Pergamon

Ann. occup. Hyg., Vol. 41, Supplement 1, pp. 384–389, 1997

0003–4878/97 $17.00 + 0.00
Inhaled Particles VIII

PII: S0003–4878(96)00092–0

RELATIONSHIPS BETWEEN LUNG DUST BURDEN, PATHOLOGY AND LIFETIME EXPOSURE IN AN AUTOPSY STUDY OF U.S. COAL MINERS

E. D. Kuempel,*† E. J. O'Flaherty,† L. T. Stayner,* M. D. Attfield,‡ F. H. Y. Green§ and V. Vallyathan‡

*National Institute for Occupational Safety and Health (NIOSH), Education and Information Division, 4676 Columbia Parkway, MS C32, Cincinnati, OH 45226; †University of Cincinnati, Department of Environmental Health, Cincinnati, OH; ‡NIOSH, Division of Respiratory Disease Studies, Morgantown, West Virginia, U.S.A.; and §University of Calgary, Department of Pathology, Calgary, Alberta, Canada

INTRODUCTION

Previous pathological studies of U.S. miners have described correlations between radiographical and pathological evidence of coal workers' pneumoconiosis and lung dust burden (Vallyathan *et al.*, 1996; Attfield *et al.*, 1994). The present study includes estimates of miners' lifetime cumulative exposures to respirable coal mine dust and investigation of the relationships between duration and cumulative exposure, lung dust burden and pathological response. Also investigated is the estimated mean lung dust clearance during the retirement period.

METHODS

Cases were collected systematically from 1957 to 1971 by the late Dr Laqueur in the Beckley, West Virginia, area from consecutive autopsies of approximately 700 former coal miners (Attfield *et al.*, 1944). The coal mined in that area is primarily high volatile bituminous. Whole lung sections were evaluated for macules, micronodules, macronodules and progressive massive fibrosis (PMF), using a four-point scale (absent, slight, moderate, severe) described in Vallyathan *et al.* (1996) and the guidelines of Kleinerman *et al.* (1979). For 131 miners, the mass and composition of dust (coal, noncoal, silica and total dust) in the lungs were determined using gravimetric or spectrophotometric analysis (Carlberg *et al.*, 1971). Occupational and smoking histories were determined from the next-of-kin. Cumulative exposure was estimated from tenure in each job and job-specific measurements of mean concentration of respirable coal mine dust, using the approach of Attfield and Morring (1992). Table 1 describes characteristics of the cohort.

Lung dust burden was used as either a response variable (in exposure–dose relationships) or a predictor variable (in dose–response relationships) Lung dust burdens are expressed in mg dust g^{-1} dry lung. Initial linear and logistic regression analyses were performed using all available measures of lung dust burden—coal, silica, noncoal and total dust. Further analyses focused on coal lung dust because it

Table 1. Characteristics of autopsy study population of U.S. miners*

Variable (units)	Smokers (n = 91)	Nonsmokers (n = 24)	Whole cohort† (n = 131)
		Mean (SD)	
Age (years)			
Start of mining	20 (7.1)	20 (8.3)	21 (7.8)
Retirement	56 (7.4)	61 (6.9)	57 (7.3)
Death	66 (9.4)	74 (9.0)	67 (9.8)
Exposure‡			
Cumulative (mg-year m^{-3})	108.4 (42.7)	122.1 (49.0)	107.8 (43.4)
Duration (years)	36.2 (9.6)	40.8 (10.6)	36.0 (10.0)
Intensity (mg m^{-3})	3.0 (0.9)	2.9 (0.6)	3.0 (0.8)
Post-exposure‡ duration (years)	9.8 (6.5)	12.8 (6.7)	10.3 (6.7)
Lung dust burdens (mg g^{-1} dry lung)			
Total dust	67.3 (40.0)	82.3 (42.7)	69.1 (40.3)
Coal dust	42.0 (34.0)	61.9 (35.4)	45.5 (34.7)
Noncoal dust	26.1 (21.1)	20.4 (13.0)	24.1 (19.1)
Silica dust	1.8 (1.1)	2.2 (1.3)	1.9 (1.1)
		Percentage (count)	
Pathological responses§ (%)			
No disease	1 (1)	8 (2)	3 (4)
Macules	87 (79)	83 (20)	84 (110)
Micronodules	79 (72)	75 (18)	77 (101)
Macronodules	42 (38)	58 (14)	47 (61)
PMF	24 (22)	42 (10)	30 (39)
Race (%)			
White	73 (66)	46 (11)	66 (86)
Black	25 (23)	54 (13)	31 (41)
Other	2 (2)	0 (0)	3 (4)

* Subset of Laqueur autopsy study (Attfield *et al.*, 1994) for which lung dust burden data and occupational histories are available; all miners in the study are male.
† Smoking status is unknown for 16 miners.
‡ Respirable coal mine dust exposure.
§ Macules: moderate severity or greater; micronodules, macronodules, and PMF: slight severity or greater.

was a significant predictor of all pathological responses evaluated in the study. Pathological response was defined in logistic regression analyses as the presence or absence of a given response and all responses of higher severity.

