for attributing the decrement in FEV₁ to exposure to dust are explained clearly in the source paper¹⁰; and just as we are not yet clear on the functionally important pathological changes related to dust, we also have little basis on which to judge the relevance of Morgan's point on pulmonary hypertension or cor pulmonale. Incidentally, the study by Fernie et al included only eight non-smoking miners without progressive massive fibrosis,¹¹ too small a group to provide substantial support for Morgan's argument.

References


Drs Heldaas, Laugård and Andersen reply:

Ten Berge seems to put a great deal of emphasis on the statistical inference of the results in our study.¹ We are less concerned about the statistics; in our view the emphasis should be put more on the design of the study. We think that the quality of epidemiological studies in occupational medicine should be judged primarily by the characterisation of the level and duration of exposure to the potentially harmful agent, and to what extent selection has been avoided, and whether confounding has been dealt with in a proper way. Occupational diseases with presumed long latency periods have also to be dealt with in a manner which takes care of this phenomenon.

A small sample size is a common weakness in the design phase of small studies. Ten Berge, however, seems to interpret this problem of small sample size and failure to obtain "statistical significance" as being evidence for non-causality. It is not obvious from Ten Berge's letter how he has tested statistical significance.

Incidence of cancer among vinylchloride and polyvinylchloride workers: further evidence for an association with malignant melanoma

Sir—Recently Heldaas et al presented the results of a cancer morbidity study in vinylchloride exposed workers (1987;44:278–80). They are suggesting a relation between exposure to VC and the incidence of malignant melanomas. This suggestion is based on visual comparison of observed/expected cases in subgroups, stratified on levels of exposure or on years from first exposure (resp tables 1 and 2).

A statistically significant trend between duration or level of exposure and specific cancer morbidity may be tested according to Breslow et al. This test on significant trend was applied on the observed/expected cases of melanoma in relation to level of exposure (table 1) or in relation to years from first exposure (table 2). The probability, that the distribution of observed/expected cases of melanoma in the subgroups of table 1 and 2 was due to chance, was respectively 65% and 22%.

The only significant finding is the increase in the number of cases of melanoma in the total group of workers. Such an increase, however, was also found in cohort studies of workers with widely differing occupations. Moreover, in all other cohort studies of workers exposed to vinylchloride no increase of mortality from melanoma was found.² Therefore, the present epidemiologic evidence does not support a causative relation between the incidence of melanoma and exposure to occupational vinylchloride.

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References

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He has, however, avoided discussing the six cases of melanoma versus one expected, which we consider to be the most important result. As pointed out in the previous study, studies of cancer incidence have advantages compared with studies of mortality, particularly for tumour sites that are successfully cured.

We feel confident that the methodological aspects have been properly considered in our study. Consequently, we are less concerned as to whether the results are “statistically significant” or not. We consider the fact that two cases of melanoma developed in the a priori high risk group selected from the same VCM exposed population before the performance of the previous study as being of more significance for the interpretation of possible causality than the presence of statistical significance. Development of new cases in a preselected risk group may be of greater significance in a causality discussion than is the presence of “statistically significant” results. As opposed to “statistical significance,” a previously selected a priori high risk group cannot be manipulated.

A recent study from Du Pont, USA, seems to support our finding, but apparently our results have not attracted the author’s attention.

The current lack of adequate animal and in vitro models for studying the development of malignant melanomas makes the study of the possible causal relation between VCM exposure and this tumour complicated. Even so, Maltoni et al succeeded in producing malignant melanomas of the skin in Syrian golden hamsters exposed to a wide range of VCM levels, and they concluded that the tumours were related to the exposure.

References


Pulmonary fibrosis in asbestos insulation workers with lung cancer

SIR—Rudd’s letter (1987;44:428–9) points to several interesting questions.

1. Histopathological pulmonary findings in asbestos insulation workers with long exposure to the dust. I reviewed lung parenchyma sections submitted to me by pathologists in various institutions in the United States and Canada. As expected, the material was taken from various parts of the lung, often unspecified. It is widely accepted that pulmonary asbestosis is characterised microscopically by diffuse interstitial fibrosis caused by inhaled asbestos fibres. This was sought in my examinations in available parenchyma; Rudd argues that the subpleural areas be excluded, a rather arbitrary preference in view of the absence of data that parenchyma here differs from parenchyma elsewhere; particularly since this part of the lung often has a considerable concentration of asbestos fibres, the result of “pleural drift” of inhaled dust. Parenthetically, lung cancer after asbestos inhalation is not infrequently peripheral in origin.

2. I reported the presence or absence of microscopically evident diffuse interstitial fibrosis. I also reported that in 130 of 138 one or more asbestos bodies were seen. It is commonplace that in single thin (5μ) sections, asbestos bodies may be absent. Does this mean that they are not present (sometimes in large numbers) in the lung? Of course not. The likelihood of showing asbestos bodies varies directly with the amount of tissue studied. They are more readily seen in thick (30μ) sections than thin, more when bulk tissue is digested and filtered than in sections, more when exposure has been to amphiboles than chrysotile, and more when long and thick fibres were inhaled than short and thin. It is thus not enough to say that so many or so many asbestos bodies are seen; one should immediately add comment regarding how much tissue was available for examination and how they were sought. Indeed, in our study, we did not expect to find so many cases (since, occasionally, there was only a single thin section available for review) in which at least one asbestos body was to be seen. My colleagues consider that perhaps this was related to the diligent, prolonged examination to which each slide was subjected.

3. I was rather surprised to learn from Rudd that in the United Kingdom when there are “too few” asbestos bodies in slides of asbestos workers’ lungs the diffuse interstitial fibrosis is not infrequently categorised as cryptogenic fibrosing alveolitis. There must be a great deal of this disease nowadays in the United Kingdom among asbestos workers. And many asbestos workers with diffuse interstitial fibrosis are not eligible for disability compensation.

4. Asbestos bodies again. I am sure that Rudd is as familiar as we are with the multitude of observations that in lung tissue of asbestos workers with or without lung cancer there tend to be myriads of asbestos fibres uncoated by the iron protein material that allows them to be visible by (relatively insensitive) optical microscopy and thereby seen as asbestos bodies. Generally, the uncoated fibres are demonstrable only by