Quantitative relation between emphysema and lung mineral content in coalworkers

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Abstract

The relation between quantified emphysema and measured lung content of coal and silica was investigated in the lungs of 264 deceased underground coalworkers who had been exposed to mixed coal and silica dust. Lung specimens obtained at postmortem and inflated and fixed under standard conditions were used to quantify the extent of emphysema and then to measure the amount of coal and silica present in the lungs at the time of death. These data were combined with clinical and other pathological information from the subjects. Multiple regression analysis showed that the extent of emphysema (E score) had a strong positive quantitative relation with coal content of the lungs ($p < 0.0003$), age ($p < 0.0001$), and smoking ($p < 0.0001$). There was a significant negative interaction of uncertain biological importance between coal content of the lungs and smoking ($p < 0.004$; E score = $-1.79 + 0.62 \text{ coal} + 0.06 \text{ age} + 0.21 \text{ smoking} - 0.17 \text{ coal} \times \text{smoking}$; adjusted $R^2 = 0.25$). In lifelong non-smokers emphysema was particularly strongly related to coal content and age (coal: $p < 0.001$; age: $p < 0.002$; E score = $-1.56 + 0.78 \text{ coal} + 0.06 \text{ age}$; adjusted $R^2 = 0.66$). The relation was basically unchanged by adding a lung silica content term. Emphysema score was highly negatively correlated with forced expiratory volume in one second (FEV₁; % predicted, obtained within five years of death) ($r = -0.44$, $p < 0.0001$). Degree of lung fibrosis was highly positively associated with lung silica content ($\chi^2_1 = 12.9$, $p < 0.0003$). These results provide strong evidence that emphysema in coalworkers is causally related to lung coal content. The role of silica in development of emphysema, however, remains unclear.

(*Occup Environ Med* 1994;51:400-407)

The relation of emphysema to coal dust and silica dust content in the lungs of coal workers exposed to mixed dust remains controversial, despite considerable recent research.¹⁻⁶ Well designed large studies on postmortem pathological material have shown that emphysema, especially centriacinar emphysema, is qualitatively related to the coal dust content of lungs⁷⁻⁹ and quantitatively related to severity

of pneumoconiosis, years at the coal face, and indices of obstructive lung disease obtained during life.^{10 11}

Previous workers have found an association between prevalence of emphysema and coal content of the lungs⁷⁻⁹ but not between extent of emphysema and measured coal content. In a hospital based case-control study, Cockcroft *et al*⁷ found an excess of emphysema in coalworkers compared with non-coalworkers, and an association between severity of emphysema and dust exposure. The dust exposure score was, however, based on pathological assessment of lung specimens rather than on measured lung dust content or exposure measurements. Ruckley *et al* showed a clear relation between the presence of centriacinar emphysema and higher coal dust exposures (whether as inhaled dust or lung content of dust), but were unable to find a relation between the amount of emphysema and exposure to coal dust. They suggested that this may have been due to problems with lung inflation and tissue fixation or an indication that coal initiates the emphysema but other factors influence its progression.^{8 9}

Recent studies of coalworkers have suggested that emphysema is relatively less likely with high lung silica content.^{9 12} By contrast, emphysema is related to exposure to silica dust in goldminers.^{13 14}

Estimation of the relation between emphysema and exposure to coal dust by evaluating pneumoconiosis pathologically is potentially biased because the coal dust lesions draw attention to the emphysema. This can be partly avoided by the use of radiological pneumoconiosis scores.¹¹ The radiological appearances may not, however, be due to coal. The most objective exposure index, not subject to these biases, is actual coal content of the lungs.

Underground coalworkers in the New South Wales (Australia) coal industry are exposed to high rank bituminous coal (% carbon dry ash free 82%-90%). Silica content of the New South Wales coal seams is on average less than 2%.¹⁵ Some workers would have been exposed to higher silica levels when working in shaft development and in other mines, predominantly in the United Kingdom. Some of these workers would have been exposed to much higher dust levels than those obtaining today.

