Radiographic and Pathologic Correlation of Coal Workers' Pneumoconiosis

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The relationships between chest radiographs (CXR) and corresponding pathology were investigated in 430 autopsied coal miners from West Virginia. Whole-lung sections were reviewed and graded on four-point severity scales for the following lesions of coal workers' pneumoconiosis (CWP): macules, micro- and macronodules (small and large fibrotic nodules), and progressive massive fibrosis (PMF). Antemortem CXR were classified by three B readers using the 1971 International Labor Office (ILO) U/C classification (6). On pathologic examination, 96% of miners had macules, 70% micronodules, 45% macronodules, 15% silicosis, and 28% PMF. By CXR, 69% of the miners had small, rounded opacity profusions of category ≥ 0/1. Data analysis revealed increasing odds that small opacities of category ≥ 0/1 would be detected with increasing grade of nodules. Profusion category 0/0 was often reported for cases with macules of mild to moderate grade and mild levels of micronodules. Overall, q-type opacities were associated with macules and micronodules, whereas the large r-type opacities were associated with macronodules. By CXR, large opacities showed good correlation with pathologic PMF. However, about one-third of cases identified as having large opacities by CXR were not substantiated as PMF by pathology. One-fourth of these cases could be explained by lung lesions such as Caplan's nodules, tuberculosis scars, and tumors. Similarly, 22% of cases classified as PMF on pathology had no large opacities by CXR. In half of these cases, the radiologists had noted other abnormalities (cancer, tuberculosis) by CXR as large opacities. Overall, the study showed good agreement (Somer's d = 0.64) between the predicted probabilities and observed responses of a profusion category ≥ 0/1 for pathologic CWP lesions. However, the study also showed that CXR were insensitive for detecting minimal CWP lesions, and were unreliable indicators in the presence of concomitant pulmonary pathology.

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Inhalation of coal mine dust (i.e., coal dust combined with other mineral dusts) may lead to the development of coal workers' pneumoconiosis (CWP), silicosis, chronic bronchitis, emphysema, and Caplan's syndrome (1–5). CWP and silicosis are categorized radiographically according to the International Labor Office (ILO) Classification, using a system to standard reference films (6). The most common radiographic abnormality in simple CWP consists of small rounded opacities located predominantly in the upper zones of the lungs (1, 3, 6). Complicated CWP, also known as progressive massive fibrosis (PMF), is defined on the basis of one or more large opacities of 1 cm or more in diameter (6).

The radiographic category of simple CWP is determined largely by the dust content of the lung and to a lesser degree by fibrotic reaction (7, 8). With respect to the relative effects of the components of coal mine dust, autopsy studies of coal miners have shown that minerals in the lung had nine times the effect of carbonaceous materials on radiographic appearance (9). A positive correlation between the total dust load and radiographic category of CWP has also been observed in other studies (9–11).

In general, category 1/0 or above is seldom recorded until dust accumulation in the lung exceeds a threshold level in the range of 8 to 10 g (9, 11); milder forms of CWP are often not apparent on chest radiographs (CXR) (3, 8, 10, 12). The sensitivity of the radiograph is also influenced by other factors such as size of the lesions, summation effect, background density, contrast effect, and thickness of the chest wall (1–3).

Compared with standard radiographic examination, pathologic assessment provides a direct means of assessing CWP with greater sensitivity and specificity (10). However, the greatest sensitivity and specificity of CWP can be achieved only by examining whole-lung sections obtained at autopsy (3). Because the CXR remains the most widely used tool for diagnosing CWP during life, it is important to understand the relationship between the radiographic appearance of CWP and the lesions in the lungs.

Several correlative studies have been reported from the British (9, 13–15), German (16), and Australian (17) coal fields. In general, the published studies have shown a moderate to good correlation between pathologic grade of pneumoconiosis and radiographic category of CWP. They have also provided important insights into radiographic correlates of specific forms of CWP and the confounding effects of diseases such as emphysema (5, 8). Factors such as rank of coal, method of mining, and concentrations of minerals in the coal mine dust have all been

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shown to play a part in the prevalence, severity, and type of disease. In addition, other unknown to partially characterized factors are probably also important (4).

In a rather small, postmortem study of 77 coal miners from Pennsylvania, the radiologic category of pneumoconiosis was compared with pathologic findings (10). A good correlation was found between category of pneumoconiosis and quantitative morphometric measurements of macules, nodules, and silica and collagen contents in tissue sections (10).

Because it is well established that prevalence and type of disease vary between countries and between regions within a country (18), and because existing information on United States miners is limited both in scope and geographically, the present study was undertaken. Its objective was to enhance knowledge about the relationships between postmortem pathologic abnormalities and the corresponding changes in the antemortem CXR by study of a group of autopsied coal miners from southern West Virginia.

