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**Public Comments on MSHA's
Proposed Rule:
Lowering Miner's Exposure to
Respirable Coal Mine Dust,
Including Continuous
Personal Dust Monitors**

RIN 1219-AB64

**Specific Comments on:
MSHA Review of Medical
Monitoring and Epidemiologic
Studies**

AB64-COMM-92-5



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**Specific Comments on: MSHA
Review of Medical Monitoring and
Epidemiologic Studies**

Prepared for

Murray Energy Corporation
29325 Chagrin Boulevard, Suite 300
Pepper Pike, OH 44122

Prepared by

Michael Kelsh, PhD, MPH
Martha L. Doemland, PhD, MS
Exponent
1800 Diagonal Road, Suite 500
Alexandria, VA 22310

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Qualifications

1.1 Michael A. Kelsh, PhD, MPH

Dr. Kelsh is a Principal Scientist with Exponent[®], a scientific research and consulting company headquartered in Menlo Park, California. Dr. Kelsh works in Exponent's Health Sciences practice in the Center for Epidemiology, Biostatistics, and Computational Biology, specializing in the application of epidemiology and biostatistics to occupational and environmental health issues. Dr. Kelsh is a former adjunct professor at the University of California, Los Angeles (UCLA) School of Public Health, Department of Epidemiology, where he taught seminars in occupational epidemiology and exposure assessment.

Dr. Kelsh holds two graduate degrees in public health and epidemiology: a Master of Public Health (MPH) in Epidemiology from the University of California, Los Angeles (UCLA), and a Ph.D. in Epidemiology also from UCLA.

Dr. Kelsh's areas of scientific research include epidemiology, occupational and environmental health, and exposure assessment for epidemiologic studies. He has conducted numerous epidemiologic studies of occupational cancer across a wide variety of occupations and industries and diverse potential occupational exposures. This epidemiologic research includes occupational studies of electric utility workers, petroleum research workers, aerospace workers, miners, electronics workers, and construction workers, as well as environmental or occupational studies of potential exposure to perchlorate, arsenic, trichloroethylene (TCE), and extremely low-frequency electromagnetic fields (EMFs) and radiofrequency exposures. In addition, Dr. Kelsh has conducted an occupational study of respiratory disease among beryllium miners, an analysis of lung function testing among surface miners, and several studies of work-related injury, musculoskeletal diseases, and exposure assessment. In addition to conducting original studies, Dr. Kelsh has participated on numerous comprehensive literature reviews, including pooled and meta-analyses. Examples of such work include meta- or pooled analyses studies on childhood leukemia and residential EMF exposure, occupational TCE exposure and cancer,

occupational chromium exposure and gastrointestinal cancers, hair dye use and bladder cancer, and automobile mechanic work and mesothelioma and lung cancer risk.

1.2 Martha L. Doemland, PhD, MS

Dr. Martha L. Doemland is a Senior Managing Scientist in Exponent's Health Sciences Center for Epidemiology, Biostatistics, and Computational Biology. Dr. Doemland has over 30 years experience in the design, implementation, management, analysis, and interpretation of epidemiologic studies in occupational and non-occupational settings. Dr. Doemland holds both a Masters degree and a Ph.D. in Epidemiology from the State University of New York at Buffalo.

Dr. Doemland has conducted mortality studies among automotive workers and electrical capacitor workers, and examined risks associated with environmental exposure to perchlorate, PCBs, and DBCPs. While serving as Director of Epidemiology in the pharmaceutical industry, Dr. Doemland designed studies to measure the incidence and prevalence of infectious diseases, and to assess disease diagnostic capabilities, potential pharmacoepidemiologic issues, and disease risk factors, and to establish profiles for the "at risk" population.

The full *curricula vitae* of Dr. Kelsh and Dr. Doemland are included as Attachments A and B, respectively, to these comments. Exponent staff (Drs. Kelsh and Doemland) were engaged by Murray Energy Corporation (MEC) to conduct a review of the MSHA proposed rule. In particular, we were asked to review and evaluate the available epidemiologic studies on coal miners that were relied upon by MSHA in assessing health risks and benefits.

Executive Summary

- MSHA relied heavily on disease prevalence data from the Coal Workers Health Surveillance Program (CWHSP) as a basis for developing the proposed new rule. However, in the context of the standard-setting process, a more balanced and comprehensive critical evaluation of the specific programs within the CWHSP and a critical assessment of data reported from the CWHSP are still required. Due to a number of limitations, CWHSP data are not sufficient for estimating exposure-response relationships between underground coal-mine dust and coal workers pneumoconiosis (CWP) and progressive massive fibrosis (PMF).
- Findings from the occupational epidemiologic studies should be representative of all underground coal-mine workers. The health studies also should use appropriate epidemiologic study designs that include worker-specific measures on both disease and exposure and are sufficiently robust to evaluate potential dose-response relationships. Data on potential confounding and effect modification are needed to assess the validity and reliability of the reported results. Unfortunately, the current NIOSH studies of coal miners appear not to meet criteria that allow for exposure-specific interpretation of health risks.
- NIOSH reports decreasing prevalence of CWP and PMF starting in 1970 and continuing until 1999, at which time prevalence of CWP and PMF reportedly began to increase. However, trends in CWP and PMF prevalence cannot be measured directly or inferred from the CWHSP as designed and implemented. Further analyses of these data should be conducted, and any interpretation should consider the strengths and limitations of the data. Disease misclassification is a significant limitation of the CWHSP disease prevalence data. NIOSH data demonstrate unacceptably high rates of false positive and false negative findings in diagnosing CWP and PMF. Discussions regarding the well-documented lack of accuracy and precision in diagnosing CWP and PMF in general, and specifically within the NIOSH B reader program, is notably absent from the NIOSH Criteria Document, Current Intelligence Bulletin (CIB), Qualitative Risk Assessment (QRA), and the MSHA hearings. The validity of the NCD exposure-response model relied on in the QRA hinges on the accuracy, precision, and reliability of the x-ray readings for CWP and PMF.

- Low miner participation in the CWHSP effectively limits the findings to those miners who participated and the regions and specific mines studied. It is inappropriate to extrapolate findings in participants to non-participants. An apparent correlation between declining disease prevalence and declining miner participation rates highlights the need for additional analysis and cautious interpretation.
- Although MSHA exposure monitoring data show overall decreasing respirable coal-mine dust (RCMD) levels across all mines measured, such data are not necessarily indicative of individual exposure levels among those participating in NIOSH monitoring studies. Individuals may have early histories of higher exposures that are not identified by the ecologic exposure assessment procedures, a factor that needs to be addressed in the review of epidemiologic data on coal miner respiratory health risks.
- Smoking is a likely critical confounder and/or effect modifier of RCMD and lung disease. Most studies of coal miners have not adequately controlled for, or assessed, the impacts of smoking behavior. In addition, several recent articles have suggested that silica or other exposures (e.g., bioavailable iron [BAI]) may be responsible for some of the CWP risk.
- The experience of other countries such as Australia may provide valuable insights and guidance on how to prevent CWP. For example, it appears that Australia has reported no CWP cases with an exposure standard of 2.5 mg/mL (higher than the current U.S. standard) and a program of periodic exposure monitoring and comprehensive medical monitoring. A review and report on the experiences of programs that have achieved successful control of CWP would be helpful in developing an effective rule.
- In summary, better epidemiologic studies are needed to resolve many questions, such as: Why is CWP reported to cluster in certain geographic regions? In addition to underground coal mine dust, are there other factors that play a role in explaining the reported increases in CWP and PMF prevalence? Do miners who have CWP have a history of higher coal-dust exposures? Is low participation in medical monitoring and surveillance skewing results? These questions must be addressed to provide a strong basis for developing a more effective standard.