The aim of this study was to determine the relation between quantified emphysema and measured lung content of coal dust and silica dust in coalworkers.

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Accepted for publication
8 February 1994

Methods

The data analysed in this study came from workers in the New South Wales coal mining industry who died during the period July 1966 to January 1983. The New South Wales Joint Coal Board, with the assistance of relevant unions, has encouraged the conduct of post-mortem examinations on all deceased coalworkers since 1949. The proportion of coalworkers who underwent postmortem examinations is probably influenced by a number of factors, including perceived eligibility for compensation. The 264 subjects included in this study represent 70% of the 376 coalworkers (all male) who underwent postmortem examination during the study period. Inadequacy of lung specimens was the main reason for exclusion of subjects. Other subjects who were excluded from the analyses had missing data. Subjects who underwent a postmortem examination consisted of about 20% of all coalworkers who died during the study period (based on the New South Wales annual male crude death rate of 9.6/1000 in 1972 and a mean mining population of 14 000 over the study period).

TISSUE PREPARATION

After removal from the body, both lungs were perfused immediately with 10% acetate formalin via vessels and bronchi under a pressure of 120 cm water without any vessels or airways tied off, until the lungs were inflated to a volume between functional residual capacity and total lung capacity. The lungs were stored in 10% formalin in plastic containers.

Blocks for histology were taken from each lobe of each lung and from hilar lymph glands. In 35 subjects, Gough-Wentworth large lung sections¹⁶ were made of the left lung, with a 2 cm thick sagittal slice involving the hilar region.

MEASUREMENT OF EMPHYSEMA AND PNEUMOCONIOSIS

Emphysema was quantified by one of two observers by a modification of the Heard method.¹⁷ This was done on macroscopic examination of the surfaces of at least three cuts in the sagittal plane in each lung. Each cut was divided into three segments of roughly equal area. In each segment the percentage of lung area involved as abnormal holes was measured and the mean for each of the three or more cuts was calculated. Both fixed and Gough-Wentworth sections were used. When both types of sections were available for the same subject, the emphysema estimations agreed closely. The mean for all the cuts from both lungs became the final percentage emphysema score. This was then coded 1–7 (1 nil; 2 1–10%; 3 11–20%; 4 21–30%; 5 31–40%; 6 41–50%; 7 > 50%). There was good agreement shown between the two observers for separate readings of 400 lungs by this method.¹¹

Classification of pneumoconiosis was made on the basis of macroscopic and microscopical examination of lung tissue and an examination of whole lung sections. Macules and nod-

ules were classed as sparse (equivalent to International Labour Office (ILO) 1/0 or less), moderate (less than ILO 2/2), or profuse (ILO 2/2 or greater), and massive lesions documented. Distinction was made between coal only (macules), mixed coal and silica (nodules, palpable), and silica only changes. One observer made all classifications. Pneumoconiosis classification was available for 259 (98%) subjects.

ANALYSIS OF LUNGS FOR COAL AND SILICA CONTENT

Specimens were freed of non-lung tissue, cut into pieces of about 2 cm³, homogenised in a blender, dried on shallow trays at 105°C in a laboratory oven, and ground in a mill to pass a 0.5 mm screen, giving an average particle size of 200 µm. Lungs had been previously dissected at necropsy and no attempt was made to further separate lymphatic tissue. Tissue used for preparation of large lung sections was included.

Powdered lung samples were hydrolysed with a modified version of the procedure of Guest.¹⁸ Subsamples of the powdered lung (1 g) were hydrolysed in duplicate in screw capped polypropylene centrifuge tubes by heating with shaking for two hours at 60°C with concentrated hydrochloric acid (20 ml, 36%). The hydrolysis procedure was carried out three times. Each hydrolysis step was followed by dilution with ethanol (20–25 ml), separation of the solid residue by centrifuging (30 minutes, 3000 rpm), and careful siphoning off of the hydrolysis product (supernatant). The separated residue was repeatedly washed with ethanol and centrifuged as before, until the supernatant was clear (usually two to three washes).