METHODS

The study group consisted of 430 coal miners autopsied in a southern West Virginia hospital serving a coal mining community. The miners' lungs were collected systematically from 1957 to 1971 by the late Dr. W. Laqueur, (Beckley Appalachian Regional Hospital, Beckley, WV) from consecutive autopsies of current and former coal miners. All miners included in the study had at least 1 yr of coal mining exposure and had worked in coal mines within a 100-mile radius of Beckley, West Virginia. The coal mined in this area is largely high rank, bituminous coal, with a high carbon content. Demographic details of the coal miners were obtained from hospital records. Occupational histories were obtained through a standardized questionnaire sent to the next-of-kin soon after death, clinical records from family physicians, and coal mine company records. Missing information on certain variables led to fewer than 430 cases in some subanalyses.

Pathology

Whole-lung preparation. At autopsy, whole lungs were removed with the major blood vessels and bronchus intact and were inflated several times with 95% CO_2 at a constant pressure of 36 cm H_2O. The lung was then cannulated through the bronchus and infused with a 4% buffered formaldehyde solution at a constant pressure of 30 cm H_2O for 1 h. The bronchus and blood vessels were then tied and the lung floated in 4% formaldehyde solution for 3 to 4 d for complete fixation. The fixed lungs were then cut parallel to the hilum (sagittal plane), and five thick (7/8-in) slices were made on a flat tissue slicer. The third level thick slice was embedded in a gelatin solution according to the procedure of Gough and colleagues (15). Gelatin penetration was achieved at 40° C for 4 h, and the embedded slice was frozen at −20° C. Semithin sections (~200 μm) were cut on a sledge microtome. Five or more serial sections were mounted on opaque white paper, dried, and laminated. For the gross evaluation of CWP, a single section was used, selected only on the basis of its technical superiority. Left whole-lung sections were used in the majority of the cases except when trauma or neoplasm precluded their use. In such cases the right lung was prepared according to the same protocol. Approximately nine tissue blocks (range: 6 to 14) were taken for histologic examination from the right and left lungs of each case at the time of autopsy, representing all visible pathologic lesions. Paraffin sections (5 μm) thick were stained with hematoxylin-eosin (H&E), and selected sections were also stained with Van Gieson's stain to identify components of connective tissue.

Pneumoconiosis classification and grading. The whole-lung sections were evaluated by two investigators (V.V. and F.H.Y.G.) using diagnostic criteria established by the joint committee of the College of American Pathologists (CAP) and the National Institute for Occupational Safety and Health (NIOSH), with slight modifications (as subsequently discussed) (3). CWP lesions such as macules, micronodules (small fibrotic nodules measuring up to 7 mm in diameter), macronodules (large fibrotic nodules measuring from 7 to 20 mm in diameter), progressive massive fibrosis (PMF), Caplan's lesions, and silicosis were identified through gross and microscopic criteria (3, 5). Collections of coal dust-laden alveolar macrophages, in a size range of 0.5 to 6 mm within the walls of respiratory bronchioles and adjacent alveoli, and enmeshed within a fine network of reticulin and occasional collagen fibers, were classified as macules. Micronodules and macronodules were defined on the basis of two size ranges (< 7 mm and 7 to 10 mm, respectively) (3, 20). On histologic examination, CWP nodules showed round or serpiginous borders containing coal dust-laden macrophages in an irregularly arranged fibrotic stroma. Because silicotic nodules could not be reliably separated from the nodules of CWP in the grading of whole-lung sections, they were included in the categorization of micronodules and macronodules. For the purpose of classification, cases of silicosis were confirmed histologically by the presence of one or more silicotic nodules, which were characterized by their rounded profile and concentrically arranged collagen fibers (3, 5). Pigmented fibrotic lesions measuring more than 1 cm or more across were classified as PMF. This size classification was used to conform to the radiologic definition and with current U.S. Black Lung Legislation (19). Lightly pigmented pulmonary nodules with smooth borders and concentric pigmented laminations, and with diameters exceeding 1 cm, were classified as Caplan's lesions (rheumatoid pneumoconiosis) after excluding mycobacterial and fungal infection.

Macules, micronodules, macronodules, and PMF were each graded on a four-point scale corresponding to the increasing profusion and severity of these lesions within the whole-lung section. The grades were based on a series of reference standards established and scored for CWP prior to the grading process (20). The grades for macules were 0 (absent, no visible macules), 1 (mild; occasional macules occupying less than 10% of proximal acinar [centriacinar] lung parenchyma), 2 (moderate; macules involving 10 to 60% of proximal acinar lung parenchyma), and 3 (severe; macules occupying more than 60% of the proximal acinar regions of the lung). The grades for micronodules and macronodules were 0 (absent; no visible lesions), 1 (mild; nodules occupying up to 5% of the lung parenchyma), 2 (moderate; nodules occupying up to 20% of the lung parenchyma), and 3 (severe; nodules occupying more than 20% of the lung parenchyma). The grades for PMF were 0 (absent; no visible lesions), 1 (mild; discrete area or areas of pigmented fibrosis measuring more than 1 cm but less than 5 cm across), 2 (moderate; area[s] of pigmented fibrosis measuring more than 5 cm across but occupying less than one whole lobe of lung), and 3 (severe; area[s] of pigmented fibrosis which singly or in aggregate occupied one lobe or more of lung parenchyma).

