Pathology and Mineralogy Demonstrate Respirable Crystalline Silica Is a Major Cause of Severe Pneumoconiosis in U.S. Coal Miners

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Abstract

**Rationale:** The reasons for resurgent coal workers' pneumoconiosis and its most severe forms, rapidly progressive pneumoconiosis and progressive massive fibrosis (PMF), in the United States are not yet fully understood.

**Objectives:** To compare the pathologic and mineralogic features of contemporary coal miners with severe pneumoconiosis with those of their historical counterparts.

**Methods:** Lung pathology specimens from 85 coal miners with PMF were included for evaluation and analysis. We compared the proportion of cases with pathologic and mineralogic findings in miners born between 1910 and 1930 (historical) with those in miners born in or after 1930 (contemporary).

**Results:** We found a significantly higher proportion of silica-type PMF (57% vs. 18%; \(P < 0.001\)) among contemporary miners compared with their historical counterparts. Mineral dust alveolar proteinosis was also more common in contemporary miners compared with their historical counterparts (70% vs. 37%; \(P < 0.01\)). *In situ* mineralogic analysis showed that the percentage (26.1% vs. 17.8%; \(P < 0.01\)) and concentration (47.3 \(10^8\) vs. 25.8 \(10^8\) particles/cm\(^3\); \(P = 0.036\)) of silica particles were significantly greater in specimens from contemporary miners compared with their historical counterparts. The concentration of silica particles was significantly greater when silica-type PMF, mineral dust alveolar proteinosis, silicotic nodules, or immature silicotic nodules were present (\(P < 0.05\)).

**Conclusions:** Exposure to respirable crystalline silica appears causal in the unexpected surge of severe disease in contemporary miners. Our findings underscore the importance of controlling workplace silica exposure to prevent the disabling and untreatable adverse health effects afflicting U.S. coal miners.

**Keywords:** silicosis; coal workers; dust
The 21st century has seen increases in pneumoconiosis globally (1). In the United States, the prevalence of coal workers’ pneumoconiosis (CWP) and its most severe forms, rapidly progressive pneumoconiosis (RPP) (2) and progressive massive fibrosis (PMF) (see the data supplement for definitions of these terms), has more than doubled since the late 20th century, from 5% to more than 10% for simple CWP (3, 4). Cases have been concentrated in the central Appalachian states of Kentucky, Virginia, and West Virginia, where the prevalence of PMF has increased from 0.33% to 3.2% in miners with 25 years or more of tenure (2, 4–8). Although the prevalence of disease declined after the institution of modern dust controls in the 1970s (9), this trend has unexpectedly reversed. This has affected active working miners participating in the Coal Workers’ Health Surveillance Program, where the prevalence of central Appalachian miners with PMF has increased 10-fold among longer tenured miners (4, 10) and 14-fold in former miners applying for federal Black Lung Program benefits (6). Large series of PMF cases have also been reported from individual clinics (5, 7).

Several lines of evidence point to excessive crystalline silica exposure as the main driving force behind this resurgent epidemic (11, 12). Improvements in mining equipment and processing technology have enabled profitable recovery of thin coal seams, which involves the extraction of large quantities of surrounding rock strata that can contain crystalline silica. In some mines, the rock strata account for more than 50% of the total mining height, but they can generate nearly twice as much respirable dust compared with the coal seam itself (13, 14). An analysis of federal dust monitoring data from 1982 to 2017 showed that respirable quartz mass percentage in mines in central Appalachia from 1982 to 2017 showed that respirable quantities of surrounding rock strata that can contribute to the development of PMF (15).

RPP and PMF are aggressive forms, rapidly progressive pneumoconiosis and mixed-dust pneumoconiosis that implicated excessive exposure to respirable silica and silicates (12). Pathologic features of silicosis were significantly associated with round opacities on chest imaging. Interestingly, pathologic features of focal alveolar proteinosis and interstitial inflammation associated with silicotic nodules pointed toward a more aggressive process than classic CWP.