The slurried residue in the centrifuge tube was transferred quantitatively to a preweighed platinum crucible with ethanol and toluene. Total lung dust, total coal, and total mineral matter (ash) were determined gravimetrically: the total lung dust after first drying the crucible contents at 110°C, the total mineral matter after ashing the crucible contents at 600°C overnight, and the total coal by calculating the difference between total lung dust and total mineral matter. Finally, silica (quartz) was determined in the ash by Fourier transform infrared spectroscopy with the potassium bromide disc technique (1 mg ash per 250 mg disc), essentially by the method of Dodgson.¹⁹ By ashing at 600°C we obtained less interference in the quartz spectra at the expense of not being able to quantitatively determine kaolin and mica. The main results consider the total amount of coal and silica in the two lungs of each subject, standardised by predicted vital capacity (from height and age).²⁰ For comparison purposes results were also expressed as proportions of coal or silica by dry weight of lung and as absolute amounts of coal and silica.

SMOKING HISTORY

Data on smoking history were obtained from a standardised questionnaire given at Joint

Table 1 Means (SD) and percentiles of main variables

	No	Mean(SD)	Percentiles		
			25%	50%	75%
Emphysema score	264	3.1(1.5)	2	3	4
Adjusted lung coal content (g/l)*	264	0.89(0.81)	0.32	0.65	1.21
Absolute lung coal content (g)†	264	3.93(3.44)	1.53	2.88	5.07
Adjusted lung silica content (g/l)*	261	0.04(0.04)	0.02	0.03	0.05
Absolute lung silica content (g)†	261	0.18(0.17)	0.08	0.12	0.21
Tobacco smoked (ounces/week)	264	3.1(2.2)	2	3	4
Age at death (y)	264	63.4(10.4)	58	64	71
FEV ₁ %‡	183	78.7(25.5)	60	81	98

*Adjusted by predicted vital capacity.

†Absolute amount of lung coal or silica per subject.

‡Measured FEV₁ as a percentage of predicted (using height and age).²⁰

Coal Board routine clinical examinations, which were held every two to three years. Smoking was expressed as ounces of tobacco smoked per week (1 ounce = 28 g), based on a lifetime average of tobacco intake.

LUNG FUNCTION MEASUREMENTS

Forced expiratory volume in one second (FEV₁; body temperature, atmosphere pressure, and saturation) was measured with a Vitalograph spirometer and the results were recorded as the higher of two satisfactory efforts. The measurements were performed at the routine clinical examinations. Measurements were only accepted for this study if taken within five years of death. Results were available for 183 (69%) miners. Values were expressed as percentage predicted (FEV₁%).²¹

YEARS AT FACE

Information on years worked at the coal face was obtained from the detailed occupational histories taken at each routine Joint Coal Board clinical examination.

STATISTICAL METHODS

Calculations were performed with standard simple parametric and regression techniques as programmed in the Statistical Analysis System,²² with appropriate checking of residuals in regression models. Statistical significance was determined at the 5% level (two sided).

Results

Table 1 gives the frequency distributions, means, SDs, and quartile values for emphysema score, lung coal content, lung silica content, smoking amount, age at death, and FEV₁%. Age, smoking, and FEV₁% had normal distributions, with similar medians and means. By contrast, the lung dust content

Table 3 Mean coal and silica content by type of pneumoconiosis

Pneumoconiosis type	Lung content (g/l predicted vital capacity)	
	Coal* Mean(SD)	Silica† Mean(SD)
Sparse (n = 123)	0.53(0.41)	0.03(0.02)
Coal (n = 86)	1.15(0.84)	0.05(0.03)
(moderate, profuse, massive)		
Mixed (n = 46)	1.41(1.11)	0.07(0.06)
(moderate, profuse, massive)		

*Mean lung coal content significantly different for each group (F = 31.8, p < 0.0001) by Duncan's multiple range test.

†Mean lung silica content significantly different for each group (F = 30.6, p < 0.0001) by Duncan's multiple range test.

variables and emphysema score were positively skewed.