The evaluations were made independently by each reader, in random order, and without knowledge of historical information, radiographic classification, or diagnosis at the time of autopsy. Items of disagreement were subsequently resolved by consensus with reference to the standard lung sections, and the consensus scores were used in the analyses.

Radiology

For each miner, three or more CXR were available for radiologic-pathologic correlations. All the radiographs were full sized posterior-anterior (PA) films obtained during the periodic screening program administered by the Appalachian Regional Hospital, Beckley, WV. Coal miners, on a voluntary basis, were surveyed radiographically at approximately 5-yr intervals during working life and after retirement, at the hospital clinic. For this study, the most recent radiograph was used; most of these (90%) had been taken within 3 yr of death. Without knowledge of exposure history or other details, the radiographs were randomly ordered and classified independently by each of three NIOSH-certified B readers using the 1971 ILO U/C classification system (6). Each reader recorded the profusion and type of small rounded opacities and small irregular opacities, and the profusion of the combined small opacities, as well as the category of large opacities.

For each film, profusion was summarized by taking the median of the three readers' combined small-opacity-profusion categories. Fourteen percent of the films had only two readers because one reader stated that the film was unreadable. In these 14% of films, when there was no agreement between the two readers (n = 39), the highest profusion category was assigned. A summary indicator for the predominant type of small opacities was derived as follows. If the median profusion of small rounded opacities was greater than the median profusion of small irregular opacities, the predominant type was said to be rounded. In this case, if two of the three readers agreed on the small rounded type of opacity (i.e., p, q, or r), that type was taken as the predominant category. If no agreement was reached, the case was assigned a mixed rounded (MR) category. A similar procedure was followed for the situation in

which the median profusion of irregular opacities (i.e., s, t, or u) was greater than the median profusion of small rounded opacities. In cases in which the median profusions of small rounded and small irregular opacities were equal (apart from categories 0/- and 0/0), the cases were assigned a mixed-type (M) category. In cases of large opacities, an average score was generated by converting the categories (None, A, B, C) as classified by each reader to integers (0, 1, 2, 3), taking the median, and converting back to the letter scores.

Statistical Analysis

For examination of the relationship between the radiologic and pathologic variables, logistic regression was performed (21). Two radiologic variables were formed by dichotomizing the profusion category scale of small opacities between: (*1*) categories 0/0 and 0/1; and (*2*) categories 1/2 and 2/1. For each pathologic variable (macule, micronodule, macronodule), k-1 design variables were defined on the basis of the k grades available for each variable. There were three design variables for the four grades of each pathologic variable (normal, mild, moderate, severe). However, in some cases, adjacent categories were combined prior to analysis when the size of the group was too small for reliable analysis. The logistic regression function was

$$\pi = \frac{e^Y}{1 + e^Y} \qquad (1)$$

where

$$Y = \beta_0 + \sum_{i=1}^{3} \sum_{j=1}^{k_i - 1} \beta_{ij} D_{ij} \qquad (2)$$

was used. D_{ij} are the $k_i - 1$ design variables for each of the three pathologic variables, and π is the probability that a film would be classified as positive (e.g., the median classification was 0/1 or greater rather than 0/0) given the pathology variables. Diagnostic statistics, such as residuals ($\Delta\chi^2$) and influential measures ($\Delta\beta$), were computed to assess the extent to which individual observations influenced the overall fit of the models (21).

Logistic models were also fitted to subsets of the complete data set, which were formed by omission of cases with PMF by pathologic examination, and by omission of cases with either PMF or large opacities from the radiographic classification. The latter analyses were undertaken to determine if the relationship between the radiographic and pathologic variables was affected by the presence of complicated pneumoconiosis.

Other statistical analyses were performed, such as the chi-square test of independence and Kendall's (tau-b) and Somer's d measures of association. All statistical parameters were tested at a significance level (α-level) of 0.05.

RESULTS

The average age at death for the 430 coal miners in the study was 68 yr, with the youngest dying at 31 yr and the oldest at 91 yr. On average, the miners had about 34 yr of exposure in coal mining, with a range of from 4 to 64 yr. Fifty-eight percent were ever-smokers (current and ex-smokers), 18% were never smokers, and 24% were of unknown smoking status. All 430 coal miners were males; 70% were white, 29% were black, and 1% were of other classification.

The basic pathologic profile showing the percent frequency distribution for macules (present in 96%), micronodules (70%), macronodules (45%) and, PMF (28%), along with their grades of severity, is presented in Figure 1. Silicosis (based on histologic criteria), not shown in the figure, was found in 15% of the cases and was not graded for severity. Caplan's lesions were found in eight cases. Macules and nodules of any type were absent in 3% of the cases.