2 Background

The following comments summarize and expand upon the presentation made by Dr. Michael Kelsh at MSHA's Salt Lake City hearing on January 25, 2011. The focus of that presentation was on limitations in the design, implementation, and resulting data from the Coal Workers Health Surveillance Program (CWHSP)¹ in the context of the standard-setting process. The comments submitted here extend that discussion to include critical issues related to the accuracy and precision in the detection and diagnosis of CWP and PMF in U.S. coal miners, and provide further comments on study design issues and limitations present in the epidemiologic studies of coal-mine workers. Given that NIOSH reports from the CWHSP in large part initiated and were relied on in the current proposed rule, a comprehensive, critical evaluation of the CWHSP data should be conducted by independent scientists. Such an evaluation would help to determine whether the data are sufficiently valid, reliable, and scientifically robust for use in the regulatory process. Relying on disease measurement data collected in a small, self-selected subset of active coal miners using inaccurate and imprecise CWP and PMF detection and diagnostic methods, in targeted areas of the country, to inform and drive a national standard—because it is the only available data set—will not necessarily produce a beneficial, health-protective standard.

We acknowledge the health risks of CWP and PMF among underground coal miners that have resulted from exposure to respirable coal-mine dust (RCMD) and the urgent need for better research and more effective medical surveillance programs to manage this risk in coal miners. We also recognize that other clinical and medical information such as longitudinal lung function data were used in addition to the disease prevalence data from the CWHSP. Substantial efforts have been made toward understanding the complex interplay between lung pathology and lung dust content, as well as extensive monitoring and surveillance efforts undertaken by NIOSH. Unfortunately, these efforts have not translated to success in determining dose-response relationships between respirable coal-mine dust and lung diseases. Now, 40 years following the

¹ Designed by NIOSH and managed by NIOSH/MSHA, the CWHSP include The National Study of Coal Workers Pneumoconiosis-NCWPS (1969–1988), the Coal Workers X-Ray Surveillance Program-CWXSP (1970–present), the Miners' Choice Program – MCP (1999–2002), and the Enhanced Coal Workers Health Surveillance Program ECWHSP (2006–present).

mandate to study, monitor, and reduce black lung disease, it is still an important health and safety issue in U.S. coal miners. It is critical that efforts move beyond disease detection to more rigorous epidemiologic studies incorporating better study design, higher miner participation, and use of more sensitive diagnostic tools and exposure assessment protocols. Studies designed by multidisciplinary research teams consisting of miners, independent and academic researchers, biomedical engineers, clinicians, health psychologists, and industry experts are required to develop effective research, medical surveillance, and exposure monitoring programs.

As the sole source of CWP and PMF prevalence data among U.S. coal miners, it is essential that the CWHSP program and reported data undergo a comprehensive evaluation and critical review. The ability to evaluate and critique the CWHSP programs, however, is significantly hampered by the lack of information and detail in NIOSH reports, presentations, and publications, as well as information provided on the NIOSH website. Insufficient information is provided on the overall program and study design, study objectives, methodology, and characterization of miner participation patterns. Relevant information on participants such as demographic data, occupational history, medical history, and other risk-factor data are also missing.

Briefly, the current proposed rule to lower the RCMD limit was initiated as a result of NIOSH reports from the CWHSP, which reported: 1) continued occurrence of coal worker pneumoconiosis (CWP) and PMF in active coal miners; 2) an increase in the prevalence of CWP and PMF in active coal miners starting in 1999, reversing a 30-year decline; and 3) cases of rapidly progressing disease.

The CWHSP was not designed to provide the quality of data or level of detail required for use in the standard-setting process; however, these data were relied on in the NIOSH Criteria Document (NCD), 2003 Notice of Proposed Rule Making (NPRM), Quantitative Risk Assessment (QRA), and the current proposed rule, to initiate and demonstrate the need to lower the current RCMD standard.

Our evaluation of the reported disease prevalence data from all programs within the CWHSP (albeit limited by the lack of available information) reveal several potential biases of unknown direction and magnitude resulting from issues related to the accuracy and precision in the

diagnosis of CWP and PMF, low miner participation rates, limited exposure data, and other design and analysis limitations. A summary of Dr. Kelsh's Salt Lake City presentation and the responses to the panel's outstanding questions are presented in these comments.

3 Comments Regarding Epidemiologic Research Among Coal Miners

3.1 Study Design

Critical aspects of study design characteristics of the CWHSP program and further elaboration on the CWHSP data are needed to determine the strengths and limitations of the CWHSP data, and to assess the ability of these data to establish risk for a given level of RCMD exposure—a critical piece of information for developing an appropriate coal-mine dust standard. The lack of the most basic information and analyses in reports, presentations, and publications from the NCWHS preclude the level of critique needed for all data used in the standard-setting and regulatory process. Answers to the questions and requests for additional analyses that we presented during the MSHA hearings in Salt Lake City are needed to adequately critique the NCWHS data. Specifically, information on differences between miners who participate and those who do not, with respect to age, race, tenure, hours per week in the mine, geographic location of mine, county of residence, mine size, time mine has been in operation, number of mines worked in lifetime, education level, marital status, smoking status, other tobacco use, non-coal mine employment history, and time away from coal mining are also requested of MSHA and NIOSH in order to properly analyze the CWHSP data. Important information not published by NIOSH includes the distribution among miners with and without CWP/PMF for: 1) specific jobs in the mine; 2) number of job changes during employment; 3) time in specific jobs; 4) number and size of mines worked in; 5) time employed in different mines of different sizes, in different geographic areas is important information not published by NIOSH.

Dr. Kelsh's presentation can be found as an attachment to these comments and on the MSHA website: <http://www.msha.gov/REGS/Comments/2010-25249/Transcripts/Kelsh-DoemlandSaltLakeCity.pdf>

3.2 Diagnostic Issues

Accurate diagnosis of CWP and PMF is an important and critical issue in estimating health risks, however, discussion regarding the well-documented lack of accuracy and precision in

diagnosing CWP and PMF in general, and specifically within the NIOSH B reader program, is notably absent from the NCD, Current Intelligence Bulletin (CIB), QRA, and the MSHA hearings. The validity of the NCD exposure-response model on which the QRA relied hinges on the accuracy, precision, and reliability of the diagnostic methods and disease classification scheme for CWP and PMF used during the fourth round of the NCWPS.² This is a critical issue, because it was these data that were used in the NIOSH criteria document that was used to estimate risks of disease for exposures to underground coal-mine dust at levels less than 2 mg/m³. The lack of accuracy and precision in using chest x-rays, as reported by NIOSH, should have precluded the use of these data to model the RCMD exposure response relationships. These limitations should necessarily affect the interpretation of epidemiologic data and the validity of the QRA risk/benefit analyses.

Interpretation of film chest x-ray, the diagnostic tool for CWP and PMF used by NIOSH in the CWHSP, is highly subjective and suffers from considerable variability between readers and within readers (when a reader classifies the same x-ray differently at a different time). To address issues related to poor accuracy and lack of precision, NIOSH developed the B-reader program, which was designed to train physicians in the use of the International Labor Organization (ILO) system for classifying x-rays for the presence of CWP and PMF for both surveillance and for miner compensation programs. Evaluation of early results from the first few years of the B-reader program revealed unacceptably high variability among readers, so additional training and a certification program were instituted shortly before 1978. In 1984, a recertification requirement (every 4 years) was instituted (see <http://www.cdc.gov/niosh/topics/chestradiography/breader.html>).