Analyses were performed separately for smokers and nonsmokers because of possible differences in the deposition and retention of dust in the lungs of smokers and nonsmokers and because of observed differences in factors that may influence pathological response (age of retirement, age of death, cumulative exposure, lung dust burden) (Table 1). Departures from linearity were evaluated using quadratic and cubic terms of duration of exposure, cumulative exposure and lung dust burdens; two-way interactions between covariates were evaluated.

Mean clearance rates of dust from the lungs were estimated from the slope of the relationship between the lung dust burden (normalized on cumulative exposure) and the post-exposure duration (years between retirement and death). These values were computed in linear regression analyses of the whole cohort, smokers and nonsmokers, and smokers stratified by lung dust burden (tertiles) for each of the measured lung dusts.

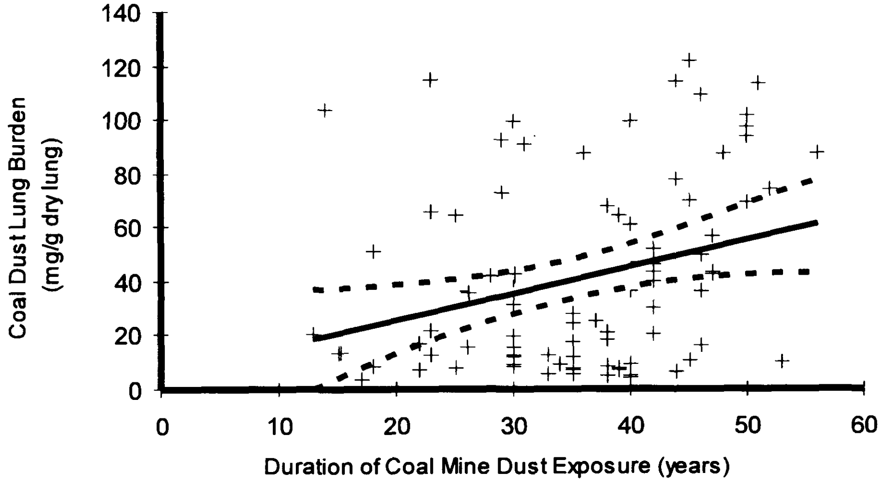

Fig. 1. Actual and predicted coal dust lung burden by duration of exposure to respirable coal mine dust in smokers (95% confidence intervals).

RESULTS

Exposure–dose

Coal lung dust burden increased in a linear relationship with duration of exposure ($P < 0.006$, $r^2 = 0.08$) (Fig. 1). Coal lung dust burden also increased with cumulative exposure ($P < 0.0001$; $r^2 = 0.17$) (Fig. 2). Departure from linearity was suggested by marginally significant quadratic and cubic terms for cumulative exposure ($P < 0.05$; skewness observed in residuals). The model fit shown in Fig. 2 excludes the two highest cumulative exposures; exposure–dose was also significant with these cases included ($P < 0.007$). Smoking status was a significant, negative