Excluded subjects had a similar mean emphysema score (3.1), age (67 years), smoking amount (3.1 ounces/week), FEV₁% (74% predicted), and years worked at the coal face (21) as subjects included in the analyses. Subjects without FEV₁ data had a higher mean emphysema score (3.6 v 2.8), higher mean lung coal content (1.25 v 0.73 g/l), higher mean lung silica content (0.051 v 0.037 g/l), and were older (67 v 62 years), but had smoked a similar amount (2.9 vs 3.2 oz/week) and had worked a similar number of years at the coal face (21 v 19) as subjects with FEV₁ data.

Most subjects had minimal or mild pneumoconiotic changes and there were only four with silica only changes (table 2). Mean coal and silica content in the lungs were highest in those subjects with a mixed pneumoconiosis, next highest in those subjects with primarily coal pneumoconiosis, and lowest in subjects with minimal changes. All differences were statistically significant (table 3). Lung fibrosis was highly significantly related to lung silica content (p < 0.005) and age (p < 0.0001) but not to lung coal content (p > 0.55) when examined in the same model by logistic regression.

The distribution of emphysema score was positively skewed, suggesting that a log transformation might be appropriate for regression techniques. Results from the regression equations were similar, however, with and without transformation. A slightly better fit was obtained when the log transformation of emphysema score was used. Residuals were appropriately distributed whether the emphysema score or its logarithm was used as the outcome variable. For clarity, only the analyses with the untransformed emphysema score are presented. Table 4 shows the correlation matrix for variables of interest.

Emphysema score (E score) increased significantly with coal content of the lungs, age, and amount of smoking (equation 1).

$$\begin{aligned} \text{Equation 1:} \\ E \text{ score} = & -1.73 & t = 3.12 & p < 0.002 \\ & + 0.22 (\text{coal(g/l)}) & t = 2.05 & p < 0.05 \\ & + 0.07 (\text{age (years)}) & t = 8.18 & p < 0.0001 \\ & + 0.10 (\text{smoking} & & \\ & \quad (\text{ounces/week})) & t = 2.50 & p < 0.02 \\ & (\text{adjusted } R^2 = 0.23) \end{aligned}$$

Silica content of the lungs did not contribute significantly to the model. Addition of a

Table 2 Distribution of pneumoconiotic changes

Pneumoconiosis type	Pneumoconiosis severity				
	Sparse No(%)	Moderate No(%)	Profuse No(%)	Massive No(%)	Total No(%)
Coal	—	72 (28)	10 (4)	4 (2)	86 (33)
Mixed	—	29 (11)	11 (4)	6 (2)	46 (18)
Silica	—	4 (2)	—	—	4 (2)
Sparse	123 (47)	—	—	—	123 (47)
Total	123 (47)	105 (40)	21 (8)	10 (4)	259 (100)*

*5 subjects did not have data regarding pneumoconiotic change. Errors in total percentages are due to rounding.

Table 4 Correlation matrix of main variables (Pearson correlation coefficient (*r*))

	Emphysema (n=264)	Coal (n=264)	Silica (n=264)	Age (n=264)	Smoking (n=264)	Years at face (n=264)	FEV ₁ % (n=183)
Emphysema (score)	1.00						
Coal (g/l)	0.20**	1.00					
Silica (g/l)	0.19**	0.54****	1.00				
Age (y)	0.46****	0.23***	0.26****	1.00			
Smoking (ounces/week)	0.04	-0.15*	-0.25****	-0.17**	1.00		
Years at face	0.24****	0.27****	0.26****	0.45****	-0.19**	1.00	
FEV ₁ %	-0.44****	-0.01	0.05	-0.31****	-0.02	-0.11	1.00

* *p* < 0.02; ***p* < 0.005; ****p* < 0.001; *****p* < 0.0001.