The frequency distribution of combined small-opacity profusion overall and by grade of macules, micronodules, and macronodules is shown in Table 1. Sixty-nine percent (298 of 430) of the chest films were classified as 0/1 or greater (≥ 0/1) for

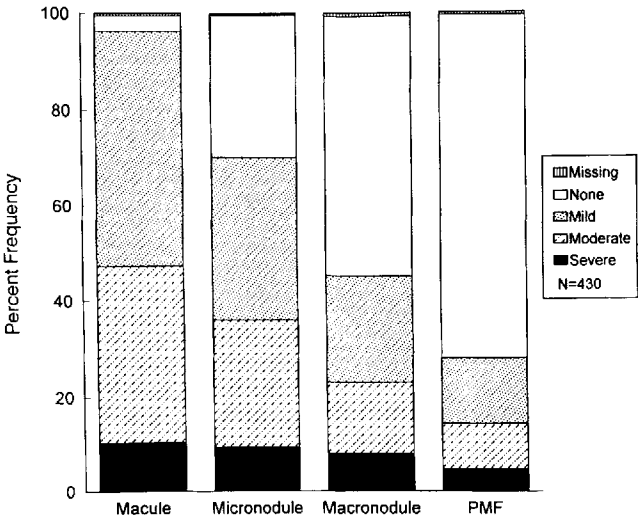

Figure 1. Percent frequency distribution of pathologic lesions of CWP by severity in 430 autopsied coal miners.

small-opacity profusion, and 41% were classified as 2/1 or greater (≥ 2/1). An increasing prevalence of category ≥ 0/1 was seen for an increasing grade of each of the three pathologic variables, rising to nearly 100% for moderate and severe grades of micronodules and macronodules. The results were similar for category ≥ 2/1, except that no consistent trend was evident across the macule grades.

A clearer idea of the effect of macules *per se* on radiographic category can be gained by restricting the data to those cases without nodules (lower part of Table 1). In this, there was some indication of a trend in prevalence of category ≥ 0/1 by macule grade, although there were too few cases in the severe grade for reliable interpretation. There was the appearance of a possible increase from normal (0%, n = 10) to abnormal (i.e., about 16% for mild to severe) for category ≥ 2/1; however, no trend was seen from mild to severe grade. The corresponding results by micronodule grade for the subset without macronodules are given at the bottom of Table 1. Clear trends are evident for category ≥ 0/1, suggesting a doubling and tripling of the percentage of positive X-rays with an increase in micronodule grade from normal to mild and normal to moderate, respectively. Similar findings were evident for category ≥ 2/1.

The relationship between profusion category of small opacities on the chest film and severity of pathologic lesions (macule, micronodule, macronodule) was examined by performing logistic regression. Two logistic models were of primary interest, the results of which are shown in Table 2. Models 1 and 2 explain the relationship between the pathologic variables and the absence or presence of the different profusion categories ≥ 0/1 and ≥ 2/1.

For each of these models, the parameters represent design-variable coefficients for the various grades of macules, micronodules, and macronodules. All coefficients represent a comparison with the normal grade (i.e., mild to normal, etc.) or to the normal combined with the mild grade for those analyses in which the lower two grades had been pooled.

For Model 1 (Category ≥ 0/1), all estimated parameters were positive, indicating that the odds that a positive chest film (i.e., positive radiographically for simple CWP) will be found increases when any abnormality is present in terms of pathologic findings. The strongest effects, statistically, were observed for micronodules and macronodules. In this, the odds ratios (OR) that a category ≥ 0/1 radiograph would be reported for mild and

TABLE 1

FREQUENCY DISTRIBUTION OF PATHOLOGIC LESIONS BY SMALL OPACITY PROFUSION CATEGORY

		Radiographic Profusion Category					
	n	0/0	0/1	1/0–½	≥ 2/1	% (≥ 0/1)	% (≥ 2/1)
Overall	430	132	11	111	176	69	41
Macule							
Normal	14	10	–	4	–	29	0
Mild	211	70	6	45	90	67	43
Moderate	158	43	5	45	65	73	41
Severe	45	9	–	16	20	80	44
Micronodule							
Normal	127	82	7	20	18	35	14
Mild	147	39	3	49	56	73	38
Moderate	114	10	1	33	70	91	61
Severe	41	1	–	9	31	98	76
Macronodule							
Normal	232	113	9	55	55	51	24
Mild	95	15	2	33	45	84	47
Moderate	65	3	–	16	46	95	71
Severe	35	–	–	7	28	100	80
Macules alone							
Normal	10	9	–	1	–	10	0
Mild	70	45	5	8	12	36	17
Moderate	36	22	1	8	5	39	14
Severe	6	5	–	–	1	17	17
Micronodules without macronodules							
Normal	122	81	6	17	18	34	15
Mild	85	28	3	31	23	67	27
Moderate	24	4	–	6	14	83	58
Severe	1	–	–	1	–	100	0

moderate/severe grades of micronodules, compared with the normal grade, were 3.3 and 11.4, respectively. For presence/absence of macronodules, the OR that a category ≥ 0/1 radiograph would be reported was 3.1. The effect of macules was smaller, and the coefficients were not significantly different from zero. The overall fit of the model was good, with a chi-square value of 129.8 ($p = 0.0001$), and there was good agreement (Somer's $d = 0.64$) between the predicted probabilities and observed responses for a category ≥ 0/1 radiograph.