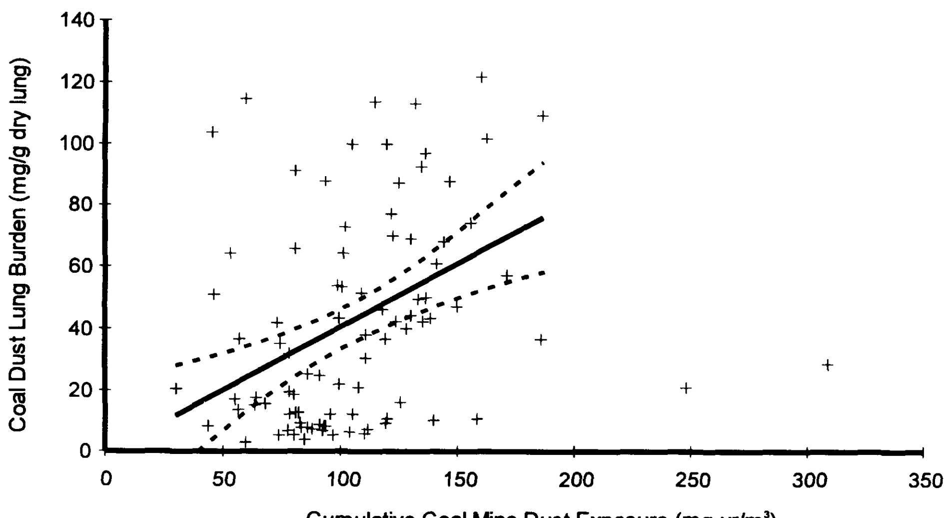

Fig. 2. Actual and predicted coal dust lung burden by cumulative exposure to respirable coal mine dust in smokers (95% confidence intervals).

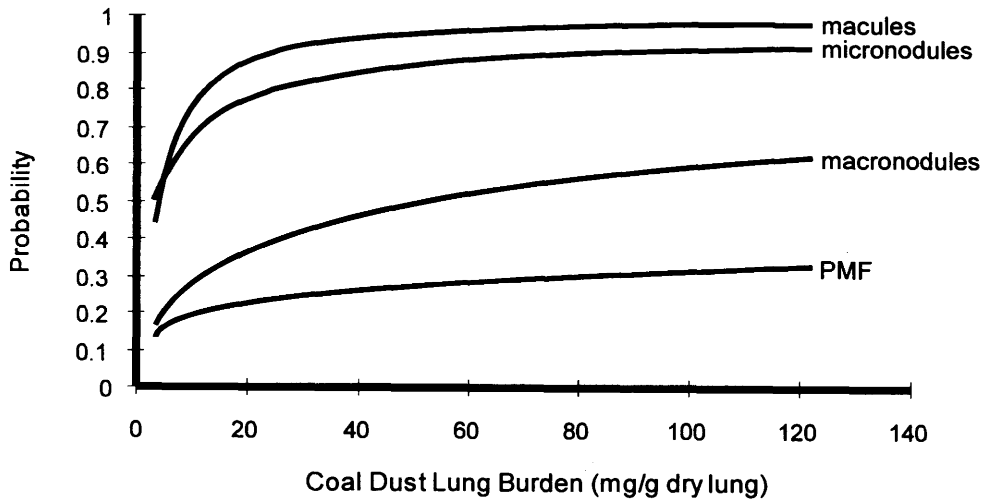

Fig. 3. Probability of pathological response associated with (log) coal dust lung burden in smokers.

predictor of coal dust lung burden ($P < 0.02$), apart from the positive effect of cumulative exposure (effect of smoking: -17 mg g^{-1} dry lung).

Dose–response

The presence and severity of pathological lesions (macules of moderate or greater severity, nodules and PMF) were significantly associated with the coal, silica and total lung dust burdens in the whole cohort (P values = 0.02–0.0001) and in smokers (P values = 0.04–0.003) (Fig. 3). The best predictor of macules was coal lung dust burden, while the best predictor of nodules and PMF was silica lung dust burden (based on comparison of model likelihoods). Smoking status was not a significant predictor of macules, nodules, or PMF (P values = 0.2–0.6). Age at death was a significant and positive predictor of all pathological responses evaluated except moderate or severe PMF.

Exposure–response

Lung dust burden was a better predictor of pathological response in the whole cohort than was duration of exposure or cumulative exposure to respirable coal mine dust (based on comparison of model likelihoods). Separate analysis by smoking status showed improved model fit for exposure–response in smokers (Fig. 4).

Clearance

No evidence of lung dust clearance during the post-exposure period was observed in the full cohort, smokers, or nonsmokers for any of the dusts evaluated—total, coal, noncoal, silica lung dust burdens (P values = 0.15–0.9). Post-exposure lung dust clearance was not detected even in the lowest coal lung dust burden stratum (9.8 mg g^{-1} dry lung, SD = 5.2), thus no dose-dependent clearance was observed.