Table 5 Regression parameters for various measures of lung coal content

Parameter	Measure of coal used in final regression equation					
	Adjusted by vital capacity		Proportion of lung dry weight		Absolute amount per subject	
	<i>t</i> Value	<i>p</i> > <i>t</i> *	<i>t</i> Value	<i>p</i> > <i>t</i> *	<i>t</i> Value	<i>p</i> > <i>t</i> *
Coal	3.64	0.0003	3.53	0.0005	3.79	0.0002
Age	7.76	0.0003	7.86	0.0001	7.87	0.0001
Smoking	3.91	0.0001	3.28	0.002	4.02	0.0001
Coal × smoking	-2.99	0.004	-1.89	0.06	-3.15	0.002
adjusted R ²	0.25		0.26		0.26	

* Probability of obtaining an absolute value of *t* as great or greater.

coal-smoking interaction term improved the model slightly, with coal and smoking having a negative interaction (equation 2). Note that the effect of lung coal content on E score must be obtained by using a combination of the coal only and coal × smoking regression coefficients, as the effect of coal depends on the level of smoking.

Equation 2:

$$E \text{ score} = -1.79 + 0.62 (\text{coal(g/l)}) + 0.06 (\text{age(years)}) + 0.21 (\text{smoking (ounces/week)}) - 0.17 (\text{coal} \times \text{smoking})$$
 (adjusted R² = 0.25)

t = 3.28 *p* < 0.002
t = 3.64 *p* < 0.0003
t = 7.76 *p* < 0.0001
t = 3.91 *p* < 0.0001
t = 2.99 *p* < 0.004

Of the other potential interactions (coal × silica, coal × age, silica × age, silica × smoking, and age × smoking) none showed a significant effect. Similar results were obtained when the coal and silica contents were expressed in an unadjusted form (as absolute weight per subject) or as a proportion of the dry weight of lung (table 5).

When the 40 non-smokers were considered separately, the positive effect on emphysema score of coal content and age was striking, with these two variables accounting for about two thirds of the variation in emphysema score (equation 3). Silica content of the lungs and all interaction terms did not contribute significantly to the model. The figure shows the univariate association between coal content of the lungs and emphysema for non-smokers.

Equation 3:

$$E \text{ score} = -1.56 + 0.78 (\text{coal (g/l)}) + 0.06 (\text{age (years)})$$
 (Adjusted R² = 0.66)

t = 1.98 *p* < 0.06
t = 5.43 *p* < 0.0001
t = 4.19 *p* < 0.0002

Emphysema score had a highly significant negative relation with FEV₁% for the 184 subjects who had available FEV₁% measurements (equation 4). Almost identical results were found when lung coal content was added to the regression model (*b*_{Emphysema} = -7.39, *t* = -

6.73, *p* < 0.0001), with coal not making a significant contribution to the model (*b*_{coal} = 2.86, *t* = 1.00, *p* > 0.32). This relation seemed to be similar for non-smokers, with the low numbers of non-smokers with available FEV₁ data (28) probably responsible for the borderline statistical significance of this relation (equation 5).

Equation 4:

$$FEV_1\% = 99.2 - 7.24 (E \text{ score})$$
 (R² = 0.19)

t = 28.22 *p* < 0.0001
t = 6.66 *p* < 0.0001

Equation 5:

$$FEV_1\% = 105.3 - 7.21 (E \text{ score})$$
 (R² = 0.11)

t = 10.24 *p* < 0.0001
t = 1.76 *p* < 0.09

Emphysema score was significantly higher in subjects with pneumoconiotic change (moderate, profuse, or massive) than in subjects with minimal or no pneumoconiotic changes (*t* = 4.90, *p* < 0.0001). This relation was independent of coal and silica content of the lungs. Mean FEV₁% was higher, but not significantly so, in subjects with minimal or no pneumoconiotic change than in those with definite pneumoconiotic change (82% *v* 76%; *t* = 1.40, *p* > 0.17).

Univariate relation between adjusted lung coal content and emphysema score for lifelong non-smokers (*n* = 40).