Wagner et al.³ conducted an analysis of the results from the NIOSH B-reader certification and re-certification examinations. Of the 992 physicians who took the certification exam, only 442 passed, and of the 328 physicians seeking recertification, only 220 passed the exam. Thus, 108 certified NIOSH B-readers failed the re-certification examination, yet these physicians were

² Attfield et al., Am J Ind Med. 1995

³ Wagner et al., JOM 1992;24(9)

actively reading x-rays and providing data to the CWXSP. This leads to obvious concerns regarding validity and reliability of the classification of x-rays in the CWXSP data.

As reported by Wagner et al.,² the group of physicians that failed the re-certification examination had a very high rate of false positive readings, approaching an average of 40% in 1987, 1989, and 1990, and 30% in 1988. On the flip side, among this group of 108 physicians, the rate of false negative readings averaged over 20% in 1987, 10% in 1988, and around 5% in 1989 and 1990, indicating that a high number of CWP cases are missed with the present diagnostic and reading system. Physicians who passed the re-certification examination did better on classification than NIOSH readers who did not pass. Their mean false positive rates approached 20% and false negative readings averaged about 8%. However, even these false positive and false negative rates are still high. Sensitivity analyses of the CWXSP data are needed to evaluate the impact of this health outcome misclassification. Such analyses will likely reveal a wide range of possible prevalence estimates. Without information on how these problems have been addressed in the current monitoring programs, it is not possible to determine whether recently reported prevalence estimates are accurate or an artifact resulting from disease misclassification or other biases. Given the history of high rates of false positive x-ray readings among certified NIOSH B readers, it is highly likely that this problem still exists, making interpretation of any data trends subject to significant error. Ignoring this important study limitation is not scientifically acceptable.

During the Salt Lake City hearings, Dr. Wagner inquired as to our awareness of the NIOSH longitudinal studies and requested "specific analyses and critique" on those longitudinal studies. What follows incorporates the requested analyses and critique on the NCWPS. The NCWPS, like the CWXSP, suffered from diminishing miner participation rates from round 1 through round 4, and with issues ensuing from changes in ILO classification schemes and with inter and intra-reader reliability within and across rounds 1-4.

During the NCWPS, three different ILO classification schemes were used to diagnose and classify CWP and PMF in coal miners. In 1998, NIOSH published their findings from a

systematic re-reading of a subset of NCWPS x-rays using the 1980 ILO classification scheme.⁴ A panel of three certified NIOSH B-readers was selected for their moderate reading tendencies, as were the original panel of certified NIOSH B-readers selected for the NCWPS. The impact of using three different ILO classification schemes on the declining trend in CWP and PMF prevalence was determined by comparing original readings (done with the ILO scheme in force at the time) with the re-readings using the 1980 ILO scheme. The authors confirm the overall decline in CWP and PMF prevalence rates using the 1980 ILO scheme; however, considerable differences in x-ray classifications were noted between the original and the re-readings, as well as a lack of consensus within the panel of re-readers for all rounds of the NCWSP.

Particularly relevant are the results for x-rays from the fourth round of the NCWPS, because disease prevalence data from the fourth round were used in the NCD exposure-response model, which was relied on in the QRA. Round 4 x-rays were originally read using the 1980 ILO classification, indicating that differences noted between original and re-readings are not related to ILO classification but attributable to reader variability. Using adjusted summary prevalence, the percentage for combined opacities in the original readings for round 4 using ILO 1980 was reported to be 2.3% for category 1+ and 0.3% for category 2+. The re-readings using ILO 1980 were 22.5% and 0.91% for categories 1+ and 2+, respectively.³ In summary, the results from the re-reading of the NCWPS chest x-rays are no more reliable or valid than the original readings and cannot be relied on to represent the “true prevalence” of disease. Thus, given the potential misclassification, using disease prevalence data collect during the fourth round of NCWPS for the exposure-response model, as done in the NCD, most likely produces inaccurate results with errors of unknown direction and magnitude.

These two studies, both conducted by NIOSH, provide sufficient data to demonstrate critical issues concerning the reliability and validity of the diagnoses and classification of CWP and PMF using chest x-rays and the NIOSH B-reader program. Using such unreliable data to measure trends across time and in exposure-response models will introduce an unacceptable level of error and produce uninterruptable findings. As discussed throughout these comments, compounding the lack of reliability and validity in the diagnostic methods are study design,

⁴ Goodwin and Attfield JOEM 1998; 40(12)

exposure assessment, miner participation, and study implementation issues within the CWHSP that also limit the use of these data.

3.2.1 Low Miner Participation in NIOSH Monitoring Programs Severely Impacts Interpretation of NIOSH data

Participation in the CWXSP was and continues to be mandatory for coal operators and voluntary for coal miners. It is mandatory for mine operators to offer x-rays to new and existing employees, but miners are not obligated to undergo x-ray screening after hire.⁵ Management and administration of the CWXSP is very complex and requires significant interaction and cooperation between MSHA, NIOSH, and mine operators. The focus of compliance is on ensuring that mine operators submit their x-ray plans within the required time limit, rather than on ensuring that all miners eligible to undergo medical surveillance actually do so.

The CWXSP was designed by NIOSH to screen individual miners for indications of CWP and PMF, not to measure general declines or increases in CWP and PMF prevalence across time, by mine size, coal rank, or geographic location. Tracking disease trends in a workforce using surveillance data can only be done using accurate diagnostic tools with substantially higher participation from the workforce. Such surveys should be implemented at consistent intervals to improve assessment of disease trends over time. Only a minority of miners have ever participated in any medical surveillance program under the CWHSP. Additionally, monitoring throughout a miner's tenure at the defined intervals as mandated⁶ is rare, as reported in the August 26, 2006 MMWR.⁷ In the 11 miners reported on, only two appeared to have undergone pre-employment chest x-rays, and only one miner underwent chest x-ray screening close to the prescribed time intervals, but only for part of their tenure. All 11 miners had periods of 10 years or more with no x-ray examinations, and 5 miners went 20 or more years without x-ray

⁵ New coal miners in underground mines must be offered and undergo a chest x-ray, either as part of a pre-placement physical examination or within six months after being hired. Three years later, a second chest x-ray must be offered, again by the mine operator, and again every 5 years after the second x-ray. If the second examination reveals evidence of pneumoconiosis, miners must be offered a third chest x-ray two years after the second.

⁶ Miners who began employment prior to 1969 were to be offered an optional x-ray every five years. For miners employed after 1969, x-ray exam is mandatory within 6 months of hire and 3 years later, and for miners with radiographic evidence of CWP, a mandatory x-ray 2 years later. For miners with no evidence, x-rays are to be offered every 5 years.

⁷ Advanced cases of coal workers' pneumoconiosis--two counties, Virginia, 2006. MMWR Morb Mortal Wkly Rep. 2006 Aug 25;55(33):909-13. Centers for Disease Control and Prevention (CDC).

examination through the CWHSP. Unfortunately, chest x-ray examinations and medical care provided to miners throughout their tenure, outside the CWHSP, was not assessed.

The CWHSP continues to suffer from very low miner participation rates, with only a minority of coal miners ever having participated after 1980. Participation rates range from near 100% in 1970 down to around 20% in the 1985–1990 round of examinations, where it has remained, with the exception of the 2000–2004 round, when x-ray results from the Miners Choice Program were added, increasing the participation rate to 42%. With such low and variable miner participation, inherent differences between miners who participate and those who do not will have a significant impact on the measure of disease prevalence.