We compared miners born between 1910 and 1930 ("historical miners") with those born in or after 1930 ("contemporary miners"). Historical miners worked mainly with conventional mining technology that relied on drilling and blasting, whereas contemporary miners spent at least a substantial portion of their mining tenure working with mechanized equipment that uses high-powered cutting heads to shear coal from the mine face (18, 19). To date, no study has compared the pathologic and mineralogic features of contemporary miners who have this resurgent form of pneumoconiosis with historical counterparts to determine if silica is indeed an important culprit. To address this uncertainty, we used brightfield and scanning electron microscopy (SEM) with energy-dispersive X-ray spectroscopy (EDS) to analyze lung tissue specimens from materials archived as part of the National Institute for Occupational Safety and Health’s NCWAS (National Coal Workers’ Autopsy Study) (20), as well as pathologic specimens from contemporary miners with PMF.

Methods

Study Population and Procedures

Contemporary coal miners attend Black Lung Clinics or approach physicians and attorneys for assistance with medical examinations for the presence and severity of CWP. Records of 1,129 coal miners seeking black lung benefits between 2016 and 2019 were reviewed to identify those with PMF and available lung pathology specimens from biopsy, resection, explantation, or autopsy. NCWAS samples were obtained between 1971 and 2013. During that time period, the program offered families of all coal miners the opportunity to have an autopsy performed to determine the presence and severity of CWP for use in black lung benefits claims. The NCWAS data set of 7,762 miners was reviewed to identify cases initially classified as PMF by National Institute for Occupational Safety and Health–contracted pathologists. Cases were included if they were born after 1910 and had engaged in ≥110 years of underground or surface coal mining and if the archived specimen was adequate for analysis as determined by slide review (F.H.Y.G., A.F.H., and M.S.O.).

Non-NCWAS miners met these same inclusion criteria and completed a standardized questionnaire eliciting demographic, smoking, and occupational histories, similar to the one completed by the NCWAS miners’ next of kin.

Miners were classified as historical if they were born between 1910 and 1930 and as contemporary if they were born in or after 1930. The study was approved by the University of Illinois Chicago institutional review board (protocol 2016-0767). Written informed consent was obtained for cases not accessioned through NCWAS.
**Pathology**

Brightfield images from hematoxylin and eosin–stained lung slides were digitally acquired at 40× magnification using Aperio XT (ImageScope version 8.2 software; Leica Biosystems). Images were classified and scored by pathologists using a standardized scoring system. Pathologists were blinded to all details of case histories other than prior employment as coal miners and that these miners were believed to have PMF. Three pathologists (J.L.A., S.S., and C.D.C.) evaluated and scored specimens individually; two pairs of pathologists (F.H.Y.G./A.D.F. and J.M./N.I.V.) evaluated specimens together and submitted joint findings. This approach yielded five separate classifications for all cases.

PMF was defined as a dust-related fibrotic lesion measuring >1 cm in longest dimension with irregular or whorled collagen fibers, with or without necrotic areas, and presence of dust consistent with coal mine dust (21).

To address the question of the role of silica, we developed a classification system characterizing three types of PMF lesions on the basis of the proportion of silicotic nodules in PMF lesions by area in the images reviewed. These were a “coal” type of PMF, defined as having ≤25% silicotic fibrosis; a “silica” type of PMF, defined as having >75% silicotic fibrosis; and a “mixed” type of PMF, having >25% and ≤75% silicotic nodules (Figure 2).

Pathologists scored the presence or absence of coal macules, coal nodules, and silicotic nodules when sufficient lung parenchyma surrounding the PMF lesion was present (12). In addition, pathologists noted the presence or absence of immature silicotic nodules (Figure 3) and mineral dust–related alveolar proteinosis (MDAP), a marker of acute silicosis (Figure 4). Discordant classifications, defined as disagreement on the presence or absence of a finding or on the type of PMF, were resolved by consensus conference involving all study pathologists. Previous work demonstrated a substantial degree of agreement (kappa = 0.62) on type of PMF among the study pathologists in a larger sample of NCWAS cases (22).

**Mineralogy**

SEM with EDS was used to characterize size, type, and concentration of mineral particles in situ using modifications of published morphometric point-counting methods (23–25). (See the data supplement for additional detail.)