Discussion

The results show clearly that content of coal in the lungs is quantitatively related to the development of emphysema, taking into account age and smoking. This is true whether the effect of smoking is controlled by regression methods or by examining only life-long non-smokers. The results indicate that a non-smoking miner with about the average lung coal content would have emphysema involving 7% to 10% more of the whole lung mass than a non-smoking person of the same age who was not exposed to coal. The influence of coal seems less pronounced in smokers, perhaps due to a negative interaction between smoking and coal. Although other possible causes of emphysema in coalworkers, apart from coal and smoking, have been suggested,²³ the high R^2 term in the regression equation for non-smokers strongly suggests that coal exposure and age are the main determinants of emphysema in non-smoking coalworkers. Biologically plausible mechanisms for a pathological effect of coal on lungs to produce emphysema are now well documented.^{24,25}

The analytical technique used in this study measures total coal and silica content of the lungs, which includes both dust in the bronchi and in the parenchyma. This measurement is used as a proxy for the true measure of interest, parenchymal dust, as it is in the parenchyma that any pathological effects that might result in emphysema presumably occur. Therefore, any process (such as dust being trapped in the increased mucus produced in bronchitis) that might alter the proportion of total lung dust in the parenchyma could affect the relation between total lung dust and emphysema. Unfortunately, it is not known how much variation in this proportion might occur due to pathological processes or differences between workers; it is too difficult to dissect out the bronchial tree from the parenchyma to allow separate measurements of dust content in each. Known particle deposition distributions suggest that the parenchymal component would be much larger than the bronchial component, except in very unusual circumstances.

An alternative explanation for the coal and emphysema association found might be that emphysema somehow impairs clearance of dust from the lungs. Greater emphysema would therefore be associated with dust in the lung because of decreased clearance rather than because the dust was causing the emphysema. The effect of emphysema on clearance is uncertain, and there is evidence from animals and humans of both decreased and increased clearance in emphysematous lungs.²⁶⁻²⁸

The strong positive association between age and emphysema found is well documented elsewhere.²⁹ An association between smoking and emphysema as found in this study has been well documented for the general community,³⁰ in coal miners,⁷⁻⁹ and goldminers.^{13,14} The negative interaction between coal and smoking does not have a clear explanation. Perhaps it is because smokers

have more bronchitis,³⁰ and the increased mucus production traps more coal in the bronchi before it reaches the lung parenchyma. Therefore, for a given amount of measured dust in the lung, more smoking may result in a smaller proportion of dust reaching the parenchyma and correspondingly less emphysema than would otherwise be expected. Alternatively, the negative interaction may be due to a form of competitive inhibition, with the individual effects of coal and smoking having a final common pathway in which the presence of one interferes with the effect of the other. This is plausible, as damage or activation of macrophages or polymorphonuclear leucocytes with subsequent release of elastase or other proteases, is a probable mechanism for the development of emphysema in both smokers³¹ and coal miners.^{24,25} Finally, the relation might simply be a result of statistical associations inherent in this data set rather than a reflection of a true biological phenomenon.

Silica content in the lung was not significantly associated with emphysema in this study. Previous investigators have found conflicting results. One group studying British coalworkers found a negative effect of silica on the prevalence of emphysema in coalworkers.⁹ This was true for lung silica content for subjects with progressive massive fibrosis and for percentage silica of lung dust or percentage silica in the lungs for subjects with any fibrotic lung disease. They postulated that silica induced fibrosis might make emphysematous change less likely. In goldminers exposed to "silica dust", the prevalence of centriacinar emphysema was related to dust exposure level and to the presence of silicosis in one study.¹⁴ By contrast, an earlier study of goldminers found a positive association between the presence of any emphysema and dust exposure levels, but no significant effect of silicosis.¹³ It is possible that the relation between emphysema and "silica dust" in these two studies was due to some other component of the dust apart from silica, although the dust is known to have had a high silica content.¹⁴