If the objective of the CWHSP was to collect disease prevalence data in a subset of miners in order to extrapolate disease prevalence data to all coal miners, a sampling strategy should have been developed and applied to the miner work force during each round of examinations. Random sampling of a subset of miners, however, conflicts with the objective of medical monitoring and surveillance for all coal miners, but was considered for the ECWHSP.⁸ The extrapolation of disease prevalence as measured in the small percentage of self-selected active coal miners to all coal miners is an inappropriate extension of that data. The limitations on generalizing the CWHSP findings imposed by the low participation rate are well recognized by NIOSH; however, NIOSH reports and presentations, and even the peer-reviewed literature, frequently fail to discuss these limitations.

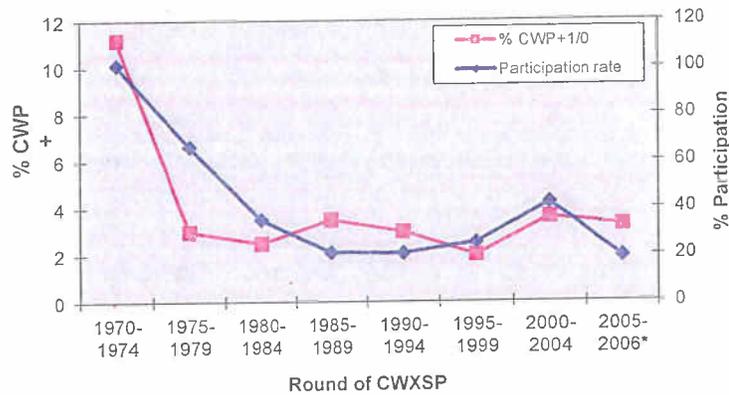
The prevalence of CWP and PMF as reported by NIOSH from the CWHSP is either an underestimate or over-estimate of the true disease prevalence in all coal miners. Unfortunately, the data required to make this determination simply do not exist.

Of particular concern is the apparent relationship of the miner participation rate to disease prevalence rates. The diminishing participation of miners in the CWXSP during 1970–2006 parallels the diminishing prevalence in CWP and PMF, as illustrated in Figure 1, suggesting a potential screening artifact (the more you screen, the more you find; the less you screen the

⁸ The study protocol for the ECWHSP incorporated the use of a sampling frame into the study design; however, it is not clear from reports of the ECWHSP that a sampling frame was ever employed.

fewer you find). Because CWHSP data initiated the current proposed ruling to lower the RCMD standard, it is essential to determine whether the reported decrease and subsequent increase in CWP and PMF prevalence is real, the result of a screening artifact, or a chance finding.

Figure 1. Percent of Coal Worker Participation in CWXSP and Prevalence of CWP +1/0 from 1970-2006



**Incomplete data for the 20056-2006 period, which will be limited until data are available for round 8 of the CWXSP; Raw data downloaded from NIOSH Ref No. 2007F02-05 and Ref. No. 2007 T02-12. Further analyses of these data may reveal no trends, or a decreasing trend.*

To properly interpret the CWXSP data, evaluation of the following information and data is necessary:

1. How many newly employed underground coal miners undergo chest x-ray screening within 6 months of hire? How many do not?
2. How many underground coal miners employed ≥ 3 years have never participated in the CWXSP by tenure, age, and year of hire?
3. How many underground coal miners with tenure greater than 10 years have never participated in CWXSP by tenure, age, and year of hire?
4. How many underground coal miners with tenure greater than 20 years have never participated in CWXSP by tenure, age, and year of hire?

5. For all coal miners with 20 years of tenure, how many have participated in all prescribed rounds of the CWXSP? What are the current age, race, tenure, geographic location of current mine, job in mine, hours per week in the mine, mine size, time mine has been in operation, number of mines worked in lifetime, family history of mining, non-coal-mine employment history, time away from coal mining, education level, history of smoking, and history of other tobacco use in this group of miners?
6. What are the differences between all miners who ever participated in the CWHSP and those who never participated with respect to current age, race, tenure, geographic location of current mine, job in mine, hours per week in the mine, mine size, time mine has been in operation, number of mines worked in lifetime, family history of mining, non-coal-mine employment history, time away from coal mining, education level, history of smoking, and history of other tobacco use.

These questions are critical to acquiring a better understand of CWXSP data, and assessing the reported trends on CWP and PMF prevalence among underground coal miners.

3.2.2 Exposure Assessment Limitations in NIOSH Studies

A critical analysis essential to quantitative risk assessment is dose-response analyses (i.e., what is the relationship of increased exposure level with disease occurrence? When there is a pattern of increasing disease risk with increased exposure level, this is interpreted as a dose-response relationship. This relationship is then extrapolated to lower exposure levels to propose regulatory standards. As noted in the NIOSH CWHSP data in conjunction with MSHA inspector and operator exposure data, the overall prevalence of CWP and PMF has reportedly decreased with decreasing average coal-mine dust levels. This relationship of group (or “ecologic”) data, however, is not based on individual-level comparisons of miners’ work history and exposures and the presence of CWP. In addition, this type of cross-sectional comparison, which evaluates only the current exposure levels and the presence of disease at the same point in time, misses characterizing the historical exposures of individuals. Information on such exposure is more important for estimating risk than current measurements. Few epidemiologic studies were able to incorporate cumulative exposure

metrics in their analyses, yet data of this type are critical for evaluation of risks at a specific exposure level. Individuals may have early histories of higher exposures that are not identified by the ecologic exposure assessment procedures.

Often in epidemiologic research, average exposure levels for a specific job title are used to develop a job exposure matrix and attempts have been made with U.S. coal miner data (Attfield and Moring, 1992). This information is then applied to an individual's work history to estimate his cumulative workplace exposure to RCMD. This method, however, can be limited and introduce biased exposure estimates if exposures have changed over time, if they vary by specific regions or specific coal type (rank), or if an individual worker actually works in different roles. For studies of underground coal-mine workers, all of these factors can have an important role in accurately estimating worker exposures—and not accounting for this variation can produce inaccurate individual exposure estimates. The characteristics and variability of individual coal miners' exposures highlight the need for region-specific, coal-rank-specific, and calendar time-period-specific exposure matrices integrated with the health outcome data for conducting epidemiologic analyses. Although some attempts have been made to develop individual coal miner exposure estimates (e.g. Attfield and Moring, 1992; Attfield and Seixas 1995); – such procedures are not applied to all of the NIOSH surveillance data.

3.2.3 Consideration of Other Exposure Factors

The following factors, while discussed as possible explanations for the recent increase in CWP and PMF, have not been systematically examined.

- Increase in volume of coal produced
- Increase from an 8-hour to a 10-hour working shift
- Changes in coal extraction techniques, resulting in changes in amount/quality of dust
- Increase in exposure to silica-rich rock resulting from mining thinner coal seams

- Inadequate compliance with current RCMD standard
- Change in biological potency of coal.

Several recent studies (discussed below) have started to examine factors such as silica exposure and bioavailable iron as components of underground coal-mine dust that may be useful in better predicting respiratory health risks among underground coal-mine workers.

3.2.4 Confounding

Smoking is a likely critical confounder and/or effect modifier of RCMD and lung disease. Most studies of coal miners have not adequately controlled for, or assessed, the impacts of smoking behavior. The CWHSP is not a suitable study design to evaluate potential confounders; however, if these data are to drive the standard-setting process, confounding factors must be identified and adjusted for.