**Statistical Analysis**

We used SAS (version 9.4; SAS Institute) for all analyses. Categorical variables were compared between historical and contemporary groups using the Fisher exact test. Continuous variables were examined across historical and contemporary status as well as PMF type using t tests with pooled or Satterthwaite results as appropriate. Analysis of variance (ANOVA) with Tukey’s pairwise comparison were used to compare mean differences in continuous variables across multiple groups. The Levene test was used to assess homoscedasticity; in cases of unequal distribution, we used the Welch test for ANOVA. A P value ≤ 0.05 was considered to indicate significance. Bonferroni-corrected P values were used for multiple comparisons.

**Results**

**Demographics**

Lung tissue from 85 miners was analyzed. We obtained tissue on 16 miners born in or after 1930 who received diagnoses of PMF from their clinical providers. Review by study pathologists confirmed PMF in 9 of these cases, and the remaining 7 cases were excluded from further study because the available specimens did not meet criteria for PMF.
An additional 14 contemporary cases of PMF were identified from the NCWAS archive. Sixty-two historical comparison cases were also selected from the NCWAS archive (Figure 1). Contemporary miners were significantly younger at the time their lung tissue was obtained (61 vs. 65 years; \( P = 0.03 \)) and had significantly fewer years of underground mining (30 vs. 35 years; \( P = 0.03 \)) as well as a trend toward fewer total years mining (31 vs. 36 years; \( P = 0.14 \)). There was no difference between groups for work in the central Appalachian states of Kentucky, Virginia, and West Virginia; race; or smoking status and total pack-years (Table 1).

Brightfield Microscopy
We found a significantly higher proportion of silica-type PMF (57% vs. 18%; \( P < 0.01 \)) among contemporary miners compared with historical counterparts. In contrast, coal miners born before 1930 had a significantly higher proportion of both coal-type PMF (50% vs. 17%; \( P < 0.01 \)) and mixed-type PMF (33% vs. 26%; \( P < 0.01 \)) (Table 2).

Specimens had varying amounts of lung parenchymal tissue surrounding PMF lesions. Five specimens had so little non-PMF parenchyma that neither coal macules and nodules nor mature and immature silicotic nodules could be evaluated. Despite differences in the quantity of lung parenchymal tissue surrounding PMF lesions, we found a trend toward increased proportions of both mature silicotic nodules (50% vs. 17%; \( P < 0.01 \)) and mixed-type PMF (33% vs. 26%; \( P < 0.01 \)) (Table 2).

Findings consistent with MDAP were also more common in contemporary miners.
compared with historical counterparts (70% vs. 37%; \( P, 0.01 \)) (Table 2). To confirm these findings, 10 specimens with MDAP lesions identified on hematoxylin and eosin stains were stained with periodic acid–Schiff diastase, and all were positive, confirming the presence of lipoproteins (Figure 4). MDAP in these specimens was confined to focal involvement of alveolar spaces adjacent to the PMF lesions.

Analysis by mining region showed that the increased proportion of silica-type PMF, MDAP, and the trends toward increased profusion of mature and immature silicotic nodules were largely due to cases of miners who worked in the central Appalachian states of Virginia, West Virginia, and Kentucky compared with those who worked outside of central Appalachia. Similar differences between historical and contemporary miners were also seen outside of central Appalachia, but the numbers were small and were not statistically significant (Table 2).

### Mineralogy

**Silica.** *In situ* mineralogic analysis was performed on lung tissues from 17 of 23 (74%) contemporary miners and 33 of 62 (53%) historical comparisons. The total concentration of mineral particles in lung specimens did not differ significantly between contemporary and historical miners, (180 \( \times 10^8 \) vs. 149 \( \times 10^8 \) particles/cm\(^3\); Table 3). Most notably, the percentage (26.1% vs. 17.8%; \( P < 0.01 \)) and concentration (47.3 \( \times 10^8 \) vs. 25.8 \( \times 10^8 \) particles/cm\(^3\); \( P = 0.036 \)) of silica particles were significantly greater in specimens from contemporary miners compared with their historical counterparts.