The lack of an emphysema and silica association in our study may be due to low silica exposures and correspondingly less silica related fibrotic lung disease, even though there was a strong relation between the presence of fibrotic lung disease (mixed coal and silica or silica only disease) and the lung content of silica. The subjects included were mostly recent miners who had a low prevalence of fibrotic lung disease. Of the 259 subjects who had data available on lung histology, 19% had mixed coal and silica or silica only nodules, with only 34% of these (6% of the total) showing profuse nodularity or massive fibrosis (ILO 2/2 or greater). By comparison, in a study of British coalworkers that showed a negative emphysema and silica association, 79% of the subjects had some fibrotic lung disease and 33% were said to have progressive massive fibrosis.⁹ A study of an earlier group of miners from the same mining regions as the subjects used in our study, but exposed to a

higher concentration of respirable dust, had a much higher prevalence of fibrotic lung disease. Forty eight per cent had mixed nodules and 54% of these (26% of the total) had ILO 2/2 or greater.¹² In this group there was a significantly lower prevalence of emphysema in those subjects with mixed nodules than in those with coal only macules, and this difference was especially pronounced in those with profuse mixed nodules. This supports the suggestion that there may be a negative association between silica and development of emphysema. Unfortunately, the lungs of these subjects were not available for the mineral analysis used in this study.

The content of silica in the lungs of subjects in this study was also lower than other studies, both on an absolute and a percentage basis. Our study showed a mean lung silica content of 0.11% of dry lung weight, compared with 0.35% in the study of British coalworkers.⁹ The comparable absolute amounts were 0.18 g and 0.30 g per subject. Percentage content of coal in the lungs could not be directly compared between the two studies because of differences in the presentation of data, but the mean absolute amount of coal per subject found in our study (3.9 g) was lower than that found in the British study (4.9 g). Content of coal in the lungs was an order of magnitude higher than silica content in our study (mean coal (g/l): mean silica (g/l) = 22:1), similar to the British study, which found a corresponding ratio of about 16:1.

Emphysema score had a highly significant negative relation with FEV₁% in our study. This result has been found previously in a larger group of coalworkers that included the subjects from our study,¹¹ and in other studies of coalworkers.^{8,9} The emphysema and FEV₁% relation was independent of coal content in the lungs suggesting that the association was not a consequence of dust exposure independently causing emphysema and a decrease in FEV₁%. The regression coefficient suggests that the emphysema found in coalworkers is of some functional relevance, with an increase of emphysema of 10% leading to a predicted decrease of FEV₁% of about 7%. This same negative relation between FEV₁% and emphysema was suggested in the analysis that included only non-smokers, but the few subjects with available FEV₁ measurements make firm conclusions difficult. Recent evidence indicates that occupational exposure to coal dust alone might produce clinically important airways dysfunction,^{23,6} although this is not accepted by all researchers.^{4,5} In this study, as the severity of pneumoconiosis increased the severity of emphysema increased. This relation seemed to be independent of dust content of the lungs and suggests a direct pathological connection between pneumoconiosis and emphysema. The FEV₁% showed a non-significant decline with increased severity of pneumoconiosis. The lack of statistical significance of this relation was possibly due to the limited number of subjects with available FEV₁ measurements.

The lung content of coal and silica were

highly correlated with each other, as would be expected because most coalworkers were exposed to mixed coal and silica dust. The lung contents of coal and silica were also both highly significantly correlated with years worked at the face, although the correlation coefficients of 0.26 and 0.27 suggest that years worked at the face gives a more qualitative estimate of the lung burden from dust exposure. Years at the face was highly significantly correlated with emphysema score, but not when age was taken into account, presumably because years at the face was acting as a proxy measure of age in the univariate correlations.

Some sources of bias are possible in a study of this type, but, for reasons outlined here, bias is not thought to have been a significant problem. Most of the emphysema found in previous studies of coalworkers was reported to be of the centriacinar type,^{7,8} with little panacinar emphysema, and this was also the case in the present study. In advanced cases, centriacinar emphysema extended to involve whole lobules and to coalesce between lobules, ultimately involving the whole lung. In accordance with current thinking,³²⁻³⁴ we regarded the two types of emphysema as part of a range and hence made no attempt to separately measure panacinar emphysema. Tissue preparation methods were the same for all lung specimens used and emphysema measurements were made by either of two observers with standard techniques, with a high degree of interobserver agreement and blinded to the other variables of interest. Assessment of emphysema by macroscopic measurements has been criticised,³² but the technique is widely used³⁵ and, in this study, emphysema score had a highly significant negative relation with FEV₁%, as would be expected clinically. The measurements of overall emphysema are therefore believed to be appropriate and reasonably accurate.