3.3 Summary of Recent Studies

Recently published studies (Laney et al. 2010a; 2010b; Wade et al. 2011; McCunney et al. 2009) on coal miners highlight the variability in prevalence rates by geographic factors and mine size, and the challenges and uncertainties in understanding the causes and prevalence of CWP and PMF. Although these studies may be interpreted as further evidence of increasing prevalence of CWP, more importantly, they suggest geographic clustering, clustering in smaller mines, and a potentially important role of silica exposure or other components of coal-dust exposures in predicting the risk of CWP and PMF. Copies of these recent publications are included as Appendix C to these comments.

The most recent CWP and PMF prevalence data set, published by Laney et al. (2010a), includes data from all rounds of the CWHSP during 1970–2009, representing 145,512 coal miners who contributed 240,067 chest x-rays for analysis. Underground coal miners from both the CWXSP and ECWHSP were included in the analysis. The objective of the analyses was to determine the extent to which coal-mine size was associated with the prevalence of CWP or PMF. The authors report that miners from smaller mines (<50 miners) experienced significantly more

CWP and PMF in the 1990s and 2000s than miners from mines with >50 employees. Only one-third of participants contributed more than one x-ray over the 39 years of monitoring, illustrating the lack of participation in the CWHSP and adherence to the monitoring schedule.

In a second report, Laney et al. (2010b) examined the role of silica in CWP in the CWXSP. The authors report that 50.7% of the 90,973 participants in the CWXSP during 1980–2008, of any tenure, were mining in Virginia, West Virginia, and Kentucky at the time of their examination. Historical data indicate that Virginia, West Virginia, and Kentucky are three of the five states that have the largest number of mines with <20 employees (Interior Bureau of Mines 1994). Laney et al. report that only miners in Virginia, West Virginia, and Kentucky experienced an increase in the proportion of category 2 and 3 opacities, and only miners in those three states experienced an increase in the prevalence of PMF. Because Virginia, West Virginia, and Kentucky have the highest number of small mines, account for half of the miners who participated in the CWXSP, and have the highest reported prevalence of CWP and PMF, the independent influence, as well as any potential interaction of these factors on disease prevalence, need to be more fully examined. These data, however, may highlight important regional trends that need to be considered in assessing respiratory disease risk among underground coal miners.

Laney et al. (2010b) also report that the prevalence of r-type pneumoconiotic opacities on the radiographs of U.S. underground coal miners has increased markedly since 1999, and that miners with r-type opacities often demonstrate classical silicotic nodules on lung pathology. The increase in r-type opacities was also most apparent among miners in Kentucky, Virginia, and West Virginia.

To properly interpret the latest findings reported by NIOSH, additional information is needed, including:

1. Why was the unit of analysis “miner from small mine,” rather than miner-specific employment time in small mine?

2. Was the individual miner's lifetime employment history used to define "miners from small mines"?
3. What was the time interval from first employed at a "small mine" to disease occurrence?
4. How many days did a miner have to work in a "small mine" to be considered a "miner from a small mine"?
5. Was time worked in a "small mine" considered in any of the analyses?
6. What methods were employed to prevent misclassification of miners (i.e., were miners with limited time in a small mine classified as "miner from small mine"?)
7. Has the interaction among number of mine employees (mine size), miner participation rates, and location of mine been examined?
8. Was the state-specific miner participation rate for each round of CWXSP and year of exam for the ECWHSP an independent variable in the regression model?
9. How many small mines were in operation in the U.S. during each round of the CWXSP and in each year of the ECWHSP?
10. What is the ratio of small participating mines to large participating mines, by state, for each round of the CWXSP and year of ECWHSP?
11. What was the miner participation rate in the "small mines" compared to non-small mines for each round of the CWXSP and for each year of the ECWHSP?
12. What analyses were done to determine how and to what extent these factors contribute to the reported increased prevalence of CWP and PMF in small mines?

13. Was any analysis conducted to examine the collinearity between disease prevalence, participation rates, mine size, and geography?

Addressing such questions should help better understand respiratory health risks among underground coal miners and help to develop more effective health studies.

3.3.1 Wade (2011)

The retrospective case-series reported by Wade et al. (2011) reports information on the natural history of 139 West Virginia underground and surface coal miners with PMF as evaluated by the West Virginia State Occupational Pneumoconiosis Board (WVSOPB) in 2000–2009. The WVSOPB began in 2000 to monitor the annual proportion of claimants with PMF lesions on chest x-rays. As part of each evaluation, a classification of the miner's x-rays for evidence of pneumoconiosis was done by WVSOPB physicians. Demographic data (age at diagnosis of PMF, height, weight, sex, and race), work history, smoking history, and spirometry data were abstracted from the record. No information was available for the total hours worked per year, use of personal protective devices, or exposure to RCMD, other than the observation that these miners worked in mines when the 1969 MSHA standard was in place. However, this study cannot provide information about dust concentrations and PMF risks. PMF cases were initially confirmed, and compensation was awarded by the Board. Each of the miner's x-rays subsequently underwent a separate interpretation using the ILO classification of pneumoconiosis by one of the investigators (ELP), who is a NIOSH B-reader and not affiliated with the Board.

While it does provide information on disease progression in the 139 miners, this case series does not provide a measure of disease prevalence or the trend in disease prevalence over time. The ability to interpret the findings reported by Wade et al. is also limited by the reliance on chest x-ray for CWP and PMF diagnosis, classification, and measurement of disease progression.

3.3.2 McCunney et al. (2009)

McCunney and colleagues recently reviewed the epidemiologic and toxicological literature of underground coal-mine workers and coal-dust composition in an attempt to identify the

component(s) of coal dust that may be responsible for CWP. If such components can be identified, it would be useful for prevention efforts, because it could be used to better characterize or predict potential health risks. They note the higher risks of CWP due to anthracite coal compared to bituminous coal, and the consistent dose-response relationship between coal rank and CWP. After a comprehensive review of information on silica and quartz exposure and the estimated risk of CWP, these authors conclude:

... it can be stated with some scientific certainty based on human epidemiology studies, animal investigations and in vitro evaluations – that quartz is not the predominant factor in the development of CWP. To the contrary, large scale epidemiological studies in Germany, the United Kingdom, France and the United States indicate varying levels of risk of CWP based on the type of coal regardless of silica content. Epidemiological studies however, have confirmed that the rank of coal mined greatly influence CWP rates among coal workers, suggesting that coal's carbon content is a critical factor in assessing CWP risk. In addition, coal from regions with lower rates of CWP (while considering similar levels of exposure to coal, both in concentration and duration) show that coal high in BAI is associated with the higher risks of CWP.

If these observations are correct, this would seem to suggest a different approach to reducing coal miners' risk of CWP than a "one-level-fits-all" approach, and that other factors beyond just coal dust concentration should be considered.

3.4 Australia Experience

The experience of other countries such as Australia, coal mining activities are extensive, may provide valuable insights and guidance on how to prevent CWP. It has been reported (Sheppard, Coal Services Australia) that, among Australian coal workers, no CWP cases have been reported while working under an exposure standard of 2.5 mg/mL (higher than the currently proposed U.S. standard). These results have been achieved with a program of periodic exposure monitoring, comprehensive medical monitoring, and strong worker education components. These Australian programs, which have achieved successful control of CWP (no reported cases in over 20 years), should be reviewed and evaluated to determine if and how their success could inform MSHA.

4 Conclusions

For the purpose of informing and driving a national standard-setting process and developing a new coal-mine standard, it is not justifiable to rely on disease measurement data collected from a minority of self-selected active coal miners based on inaccurate and imprecise CWP and PMF detection and diagnosis methods, and that were based on incomplete miner-specific exposure information, in a targeted area of the country, because it is the only available data set. Improved scientific rigor needs to be applied to the study design, recruitment of participants, disease detection and diagnosis, and exposure assessment, to provide more scientifically defensible study results.