The predicted probabilities of a category ≥ 0/1 film from

TABLE 2

TWO LOGISTIC REGRESSION MODELS REPRESENTING THE RELATIONSHIP BETWEEN THE RADIOLOGIC AND PATHOLOGIC VARIABLES

	Parameter Estimate	Standard Error	Estimated OR
Model 1, Category ≥ 0/1			
Macule			
Moderate:Normal + Mild	0.39	0.27	1.5
Severe:Normal + Mild	0.36	0.46	1.4
Micronodule			
Mild:Normal	1.18*	0.29	3.3
Moderate + Severe:Normal	2.44*	0.43	11.4
Macronodule			
Mild + Moderate + Severe:Normal	1.12*	0.34	3.1
Intercept	−0.79*	0.21	
Model 2, Category ≥ 2/1			
Macule			
Moderate:Normal + Mild	0.06	0.24	1.1
Severe:Normal + Mild	−0.13	0.37	0.9
Micronodule			
Moderate:Normal + Mild	0.81†	0.30	2.2
Severe:Normal + Mild	1.15‡	0.46	3.2
Macronodule			
Mild:Normal	0.80†	0.28	2.2
Moderate + Severe:Normal	1.58*	0.34	4.8
Intercept	−1.28*	0.19	

* Significant at an alpha level of 0.001.
† Significant at an alpha level of 0.01.
‡ Significant at an alpha level of 0.05.

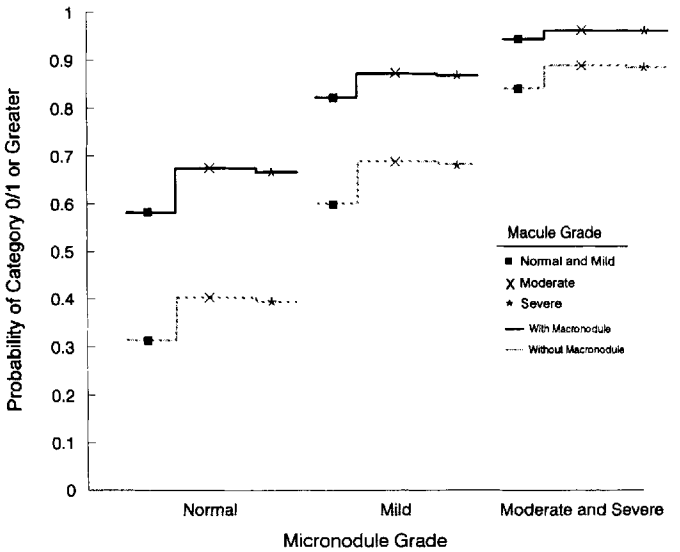

Figure 2. Predicted probabilities of classifying a chest film as having a profusion category 0/1 or greater from Model 1. *Dotted line*: cases with macules and micronodules without macronodules. *Solid line*: lungs with macules, micronodules, and macronodules. Within each micronodule grade there are three grades of macules: normal and mild grades (*small square*); moderate grades (*X*); and severe grades (*small asterisk*).

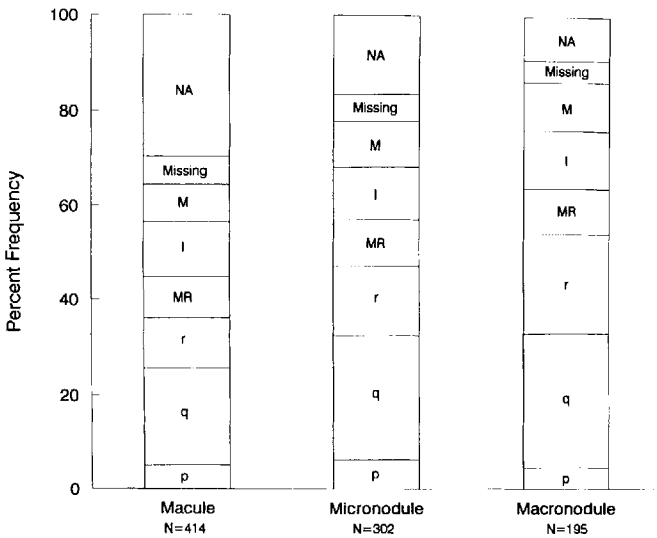

Figure 3. Percent frequency distribution of overall opacity type by pathologic lesions. The small rounded opacity types are represented by p, q, and r, and mixed rounded opacity type is represented by MR. The small irregular opacity types are represented by I (including s, t, u, and mixed irregular). The mixed opacity type (both rounded and irregular) is represented by M. "Missing" represents non classified types, and NA represents films categorized as category 0/0.