Dust analysis was performed with minor modifications of established techniques, there was good agreement between duplicate samples, and analysis was done without knowledge of the emphysema measurements made on each specimen. Lung content of coal and silica can be regarded as the best quantitative estimate of exposure as, once clearance mechanisms are saturated, accumulation of dust in the lungs is probably proportional to further exposure.³⁶

Coal and silica contents in the lungs were adjusted by means of predicted vital capacity, which was used as an estimate of lung volume, thereby providing a measure of the concentration of coal and silica in the lung. This adjustment introduces some (presumably non-differential) error. Expressing coal and silica content of the lungs as a proportion of dry lung weight would seem to give an even better measurement of the concentration of dust in the lung. Unfortunately, this measurement can be criticised on the basis that more emphysematous lungs probably contain less total lung tissue. Thus for a given amount of total lung dust, more emphysematous lungs

would have a higher concentration of dust per dry weight of lung, thereby potentially introducing a spurious positive relation between dust content and amount of emphysema. Conversely, more fibrotic lungs might contain more lung tissue and so introduce an apparent negative relation. Nevertheless, authors have expressed lung dust content on a per dry weight of lung basis,^{9 37 38} and in our study analyses with this measurement for coal and silica produced similar results to the main analyses performed with measures adjusted by predicted vital capacity. The absolute mass of coal or silica (unadjusted) does not give a measure of the concentration of dust in the lung as it does not take into account the fact that bigger lungs will contain more dust than smaller lungs. Therefore, this measure is likely to contain significant non-differential error, although analyses with these unadjusted measures gave similar results to the primary analyses.

The 264 subjects are a subset of a continuous series of 1086 postmortem examinations on coalworkers in New South Wales from 1949 to 1987. Lung tissue obtained before 1966 is no longer available for mineral analysis. Subjects who had a postmortem examination during the study period 1966–83 but were not included in this study had similar values for the main known variables of interest as subjects who were included. Because the main reason for exclusion of subjects at this stage was inadequate lung specimens it is unlikely that significant bias was introduced because of this exclusion. It is likely that those miners on whom postmortem examinations were carried out had a higher prevalence of lung disease than the overall mining population of the same age during the study period. Lung disease established at postmortem examination would be more likely to attract compensation for the families of the miners than lung disease that was not confirmed pathologically, so families of miners who suspected that they had lung disease are more likely to have agreed to a postmortem examination. There is no reason to believe, however, that selection would have been influenced by severity of emphysema and lung dust content in such a way as to artificially produce the results found.

In conclusion, the results provide strong support for the hypothesis that severity of emphysema in coalworkers is causally related to coal content in the lung and thus to exposure to coal in life. In this regard it is of interest that emphysema has recently become a prescribed disease for underground coal miners in the United Kingdom.³⁹ The importance of age and smoking in severity of emphysema is also confirmed. The results do not support a relation between exposure to silica and the development of emphysema. The lung content of silica of subjects may not have been high enough, however, to show the true effect of silica.

The skilled technical assistance of Mr D Moffat (Joint Coal Board) and Dr K White (consultant pathologist) is gratefully acknowledged. The initial work of Drs K Outhred and I

McKenzie of the Joint Coal Board (both now deceased) in establishing the pathology programme is also recognised. We thank the Occupational Medicine, Occupational Hygiene and Toxicology Units (NIOHS), and the Departments of Chemical Engineering, Geology, and Inorganic Chemistry (University of Sydney), for laboratory facilities.

The views expressed in this article are those of the authors and do not necessarily reflect those of the National Occupational Health and Safety Commission.

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