Medical monitoring and surveillance are important tools for early detection of disease, and when done properly, can provide valuable insight into factors that influence an individual's susceptibility and risk. This information is essential for developing and directing effective prevention strategies for both the individual miner and the entire coal miner work force. To optimize the goal of early detection of CWP, "best practices" for diagnosis of respiratory disease need to be employed and maintained. The excessive diagnostic error, as demonstrated by high false positive and negative x-ray readings in the CWHSP, is a severe limitation of these data in the context of estimating disease prevalence. An update on the Wagner paper⁹, extending examination results through 2009, would be useful for interpreting recent CWXSP data.

Although extensive exposure monitoring data are available from MSHA and operator exposure measurement data, these data need to be linked more directly to individual miners for risk evaluation purposes. Calendar period-specific, mine-specific, and occupation-specific job exposure matrices need to be developed for epidemiologic research purposes.

The NIOSH/MSHA medical monitoring and surveillance programs and research studies need to be redesigned. More specific data are required to move beyond simple disease detection and quantification, and the data set needs to include detailed employment histories that provide

⁹ Wagner et al., JOM 1992;24(9)

information on non-coal-mine employment, personal and family history, and in-depth medical history.

The available epidemiologic data used to characterize exposure-level-specific respiratory disease risks are very limited with respect to disease classification and exposure assessment methods. Risk assessments that rely on these data to determine potential risks of coal miners for exposures to specific levels such as 2 mg/m^3 or 1 mg/m^3 will be very limited and subject to errors.

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Supplement: Summary of Kelsh & Doemland Salt Lake City Presentation

The focus of the Salt Lake City presentation was on the limitations and interpretation of disease measurement data in U.S. coal miners collected from the CWHSP. Limitations inherent to the cross-sectional study design of the CWXSP, such as the use of prevalence rather than incidence data, and inability to estimate risk for specific coal-dust exposure levels were discussed. The negative impact of the extremely low miner participation rate on the internal and external validity of the reported findings and the inappropriate extension of findings from participants to all coal miners was reviewed and discussed in our presentation. The lack of information on important differences between participants and nonparticipants and the reliance on self-reported data such as work history data (rather than occupational records) or disease symptoms (rather than clinical diagnoses) were highlighted. Potential sources of error, such as screening artifact and misdiagnosis that limit the interpretation of the reported trend in CWP and PMF prevalence, were presented. Using surveillance data to measure trends in disease occurrence in any occupational group can only be done with near-complete participation from the entire work force. Also addressed was NIOSH's consistent lack of transparency in the reporting of coal miner health data, the need for more complete and detailed analysis, and a request for consistent acknowledgement of the limitations of disease prevalence data from the CWHSP when reporting results.

Responses to MSHA Panel Questions of Kelsh & Doemland Presentation

Question 1: Mr. Thaxton: You indicated in your slides when you were going through, around slide 15, that it was difficult to achieve the new lower levels, you had made that determination. Can you provide us with what information and what data you've analyzed to determine it would be difficult to achieve these new lower levels? Can you still, though, provide your analysis of the data that you looked at to come to that conclusion?

Response 1: This issue is addressed in the comments submitted by Dr. Richard Reiss of Exponent. Essentially, with the proposed required frequency of exposure sampling and the new

proposed rule regarding citations where a single exceedance of the 1-mg/mL level will constitute a violation, this effectively drives the average exposure level to 0.11 if a company hopes to achieve 99% compliance with the proposed new rule. Given current trends observed in MSHA inspection data, an average level of 0.11 mg/mL has not been achieved. MSHA has not recognized the implication of the combined effects of a new exposure level, the frequency of exposure sampling, and what constitutes a citation.

Question 2: Mr. Thaxton: Can you provide what data was used for this analysis that gave you that conclusion, that this would be costly and difficult to implement and analyze, please?

Response 2: See our response to #1 above. Also see the comments provided by Dr. Robin Cantor on MSHA economic analysis of the proposed rule, as well as the comments provided by Mr. Cooper and Ms. McCarthy regarding exposure monitoring issues imposed by the proposed rule. All three of these sets of comments present feasibility and cost questions that MSHA should address before enacting the proposed rule.

Question 3: Dr. Wagner: Did you take a look at any of the longitudinal studies on which the NIOSH criteria document was based and that were integrated into consideration for the current proposed rule? So we'll look forward to learning your specific analyses and critiques for the longitudinal studies as well.

Response 3: See Diagnosis of CWP and PMF section in our comments as well as the discussion of exposure assessment issues pertaining to the longitudinal studies. In addition, we provide comments regarding the impact of low miner participation in these studies.

Question 4: Dr. Wagner: In your experience as an epidemiologist, can you describe some other occupational groups where there's more extensive information upon which to base health protective standards than you find with coal miners?

Response 4: I mentioned studies of exposure to electric and magnetic fields (EMF), primarily based on my personal research experience, where there is substantial occupational exposure information and better designed epidemiologic studies. Another group of workers who have

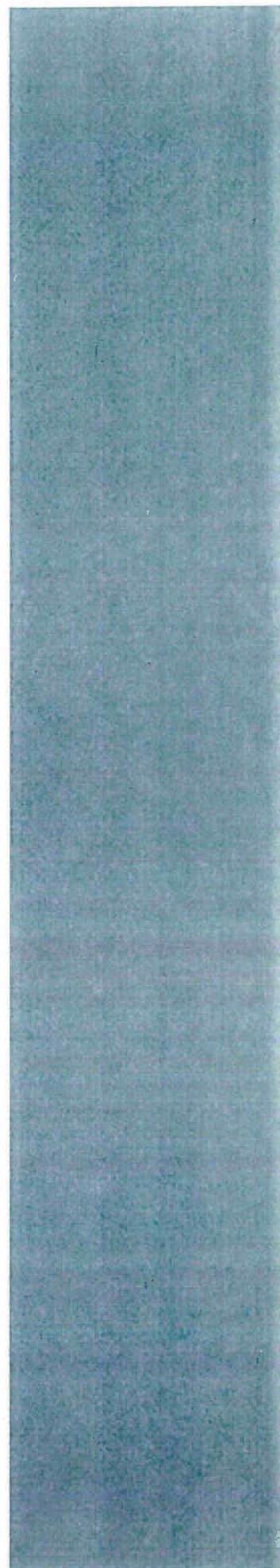
been subject to substantial exposure monitoring efforts are beryllium workers, who were continuously measured for daily beryllium exposures at the Cardiff facility in the U.K. This effort incorporated more than 300,000 area measurements, over 200,000 person lapel measurements collected from 194 workers over the period 1981-1997. But more importantly, these measurements could be tied to individuals to estimate average, maximum, and cumulative exposures for specific workers and can thus be tied to specific health outcomes among these workers.

Question 5: Dr. Wagner: Well, as you prepare your remarks, I'd appreciate it if you come up with other potential explanations. In particular, I know that the question of longer shifts has been raised and the question as to whether or not the coal-mine dust exposures that are reported are actually reflective of the exposures that individuals have and how that would play into this.

Response 5: The issues raised in this question are critically important for understanding disease risks among underground coal miners. From available studies, we do not have individual exposure information among participants in these studies. It would be important to understand when the practice of longer shifts became commonplace, and this may be a factor that results in increased exposure of miners to coal-mine dust. At this point, we do not know whether those with CWP or PMF have experienced coal-mine dust exposure at higher levels than the current 2-mg/mL standard. Keeping in mind the relative long latency of CWP and PMF for most cases, we need to be concerned about exposures in the 1970s and 1980s for many of the reported cases. Such information is not always available.