The concentration of silica particles was more than 50% greater when pathologic features associated with silica exposure were present in the sections analyzed, including MDAP, mature silicotic nodules, and immature silicotic nodules (\( P < 0.05 \); Table 4). One-way ANOVA showed nearly double the percentage of silica particles in silica-type PMF compared with mixed- or coal-type PMF (29.6% vs. 16.9% and 16.0%, respectively; \( P < 0.01 \); Table 5). Also, the concentration of silica particles appeared to be 70% higher in silica-type PMF compared with mixed- or coal-type PMF (42.4 \( \times 10^8 \) vs. 27.2 \( \times 10^8 \) and 29.6 \( \times 10^8 \) particles/cm\(^3\), respectively; \( P = 0.28 \); Table 5), but this was not statistically significant in this small sample with high variability.

**Other particles.** There was a lower percentage of aluminum silicate (SiAl and SiAlK) particles in contemporary miners’ lungs compared with historical miners (66.2% vs. 74.6%; \( P < 0.01 \); Table 3). The presence of MDAP or mature silicotic

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**Table 1.** Demographic and mine-work characteristics of study participants

|                          | Historical (\( n = 62 \)) | Contemporary (\( n = 23 \)) |
|--------------------------|---------------------------|-----------------------------|
|                          | \( n (\%) \) or Mean SD Range | \( n (\%) \) or Mean SD Range |
| Age, yr                  | 65.4 5.7 55–82            | 61.1 3.7 48–79              |
| Birth year               | 1919 4.9 1910–1928        | 1942 11 1930–1961           |
| White race, yes          | 53 (87)       | 21 (91)       | 17 (74)       | 18.6 18.4 0–60 |
| Smoker, yes              | 50 (81)       | 17 (74)       | 18.6 18.4 0–60 |
| Pack-years smoking       | 20.1 19.0 0–96          | 17 (74)       | 18.6 18.4 0–60 |
| (Work in) central Appalachia,* yes | 39 (63) | 31.4 2.2 10–42 | 30.2 8.7 10–42 |
| Years of coal mining     | 35.8 10.0 10–50         | 30.2 8.7 10–42             |
| Years worked underground | 34.9 8.9 3–50           | 30.2 8.7 10–42             |
| Years worked at the surface | 2.6 10 0–45           | 0.8 1.3 0–3               |

Definition of abbreviation: SD = standard deviation.

*Central Appalachia refers to the states of Kentucky, Virginia, and West Virginia.
Table 2. Pathologic findings in historical compared with contemporary coal miners with progressive massive fibrosis, including all cases and findings by U.S. geographic region

| Finding                              | All Regions | Central Appalachia* | Rest of the United States |
|--------------------------------------|-------------|---------------------|---------------------------|
|                                      | Historical  | Contemporary       | Historical                 | Contemporary     |
|                                      | (n = 62)    | (n = 23)            | (n = 39)                   | (n = 17)         |
|                                      | P Value†    |                    |                           | P Value†         |
|                                      |             |                    |                           |                 |
| PMF type                             |             |                    |                           |                 |
| Silica                               | 11 (18)     | 13 (57)            | 5 (13)                    | 10 (59)         |
|                                      | 0.0015‡     |                    | 0.001†                    |                 |
| Coal                                 | 20 (33)     | 6 (26)             | 10 (26)                   | 4 (24)          |
|                                      | 0.0015‡     |                    | 0.001†                    |                 |
| Mixed                                | 31 (50)     | 4 (17)             | 24 (66)                   | 3 (18)          |
|                                      | 0.0015‡     |                    | 0.001†                    |                 |
| Surrounding lung parenchyma‡          |             |                    |                           |                 |
| Silicotic nodules                    | 20 (33)     | 10 (52)            | 12 (32)                   | 7 (50)          |
|                                      | 0.17        |                    | 0.33                      |                 |
| Immature silicotic nodules           | 11 (18)     | 7 (37)             | 6 (16)                    | 4 (29)          |
|                                      | 0.11        |                    | 0.43                      |                 |
| Coal macules                         | 56 (93)     | 12 (60)            | 34 (92)                   | 10 (67)         |
|                                      | 0.0011‡     |                    | 0.035                     |                 |
| Coal nodules                         | 47 (76)     | 11 (58)            | 33 (89)                   | 8 (57)          |
|                                      | 0.018       |                    | 0.018                     |                 |
| MDAP                                 | 22 (37)     | 16 (70)            | 14 (36)                   | 12 (71)         |
|                                      | 0.021       |                    | 0.021                     |                 |

**Definition of abbreviations:** MDAP = mineral dust–related proteinosis; PMF = progressive massive fibrosis.

All values are presented as n (%).