Model 1 are shown in Figure 2 for each distinct combination of pathologic variables. In this, each variable is adjusted for the effects of the others. It is evident that the probability of reporting a film as being of category $\geq$ 0/1 increases as markedly as the severity of micronodules increases. This is true also for macronodules. In contrast, little effect of macule grade was observed.

The overall fit of Model 2 was not as good as that for Model 1 (chi-square = 88.0). However, as for Model 1, micronodules and macronodules were strong predictors of a positive chest film, and macules again were not useful predictors.

Since there was concern that the relationship between the pathologic and radiographic variables might have been affected by the presence of PMF, Model 1 was repeated after the omission of all cases with recorded PMF by pathologic examination. No changes of any consequence were noted in the observed coefficients for the macules, the OR values for moderate to normal combined with mild remaining unchanged at 1.5, whereas that for severe to normal combined with mild declined from 1.4 to 1.3. For micronodules, the OR values showed small declines, going from 3.3 to 3.0 for the comparison of mild with normal and from 11.4 to 9.2 for the comparison of moderate plus severe with normal. The single OR for macronodules showed the greatest decline, going from 3.1 for the full model to 1.95 for the restricted subset. In each of these cases the changes in the coefficients were within one standard error (SE). Omission of any cases with large opacities in addition to PMF gave rise to similar findings, but with somewhat greater declines in the OR values for micronodules and macronodules.

Examination of types of small opacities showed that rounded opacities (p, q, r, mixed rounded) predominated (63%), followed by irregular types (s, t, u, irregular mixed) (16%), and mixed types (12%), whereas 9% were missing due to incomplete data from the B readers. Overall, q-type opacities were the most common type of small rounded opacity, whereas the larger r-type opacities tended to be more prevalent in the higher profusion categories of small opacities.

The distributions of opacities of the small type among cases having macules, micronodules, and macronodules is shown in Figure 3. The percent of opacities of the small rounded type (p, q, r, mixed rounded) increased from 45% to 64% across the three groups (chi-square = 21.5; $p < 0.0001$), mainly because of an increase in the proportions of q and r type opacities. In contrast, the percentage of opacities of the irregular (s, t, u) and mixed rounded and irregular types remained about the same over all three groups. As a consequence, the ratio of the frequencies of rounded to irregular types increased as the severity of the pathologic lesion increased (i.e., from macules to macronodules).

The relationship between radiographic large opacities and PMF by pathologic evaluation of whole-lung slices is shown in Table 3. By pathologic grading, there were a total of 122 cases of PMF, of which 48% were classified as mild, 35% as moderate, and 17% as severe. Evaluation by CXR revealed a total of 142 cases with large opacities, of which 36% were graded as being in category A, 44% in category B, and 20% in category C. There was 83% agreement on the presence versus absence of PMF and large opacities, and significant overall correlation (Kendall's tau-b = 0.63; $p < 0.001$) between the size of large opacities on chest films and grading of PMF on whole-lung slices. Forty-seven (15%) of the 306 cases without PMF by pathologic evaluation were radiologically categorized as having large opacities, whereas 27 (9%) of 286 cases without large opacities on CXR were found to have PMF by pathologic evaluation.

DISCUSSION

A number of studies in different countries have demonstrated correlations between the antemortem radiographic category of CWP and the postmortem pathologic severity of pneumoconiosis (8–13, 15, 22, 23). The findings reported here on United States coal miners are consistent with these studies. In addition, we provide support for the concept that some specific radiologic features of CWP have specific pathologic correlates (8, 12, 14).

TABLE 3

RELATIONSHIP BETWEEN PMF AND LARGE OPACITY SIZE CATEGORY

Pathologic Progressive Massive Fibrosis Grade	Radiographic Large Opacity Size Category				
	Absent	A	B	C	Total
Absent (0)	259	29	14	4	306
Mild (1)	23	16	18	2	59
Moderate (2)	4	5	25	8	42
Severe (3)	0	1	5	15	21
Total	286	51	62	29	428

Most of the miners in this study were retired and had worked for long periods in coal mining (average: 34 yr). Most of their exposures had occurred prior to 1971, when the mines were considerably dustier than they are today. It is therefore not surprising that there was a high prevalence of pneumoconiosis in the group. The miners' high exposures and associated level of disease should not be taken as typical of coal miners working today. However, the presence of such high disease levels is largely an advantage rather than a disadvantage in this study, since it facilitates the examination of a spectrum of disease correlations between the radiographic and pathologic variables in CWP.

One advantage of this investigation was that the study population was relatively homogeneous, both with regard to environment and occupational exposure, being derived from a single community in southern West Virginia mining a medium-to-high-rank bituminous coal. Information about geologic variables was not available and thus was not included in the analyses of the radiographic/pathologic correlation. In addition, the methods used were consistent throughout the study, with all of the autopsies performed at a single institution using standardized protocols and under the direct supervision of one pathologist, and all of the pathologic readings made by the same two pathologists using a standardized protocol. Similarly, all of the radiographs were read by three B readers certified in the ILO/UC classification of radiographs.

