos, and that light intermittent exposure was intermediate between light continuous and no exposure. There was a slight effect of age by itself. Allowing for both age and exposure pattern accounted for a quarter of the total variation in radiographic change.

Chrysotile Asbestos Mining Industries: effect of Exposure

In the studies of 13,021 and 645 miners and millers from the Quebec and Cyprus chrysotile mining

industries, little relation was found between the profusion of irregular small opacities and dust exposure (Rossiter *et al*, 1972; Constantinides *et al*, 1972). In both surveys, age contributed as much to this profusion as did total dust exposure levels or years of employment. Only some 10 per cent of the variation in radiographic change could be accounted for in terms of dust exposure, partly because less than 1 per cent of people showed changes of category 2 or more.

Discussion

Of the dusts which cause radiographic changes, that in a coalmine is probably the most inert. The study of the relation between radiographic changes and dust in the lungs produces a close enough dose-response relation for the term pneumoconiosis to be properly applicable. This relation was also close enough to permit detailed study of the scale used for simple pneumoconiosis. This showed that the scale developed using the technique for scoring radiographs simply based on the number of readings of each category needed little modification.

It is probably true that progression of simple pneumoconiosis is closely related to dose of dust, and an analysis taking into account the differing sizes of categories should show that the low proportion of progressors from category 0/0 is just what would be expected on this basis.

This evidence that simple pneumoconiosis of coalworkers is related closely to the dust content of the lungs is supported by the general lack of relation between simple pneumoconiosis and mortality, pathology or lung function. The differences in attack rate of progressive massive fibrosis between different coalfields for the same category of simple pneumoconiosis may also be explicable just in terms of the total dust load in the lungs.

As asbestos is a more biologically active dust, radiographic changes would be expected to reflect pathological changes in the lung following exposure rather than the amount of asbestos in the lung. Thus any relation of radiographic change to dose of asbestos would only be indirect, being the resultant of two separate stages. This would imply that the relations between radiographic change and dust exposure should be lower than for coalworkers, as observed, and that mortality and lung function changes should also be related to radiographic changes and to dust exposure. These relations have been observed in the study of dockyard workers by Harries (1971), who has also reviewed the literature, and in the study of the Quebec chrysotile industry (McDonald *et al*, 1971; Becklake *et al*, 1970).

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