*Central Appalachia refers to the states of Virginia, West Virginia, and Kentucky.

†Boldface type denotes P < 0.05.

‡P < 0.0021 with Bonferroni correction for testing 24 comparisons.

§Five cases had only PMF lesions without evaluable surrounding parenchyma; total evaluated = 80.

**Discussion**

This is the first study of its kind comparing the pathology and *in situ* mineralogy of contemporary miners with PMF with those of their historical counterparts. Most prior studies of PMF have relied on chest imaging showing pneumoconiotic lesions >1 cm to diagnose PMF and therefore lacked the ability to confirm the diagnosis with an evaluation of tissue responses to mineral dust. We used an innovative multimethod approach to investigate possible contributors to the increases in proportion and severity of pneumoconiosis in U.S. coal miners. Before this study, the evidence pointing to respirable crystalline silica was indirect and relied on nonspecific clinical variables such as the prevalence of r-type opacities on chest imaging (11, 16), which have been associated with silicosis (26). Our prior case series of lung pathology in miners with RPP implicated silica and silicates, but there was no comparison group (12). This study compares contemporary and historical miners and shows significant differences between the groups.

Our data clearly show an increased proportion of pathologic features consistent with substantial exposure to respirable crystalline silica in contemporary miners. These pathologic findings have been associated with acute and subacute silicosis (27). They include the presence of foci of MDAP in association with PMF, a finding that has heretofore received little attention in the published literature (12, 28). We also developed a classification of PMF lesions into silica-, mixed-, and coal-type PMF that proved to be a useful method for characterizing lesions to better understand causal exposures. The increased proportions of mature and immature silicotic nodules seen in lung tissue adjacent to PMF lesions also point strongly toward a silica-driven

Table 3. *In situ* lung mineralogy findings in historical versus contemporary coal miners with progressive massive fibrosis: percentages and concentrations by particle type

| Finding                              | Historical Mean (SD) | Contemporary Mean (SD) | P Value* |
|--------------------------------------|----------------------|------------------------|----------|
|                                      | (n = 33)             | (n = 17)               |          |
| Total particle concentration†        | 149 (77)             | 180 (156)              | 0.43     |
| Particle type                        |                      |                        |          |
| Silica (Si)                          |                      |                        |          |
| % of particles                       | 17.8 (10.0)          | 26.1 (10.0)            | 0.007‡   |
| Particle concentration†              | 25.8 (19.7)          | 47.3 (37.0)            | 0.036    |
| Aluminum silicates (SiAl and SiAlK) |                      |                        |          |
| % of particles                       | 74.6 (9.9)           | 66.2 (9.9)             | 0.006‡   |
| Particle concentration†              | 112 (60.5)           | 120 (118)              | 0.78     |
| Titanium (Ti)                        |                      |                        |          |
| % of particles                       | 5.8 (3.0)            | 6.2 (2.3)              | 0.68     |
| Particle concentration†              | 8.8 (7.4)            | 11.4 (10.7)            | 0.32     |

**Definition of abbreviation:** SD = standard deviation.

Data for particles constituting <5% are not shown, therefore percentages in Table 3 do not total 100%.

†Boldface type denotes P < 0.05.

‡Particle concentrations are particles × 10⁶ per cm³ tissue.

*P < 0.0085 with Bonferroni correction for testing six comparisons.
etiology of disease among younger contemporary miners with significantly fewer years of mining tenure. Our findings were further informed by results of in situ analysis of mineral particles in a subset of these miners. In situ findings showed a significant increase in the percentage and concentration of silica particles in PMF lesions in lungs of contemporary coal miners compared with historical miners. There was a corresponding decrease in the percentage of aluminum silicate particles relative to silica particles in contemporary miners. This may reflect changes in geologic and/or mining conditions, including differences in silica content or dust generation from rock strata within or surrounding contemporary coal mining seams. Of note, we found a significant correlation between the concentration and percentage of silica particles and the presence of lung pathologic lesions including PMF, MDAP, and both mature and immature silicotic nodules.