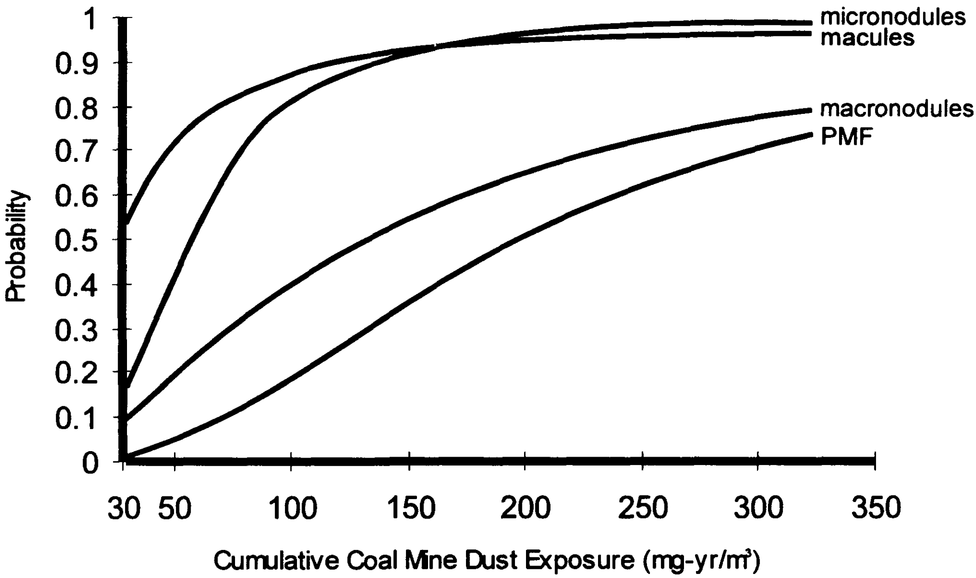

Fig. 4. Probability of pathological response associated with (log) cumulative exposure to respirable coal mine dust in smokers.

DISCUSSION AND CONCLUSIONS

The linear relationship between duration of exposure and lung dust burden suggests the absence of a time-dependent change in lung clearance during the study period, although a nonlinear relationship cannot be ruled out given the variability in the data. Lung dust burden at death increased with increasing lifetime exposure (a linear model may not be sufficient). The negative influence of smoking status on lung dust burden, after accounting for the positive effect of cumulative exposure, may suggest lower deposition of dust in the alveolar region in smokers (perhaps due to mucous hypersecretion and dust trapping in the proximal airways combined with enhanced cough clearance). No post-exposure clearance of dust from miners' lungs was observed in this study, although clearance of a relatively small portion of the total lung dust burden may have been undetectable (e.g. the alveolar dust burden relative to the interstitial dust burden).

Lung dust burden (coal, silica or total dust) was a better predictor of the presence and severity of pathological responses than were duration or cumulative exposure to respirable coal mine dust, although this distinction was less apparent when the analyses were stratified by smoking status. The significant association between increased age at death and increasing probability of having macules, nodules, or PMF (slight severity) may reflect the increased time for development and progression of these pathological responses.

The lung dust burdens of most miners in this study exceed those observed in animal studies in which overloading of lung clearance has been observed (Morrow, 1992). Further analyses of these data will include toxicokinetic modeling to evaluate hypotheses about relationships between lifetime exposures, retained lung dust, overloading of lung clearance and disease development.

REFERENCES

Attfield, M. D. and Morring, K. (1992) The derivation of estimated dust exposures for U.S. coal miners working before 1970. *Am. ind. Hyg. Assoc. J.* **53**(4), 248–255.

Attfield, M. D., Vallyathan, V. and Green, F. H. Y. (1994) Radiographic appearances of small opacities and their correlation with pathology grading of macules, nodules, and dust burden in the lungs. *Ann. occup. Hyg.* **38** (suppl. 1), 783–789.

Carlberg, J. R., Crable, J. V., Limtiaca, L. P., Norris, H. B., Holtz, J. L., Mauer, P. and Wolowicz, F. R. (1971) Total dust, coal, free silica and trace metal concentrations in bituminous coal miners' lungs. *Am. ind. Hyg. Assoc. J.* **32**(7), 432–440.

Kleinerman, J., Green, F., Harley, R. A., Lapp, N. L., Laqueur, W., Naeye, R. L., Pratt, P., Taylor, G., Wiot, J. and Wyatt, J. (1979). Pathology standards for coal workers' pneumoconiosis. *Archs. Path. Lab. Med.* **103**, 375–432.

Morrow, P. E. (1992) Dust overloading of the lungs: update and appraisal. *Toxicol. appl. Pharmacol.* **113**, 1–12.

Vallyathan, V., Brower, P. S., Green, F. H. Y. and Attfield, M. D. (1996) Radiographic and pathologic correlation of coal workers' pneumoconiosis. *Am. J. crit. Resp. Med.* **154**, 741–748.