Attachment A

***Curriculum Vitae* for
Dr. Michael A. Kelsh**



Michael A. Kelsh, Ph.D., M.P.H.
Principal Scientist

Professional Profile

Dr. Michael Kelsh is a Principal Scientist in Exponent's Health Sciences Center for Epidemiology, Biostatistics, and Computational Biology. Dr. Kelsh specializes in the application of epidemiology and biostatistics to occupational, environmental health, and pharmaceutical issues. Dr. Kelsh has extensive experience in the design, implementation, analysis, and interpretation of epidemiologic studies. Dr. Kelsh has conducted epidemiologic studies of occupational injuries, musculoskeletal diseases, cardiovascular disease, respiratory and neurological diseases, and cancer incidence and mortality. His research has also focused on exposure assessment issues, and as part of epidemiologic investigations, has evaluated the potential health effects of air pollution, arsenic, asbestos, beryllium, hexavalent chromium, electric and magnetic fields, ergonomic factors, mercury, perchlorate, radiofrequency energy, and trichloroethylene. Dr. Kelsh has conducted occupational health studies among a variety of worker groups including: Aerospace, electric utility, electronics, mining, and petroleum research workers. He has also worked on meta-analyses of trichloroethylene and cancer, arsenic and bladder cancer; auto mechanic work and mesothelioma; and magnetic fields and childhood leukemia.

Dr. Kelsh taught seminars in occupational/environmental epidemiology and exposure assessment as an adjunct professor at the University of California, Los Angeles (UCLA) School of Public Health (1996-2008). Dr. Kelsh has served on Scientific Advisory Panels covering a variety of environmental health issues for the California Department of Health Services, the New York Department of Environmental Health, and the Oregon Department of Human Services. Dr. Kelsh is fluent in Spanish and has international public health experience through consulting, research, and volunteer projects in Latin America.

Academic Credentials and Professional Honors

Ph.D., Epidemiology, University of California, Los Angeles, 1993
M.A., Latin American Studies, University of California, Los Angeles, 1986
M.P.H., Epidemiology, University of California, Los Angeles, 1984
B.A., Cellular Biology/Spanish, University of California, Santa Barbara, 1981

Fellow, InterAmerica Foundation
Fellow, American Statistical Association Conference
Traineeship, National Institute of Health, Occupational/Environmental Epidemiology, UCLA

Languages

Spanish

Publications

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Book Chapters

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Kelsh MA, Alexander DD. Occupational and environmental epidemiology. In: *Encyclopedia of Epidemiology 2007*, Sage Publications, Thousand Oaks, CA, 2007, in press.

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Mowat F, Shum M, Kelsh MA. Exposure assessment in epidemiology. In: *Encyclopedia of Epidemiology 2007*, Sage Publications, Thousand Oaks, CA, 2007, in press.

Conference Presentations

Kelsh MA, Kucera G, Erdreich L. Updated meta-analysis of mobile phone use and brain tumors. Presented at BioEM, San Diego, CA. June 8–12, 2008.

Kelsh MA. Optimal dosimetry for mobile phone studies: Factors influencing exposure and implications for epidemiologic research. Dosimetry meets Epidemiology Workshop, Swiss Science Foundation, Zurich, Switzerland, January 11, 2008 (invited speaker).

Kelsh MA, Weingart M, Mandel JH, Mink PJ, Alexander D, Basu R, Kalmes R, Goodman M. Occupational TCE exposure and kidney cancer and non-Hodgkin's lymphoma: A meta-analysis. Presented at the 2nd North American Congress of Epidemiology, Seattle, WA, June 21–24, 2006.

Mink P, Alexander D, Barraj L, Kelsh M, Tsuji J. Meta-analysis of low level arsenic exposure and bladder cancer. A poster presentation at the 2nd North American Congress of Epidemiology, Seattle, WA, June 21–24, 2006.

Mink PJ, Alexander DD, Barraj LM, Kelsh MA, Tsuji JS. Meta-analysis of low level arsenic exposure and bladder cancer: Implications for risk assessment in the United States. A poster presentation at the 45th Annual Meeting of the Society of Toxicology, San Diego, CA, March 5–9, 2006.

Weingart M, Kelsh MA, Shum M, Sheppard AR, Kuster N. Statistical analysis of the influences of technology, antenna, mobile phone shape and position on SAR measurements from FCC compliance testing data. BioEM, University College, Dublin, Ireland, June 19–24, 2005.

Shum M, Kelsh MA, Zhao K, Erdreich LS. A comparison of recall of mobile phone use with billing record data. Presented at BioEM, University College, Dublin, Ireland, June 19–24, 2005.

Kelsh MA, Sulser C, Shum M, McNeely M, Kuster N, Froehlich J, Sheppard A. Evaluation of mobile phone handset exposures using software modified phones and field phantom systems. Presented at BioEM, University College, Dublin, Ireland, June 19–24, 2005.

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Shum M, Kelsh M, Sheppard A, Chan N, Kuster N, Fröhlich J, Erdreich L, Van Kerkhove McNeely M. Improved assessment of cell phone exposure for epidemiologic studies. Presented

at American Industrial Hygiene Conference and Exposition (AIHce), Atlanta, GA, May 12, 2004.

Kelsh MA and Yager JA. Workplace injuries and illness trends in the electric energy industry: Initial results from a comprehensive occupational health and safety surveillance system. Presented at the National Occupational Injury Research Symposium, Pittsburg, PA October 28–30, 2003.

Kelsh MA. What can we learn about TCE from epidemiologic studies? Presented at the Toxicology Forum, Aspen, CO, July 13–17, 2003.

Mezei G, Cher D, Kelsh M, Chapman C, Kavet R. Cardiovascular deaths and occupational exposure to magnetic fields in the national mortality followback survey. Presented at the Bioelectromagnetics Society Annual Meetings, Wailea, Maui, HI, June 22–26, 2003.

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Kelsh MA, Exuzides KE, Cher D, Mandel JS. Heterogeneity, influence and sensitivity analyses in meta-analysis – it matters: A case study of trichloroethylene and cancer. Presented at the Society of Epidemiologic Research, Palm Desert, CA, June 18–21, 2002.

Kelsh MA. Evidence linking environmental agents to breast cancer: A review of research on electric and magnetic fields and light at night exposures. Presented at the International Summit on Breast Cancer and the Environment: Research Needs, Charminade, Santa Cruz, CA, May 22–25, 2002.

Exuzides KA, Lau E, Kelsh MA, Ebi KL. Association of weather variables with hospital admissions for asthma in Northern and Southern California regions, 1983–1998. Presented at the 13th Conference of the International Society for Environmental Epidemiology, Garmisch-Partenkirchen, Germany, Sept 2–5, 2001.

Kelsh MA, Bracken TD, Sahl JD, Shum M, Ebi K. Magnetic field exposures of garment workers: Results of personal and survey measurements and a pilot survey. Presented at the Bioelectromagnetics Society Annual Meetings, St. Paul, MN, June 10–14, 2001.

Shum M, Kelsh MA, Bracken TD, Chapman PS, Ebie K. Magnetic-field exposures of garment workers: Results of personal and survey measurements and a pilot interview study. Presented at Northern California Epidemiology Network, Berkeley, CA, February 5, 2001.

Kelsh MA, Morgan RW, Zhao K, Exuzides KA. Occupational radiofrequency exposure and cancer mortality. Presented at the Bioelectromagnetics Society Annual Meetings, Munich, Germany, June 16, 2000.

Bracken TD, Kelsh MA, Sahl JD, Rankin R. Comparing exposures among garment workers to electric utility workers for designing a study of occupational 60 Hz magnetic field exposures

and female breast cancer. Presented at the Bioelectromagnetics Society Annual Meetings, Munich, Germany, June 16, 2000.