The mineralogy findings in these cases demonstrate some of the highest concentrations of silica particles reported with this in situ method (24). For comparison, the total concentration of inorganic particles in the lungs of persons with no known dust exposures is in the range of $10^3$ and $10^5$ particles/cm$^3$ tissue. In contrast, the concentration of silica particles in PMF lesions reported in sandblasters was up to $10^7$ particles/cm$^3$ tissue. Thus, not only do our reported findings conform to the role of high silica particles in the development of PMF but they also provide evidence of the intense exposure to respirable crystalline silica particles experienced by these coal miners, nearly one-third of the concentration seen in sandblasters (29).

The findings of a higher rate of silica particle deposition in the lungs of historical miners compared with contemporary miners (31, 32) reflect the tendency of silica to coat efficiently within the lungs of historical miners. The mechanism is believed to involve the interaction of silica particles with the surface of the lungs, resulting in reduced toxicity (31, 32). The mechanism is believed to involve the interaction of silica particles with the surface of the lungs, resulting in reduced toxicity (31, 32).

### Table 4. In situ lung mineralogy–pathology correlations in coal miners with progressive massive fibrosis: percentages and concentrations by particle type

| Type of Particle | Pathology Finding | Mean (SD) | Mean (SD) | P Value* | Mean (SD) | P Value* | Mean (SD) | P Value* |
|------------------|-------------------|-----------|-----------|----------|-----------|----------|-----------|---------|
|                   | MDAP Absent       | n = 26    | n = 24    |          | n = 30    | n = 16   | n = 34    | n = 12  |
| Silica (Si)       |                   |           |           |          |           |           |           |         |
| % of particles    | 17.1 (7.3)        | 24.5 (12.4) | 0.016     | 16.9 (8.0) | 25.8 (11.6) | 0.004     | 17.8 (7.9) | 26.0 (13.8) | 0.071 |
| Particle concentration† | 24.6 (20.3) | 42.3 (13.3) | 0.030     | 24.4 (22.4) | 44.2 (31.6) | 0.017     | 26.2 (23.8) | 45.8 (32.4) | 0.031 |
| Aluminum silicates (SiAl and SiAlK) | 75.4 (7.9) | 67.8 (11.9) | 0.011     | 74.8 (8.4) | 67.5 (12.4) | 0.022     | 74.2 (8.0) | 66.7 (14.5) | 0.11  |
| % of particles    | 116.8 (96.5)      | 112.0 (67.9) | 0.84      | 110.6 (68.3) | 105.7 (60.5) | 0.81      | 108.0 (68.7) | 112.0 (56.4) | 0.85  |
| Particle concentration† | 5.70 (3.1) | 6.16 (2.80) | 0.58      | 6.2 (3.2) | 5.8 (2.9) | 0.69      | 6.1 (3.4) | 5.89 (18) | 0.76  |
| Titanium (Ti)     | 9.3 (9.6)         | 10.2 (7.7) | 0.72      | 9.4 (7.8) | 9.7 (8.6) | 0.89      | 9.3 (8.6) | 10.1 (6.1) | 0.75  |

*Boldface type denotes P < 0.05.
†Particle concentrations are particles x $10^8$ per cm$^3$ tissue.