The model-fitting revealed that both micronodules and macronodules were strong predictors of both category $\geq$ 0/1 and $\geq$ 2/1 radiographs. For category $\geq$ 0/1, the OR increased from about 3 when mild micronodules were present to about 11 when moderate combined with severe grades of micronodules were seen, as compared with radiographs free of those pathologic abnormalities. The presence of macronodules as compared with their absence gave rise to an OR of about 3 for a category $\geq$ 0/1. Similar findings resulted for category $\geq$ 2/1.

The pathologic variables used in this study represent sequential stages of disease severity, from macules through micronodules to macronodules. Because of this severity gradient, the data are unbalanced across the cells of the three-dimensional matrix formed by the three variables. For instance, when macronodules are present, macules and micronodules are both rarely absent. This imbalance in the data gave rise to concern about the validity of the model used to estimate the separate and independent effects of the three pathologic variables. However, the model appeared to behave reasonably, providing predicted effects similar to those observed. The observed OR values were calculated from the data in the lower part of Table 1, and where sufficient data were available. For moderate-to-normal combined with mild macules, the observed OR was 1.3, agreeing well with that predicted, 1.5. Similarly, for micronodules, the observed OR values were 4.0 and 10.4 for mild-to-normal and moderate combined with severe-to-normal grades, respectively (bottom rows of Table 1). These compare well with the predicted OR values of 3.3 and 11.4.

The influence of macules was found to be ambiguous. Not only were the macule coefficients statistically nonsignificant, but they differed in direction between Models 1 and 2. This phenomenon suggests increased amounts of dust deposition in categories $\geq$ 0/1, whereas that in the more advanced radiographic categories results from fibrosis. To some extent, the apparent lack of predictive ability of the macule variable for radiographic abnormality may be an artifact, resulting from there being few cases with mild disease. In addition, the adopted procedure of combining the normal and mild grades of macules for analysis, owing to small numbers, may have contributed to hiding any macule effect. In this respect, examination of the macules-only data in Table 1 shows some evidence of a difference between absence and presence of macules (i.e., 10% for the normal grade compared with 36%, 39%, and 17% for the mild, moderate, and severe grades, respectively). Although this finding is plausible, the small number of cases in the normal-grade category makes it difficult to draw a definitive conclusion about this.

Logistic regression diagnostics were performed to assess whether the overall chi-square statistics and the estimated coefficients for the predictor variables were influenced by any observations with any particular pattern of pathologic variables. Two diagnostics were computed, residuals and influential measures, and plotted against the predicted probabilities. These plots indicted that six observations were poorly fitted by Model 1 and that nine observations were poorly fitted by Model 2. Table 4 shows the diagnostic statistics, pathology patterns, radiographic readings, and predicted probabilities for these individuals. After exploring the pathologic patterns of the influential observations, it was found that six individuals from Model 1 and five individuals from Model 2 had patterns that predicted classification at profusion categories of $\geq$ 0/1 and $\geq$ 2/1, respectively. However, lower radiographic categories were actually reported (0/0 for Model 1 and 1/0 or 1/1 for Model 2). In contrast, four individuals from Model 2 had advanced profusions of small opacities, although the model predicted with low probability (0.2) that the radiographic readings would be greater than 2/1. For both models, the effect of removing the influential observations significantly increased the magnitude of the estimated coefficients. This was most apparent in the macule coefficients for the comparison of normal plus mild grades with severe grades, where the increase was 2-fold for model 1 and 6-fold, in the negative direction, for Model 2.

When PMF occurs, the traction exerted by the large fibrotic lesion sometimes distorts the remainder of the lung parenchyma. This distortion can result in compensatory emphysema, and may also affect the appearance of simple pneumoconiosis as seen on the radiograph. In serial examinations, this effect may be so severe as to result in apparent regression of the profusion of small opacities over time. Since there is a possibility that such an effect of PMF might affect the relationship between the pathologic and radiographic signs of simple pneumoconiosis, the model-fitting was repeated after the omission of cases with PMF. Overall, there was little evidence of a large interfering effect of PMF. The coefficients for micronodules declined slightly, by about 10%, and those for macronodules declined rather more so, although in both cases the changes were within 1 SE, and thus could be due to chance. One explanation for the reduction in magnitude of the coefficients is that the physical tensions induced by the PMF lesions, especially if large, caused the other pathologic abnormalities to become more clustered instead of being more randomly distributed. Although the pathologist might still record the same number and severity of lesions, the X-ray reader might detect less abnormality on the radiograph, since the resulting areas of emphysematous tissue in which few pneumoconiotic lesions occur might overly influence the overall classification.