Definition of abbreviations: MDAP = mineral dust–related proteinosis; SD = standard deviation; Sil Nod = silicotic nodules.
silica, it is possible that relative depletion of silicate minerals may also be a contributing factor to disease. In addition to surface occlusion, the toxicity of crystalline silica is dependent on other important factors, including particle size (36), presence of highly reactive silicon free radicals (37, 38), and formation of ‘nearly free’ surface silanols when freshly fractured (39). Fresh fracturing upsets the long-range ordering of silica’s crystal lattice and imparts surface disorder. Future studies could help determine which, if any, of these factors are associated with the recent upsurge in RPP-dependent disease and progress in the role of silica in this disease received less attention until the current resurgence of disease in central Appalachia was identified beginning in 2005 (2). Strengths and Limitations

Our study has several strengths. One is the independent blinded review of pathologic materials by seven pathologists, with discrepancies addressed through rigorous consensus determination. Study pathologists had no access to clinical and historical information associated with the subjects, therefore minimizing information bias in interpretations. The same was true of the in situ mineralogic analyses. Other strengths include the unprecedented number of specimens available for analysis, supplemented by relevant demographic and occupational history data that enabled comparison of contemporary and historical miners. We also developed a standardized scoring system for brightfield microscopy findings. This system ensured detailed attention to previously overlooked findings such as immature silicotic nodules and MDAP. We used digital microscopy platforms, which enabled scoring and consensus review of materials by pathologists separated by long distances. We also used two different microscopy methods to analyze materials and compare findings.

Our study also had several limitations. One limitation was the relatively small (n = 23) number of specimens from contemporary miners. This is likely related to the small number of miners with advanced disease who underwent surgical lung biopsies, resections, transplantation, or autopsies. Despite the small number, we were able to show significant changes in the pathology and mineralogy of PMF over time. Our small sample size may also reflect participation bias. Subjects who participated in NCWAS, the source of our historical cases, were likely to have had less severe disease and therefore needed the additional pathologic evidence for their claims compared with nonparticipating miners, who may have had stronger claims on the basis of imaging and physiology alone. However, this would not likely have affected our results, as our focus was on comparing the most severe disease, PMF, in contemporary miners with historical counterparts. Also, there were limitations in clinical and questionnaire data available for NCWAS specimens, such as chest imaging results and details on mining job duties. This is unlikely to have affected our

Table 5. Lung mineralogy–pathology correlations by progressive massive fibrosis type: percentages and concentrations by particle type

| Type of Particle | Silica Type Mean (SD) (n = 16) | Mixed Type Mean (SD) (n = 13) | Coal Type Mean (SD) (n = 21) | P Value* |
|------------------|-------------------------------|-----------------------------|-----------------------------|-----------|
| Silica (Si) | 29.6 (12.5) | 16.9 (5.5) | 16.0 (6.8) | <0.001† |
| % of particles | 42.4 (33.6) | 27.2 (20.0) | 29.6 (28.0) | 0.28 |
| Particle concentration‡ | 62.3 (11.2) | 76.8 (6.7) | 75.8 (7.1) | <0.001† |
| Aluminosilicates (SiAl and SiAIK) | 75.6 (39.7) | 137.6 (118.5) | 129.8 (74.5) | 0.07 |
| % of particles | 6.2 (2.9) | 5.0 (2.2) | 6.2 (3.4) | 0.44 |
| Particle concentration‡ | 7.7 (5.6) | 8.4 (8.7) | 12.1 (10.2) | 0.25 |

Definition of abbreviations: PMF = progressive massive fibrosis; SD = standard deviation.

*Boldface type denotes P < 0.05.
†P < 0.0085 with Bonferroni correction for testing six comparisons.
‡Particle concentrations are particles × 10⁶ per cm³ tissue.
findings, as we had the most relevant demographic and work history information, including age, smoking status, mining tenure, and geographic location, and pathologic findings that supersede chest imaging for the diagnosis of PMF. The SEM with EDS analysis was constrained to analyzing inorganic particles >0.2 μm in diameter, precluding sizing and counting of smaller particles as well as coal dust particles that may have important roles in disease pathogenesis. Finally, the SEM with EDS analysis provides information about elemental content but not about crystalline structure.

Conclusions
On the basis of integrated pathologic and mineralogic findings in lung tissues from two well-defined coal miner case series with PMF, our study demonstrates that exposure to crystalline silica appears causal in the unexpected surge in severe disease in contemporary miners. Our findings underscore the importance of controlling workplace silica exposure to prevent the disabling and untreatable adverse health effects afflicting U.S. coal miners (42).

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Cohen, Rose, Go, et al.: Pathology and Mineralogy of Severe Pneumoconiosis

1477
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