TABLE 4

LOGISTIC REGRESSION DIAGNOSTIC MEASURES, PATHOLOGY VARIABLES, RADIOGRAPHIC READINGS, AND PREDICTIVE VALUES FOR THE INFLUENTIAL OBSERVATIONS IN MODEL 1 AND MODEL 2

	Pathology Variables					Diagnostics	
Observation	Macule	Micronodule	Macronodule	Radiology Reading	Predicted Probability	Residuals ($\Delta\chi^2$)	Influential Measures ($\Delta\beta$)
Model 1							
1	1	2	1	0/0	0.94	16.1	0.12
2	1	2	2	0/0	0.94	16.1	0.12
3	1	2	2	0/0	0.94	16.1	0.12
4	2	2	1	0/0	0.96	23.8	0.16
5	3	2	1	0/0	0.96	23.1	0.26
6	3	3	1	0/0	0.96	23.1	0.26
Model 2							
1	1	3	2	1/0	0.81	4.3	0.12
2	1	3	2	1/1	0.81	4.3	0.12
3	1	3	3	1/0	0.81	4.3	0.12
4	1	3	3	1/1	0.81	4.3	0.12
5	2	3	3	1/0	0.82	4.6	0.13
6	3	0	0	2/2	0.20	4.2	0.09
7	3	1	0	2/2	0.20	4.2	0.09
8	3	1	0	2/3	0.20	4.2	0.09
9	3	1	0	3/3	0.20	4.2	0.09

The relationship between the radiographic appearance and specific lesions of pneumoconiosis has been considered by many investigators (8, 24, 25) and studied on deconstructed autopsy lungs (22), layers of plastic lattices, and with model lungs fabricated from plastic foam (26). These studies have shown that individual lesions less than 3 to 5 mm in diameter are unlikely to be resolved on the chest film. Because macules are generally below this size range, their appearance on the radiograph depends largely upon the effects of summation (26). Radiographic images are influenced by the density of lesions in a unit volume of lung, as well as by the background density, thickness of the chest wall, shape and composition of the lesions, and contrast effects produced by other diseases such as emphysema (1, 5, 24). It is therefore not surprising that all studies reported to date have shown that the correlation between the antemortem radiographic appearances and postmortem findings in CWP is better for the larger lesions (micronodules and macronodules) and for the more severe categories of disease (12–14). Conversely, the ability of the CXR to reveal mild and moderate grades of CWP is poor. In this study only 2% of all lungs were classified as negative for CWP by the pathologists, whereas 31% of all chest films were classified as being in radiographic profusion category 0/0. This effect was greatest for those lungs showing macules, for which 29% of the radiographs were classified as being in category 0/0, respectively. From these results, it is evident that radiology had a low sensitivity for detecting mild to moderate grades of CWP. Nevertheless, a good overall correlation between radiologic and pathologic findings is evident in Figure 2.

Although there was a good correlation between the pathologic findings for PMF and the radiographic findings for large opacities, 47 cases negative for PMF by pathologic examination showed large opacities on the CXR. Examination of the pathologic information for these cases revealed that 10 had been noted to have lung lesions that could easily have been mistaken for PMF on the radiograph. These included healed tuberculosis scars (two cases), Caplan's nodules (two cases), and tumor nodules (six cases). There were no obvious explanations for the other 37 cases. However, the pathologic assessment was made on a single sagittal slice of one lung, and it is therefore possible that it may have missed some PMF lesions. To examine this potential bias, one of the authors (V.V.) reviewed all of the postmortem pathology reports from cases in which pathologic examination for PMF was negative and the CXR was positive. However, no evidence of PMF in these cases was found from the comprehensive pathology reports of the entire (right) lung and the remaining four thick slices and four serial whole sections of the left lung. One explanation for the discrepant findings may be that the cases were misclassified as large opacities owing to the nodule summation effect.

In 27 cases said to have PMF pathologically, the median radiographic category was negative for large opacities. However, examination of the radiographic information from the B readers' records revealed that many of these cases had been noted to have some abnormality consistent with large opacities on the CXR. For example, for these 27 cases, one of the three readers noted large opacities for nine of the 23 CXR he considered readable. Tuberculosis was noted in seven cases and lung cancer in two. Other significant abnormalities were noted in four cases. Hence, it is clear that abnormalities were being detected by a majority of CXR readers. However, variation among them, in classification as well as sensitivity, led to lack of consensus, resulting in median scores negative for large opacities.

Despite the foregoing limitations, the CXR remains in general use as a tool for clinically detecting and classifying CXR during life. Radiographic documentation of CWP is important for diagnosis, surveillance, compensation, and disease prevention. The findings of this study help to clarify the limitations of the standard postero-anterior CXR in the diagnosis of simple CWP and of PMF, specifically because of the insensitivity of the radiograph to milder grades of CWP and the uncertainty evident in detecting complicated CWP lesions of PMF. The use of high-contrast radiography or high-resolution computed tomography (HRCT) scans of the chest may be of value in overcoming these limitations, owing to their superior resolution and ability to differentiate superimposed parenchymal structures (27).

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