Kelsh MA, Zhao K, Yager J. Developing a surveillance database for epidemiologic analysis of occupational injuries: Experience with the electric utility industry. Presented at the American Industrial Hygiene Conference & Exposition, Orlando, FL, May 20–25, 2000.

Kelsh MA, Chapman P, Bracken TD. Assessing exposure comparability for a study of occupational 60 Hz electromagnetic fields exposure and female breast cancer. Presented at the American Industrial Hygiene Conference & Exposition, Orlando, FL, May 20–25, 2000.

Kelsh MA, Deubner D, Maier L, Kent M, Smith B, Chapman P, Shum M, Paustenbach D, Kolanz M. Medical monitoring survey results at a beryllium mine and extraction facility. Presented at the Society of Toxicology Annual Meetings, Philadelphia, PA, March 19–24, 2000.

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Greenland, S, Sheppard AR, Kelsh MA, and Kaune WT. A pooled analysis of magnetic fields wire codes, and childhood leukemia. Presented at Society of Epidemiologic Research 32nd Annual Meeting, Baltimore, MD, June 10–12, 1999.

Kelsh MA, Sahl JD, Atherton M, and Shih J. History of previous injury as a risk factor for future severe injury: An analysis among utility workers. Presented at American College of Epidemiology Annual Meeting, Bethesda, MD, October 3–4, 1999.

Yager J, Kelsh MA, Zhao K, and Mrad R. Development of an occupational illness and injury surveillance database for the electric utility sector. Presented at ACGIH Symposium: Occupational Exposure Databases and Their Application for the Next Millennium, London, England, November 1–3, 1999.

Kelsh MA. Injury and illness surveillance database pilot study. Invited speaker at EPRI Health and Safety Advisory Meetings, Chicago, IL, October 1, 1998.

Kelsh MA. Radiofrequency exposure assessment for occupational studies: Overview and future directions. Invited speaker at the 5th Annual COST244bis Zagreb, Croatia, Workshop, November 21–22, 1998.

Sheppard AR, Kelsh MA, Kaune WT, Greenland S. Estimated attributable fraction for childhood leukemia in association with residential power frequency magnetic field exposures. Presented at Bioelectromagnetics Society Annual Meeting, St. Petersburg, FL, June 1998.

Sheppard AR, Kelsh MA, Greenland S, Kaune WT. Pooled analysis of childhood leukemia and residential power frequency magnetic field exposures: Dose response and influence studies. Presented at the 1998 Annual Review of Research on Biological Effects of Electric and

Magnetic Fields from the Generation, Delivery and Use of Electricity, Tuscon, AZ, September 14–17, 1998.

Kelsh MA. Epidemiology methods and case studies. Presented at UCLA—Sociedad Mexicana del Mexicana del Trabajo Collaborative Conference on Occupational Medicine, September 12–14, 1997.

Kelsh MA. Health and safety research among electric utilities. Invited speaker at EPRI Environmental Group Advisory Meetings, October 6–9, 1997.

Kelsh MA, Kheifets L, Smith RW. The impact of work location on occupational summaries of magnetic field exposures among electric utility workers. Presented at the 1997 Annual Review of Research on Biological Effects of Electric and Magnetic Fields from the Generation, Delivery and Use of Electricity, San Diego, CA, November 9–13, 1997.

Bowman JD, Kelsh MA, Kaune WT. A manual of methods for measuring occupational electric and magnetic field exposures. Presented at the 1996 Annual Review of Research on Biological Effects of Electric and Magnetic Fields from the Generation, Delivery and Use of Electricity, San Antonio, TX, November 1996.

Kelsh MA, Kheifets LI, Smith RW, Haines KD, Senior R, Bracken TD, and Riege LE. Comparative analyses of occupational magnetic field exposure data among electric utility workers. Presented at Bioelectromagnetics Society Annual Meeting, Victoria, British Columbia, June 1996.

Kelsh MA, Sheppard AZ, Florig K, Atherton MA, and Bernstein BB. Estimating potential health costs for cost–benefits analysis of policy options for school exposures to electric and magnetic fields. Presented at the 1996 Annual Review of Research on Biological Effects of Electric and Magnetic Fields from the Generation, Delivery and Use of Electricity, San Antonio, TX, November 1996.

Kelsh MA, Sheppard AR, Kaune WT, Atherton MJ. Pooling measures of magnetic field exposures across childhood leukemia studies: Implications for meta–analysis and attributable risk estimation. Presented at Bioelectromagnetics Society Annual Meeting, Victoria, British Columbia, June 1996.

Sheppard AR, Kelsh MA, Florig HK, Bernstein BB. Disease endpoints pertinent to cost–benefit analysis for school exposures to power frequency electric and magnetic fields. Presented at Bioelectromagnetics Society Annual Meeting, Victoria, British Columbia, June 1996.

Kelsh MA and Sahl JD. Mortality among a cohort of electric utility workers, 1960–1991. Presented at American Public Health Association Annual Meeting, San Diego, CA, October 1995.

Kelsh MA and Scott R. A strategy for monitoring magnetic field exposures among an electric utility workforce. Presented at Bioelectromagnetics Annual Meeting, Boston, MA, June 1995.

Ryan MG and Kelsh MA. Work-related injuries among county workers: Assessing impacts and identifying high-risk occupations. Presented at American Public Health Association Annual Meeting, San Diego, CA, October 1995.

Del Razo LM, Garcia-Vargas G, Ahlores A, Cebrian ME, Montero R, Ostrowsky P, Kelsh MA. Chronic high exposure alters the profiles of urinary arsenic metabolites in humans. Presented at Society of Toxicology Annual Meeting, Baltimore, MD, 1995.

Kelsh MA, Ostrosky-Wegman P, Cebrian M, Gonsebatt M, Del Razo L, Garcia-Vargas G, Riege LE, Yager J. Comparative analysis of biomarkers for arsenic exposure and early health effects among populations of Northern Mexico. Presented at SEGH Second International Conference on Arsenic Exposure and Health Effects, San Diego, CA, June 1995.

Kelsh MA and Sahl JD. Misclassification of electrical worker occupations from death certificate data: An analysis among electric utility workers. Presented at DOE/EPRI Contractors Review Meeting, Albuquerque, NM, November 1994.

Kelsh MA and Sahl JD. Sex differences in work-related injury rates among electric utility workers. Presented at the Society for Epidemiologic Research Annual Meeting, Miami, FL, June 1994.

Sahl JD, Aseltine DA, Senior RS, Rankin R, Kelsh MA, Riege LE, Smith RW, Bracken TD. An analysis of alternate summaries of magnetic field exposure data. Presented at DOE/EPRI Contractors Review Meeting, Albuquerque, NM, November 1994.

Sheppard AR, Kaune WT, Kelsh MA, Greenland S, Sahl JD. Development of a model for estimating attributable fractions for childhood leukemia and residential exposures to power frequency magnetic fields. Presented at 16th Annual Bioelectromagnetics Society Meeting, Copenhagen, Denmark, June 1994.

Kelsh MA. A review of occupational health research in power frequency electric and magnetic fields. Invited speaker at Pacific Gas and Electric Company EMF Update Conference, January 14, 1993.

Ryan MG and Kelsh MA. Work related injuries among county firefighters, 1987-1992. Presented at the American Public Health Association Annual Meeting, San Francisco, CA, October 1993.

Kelsh MA, Sahl JD, Smith RW, Aseltine DA. Sampling design for ELF magnetic field exposure assessment. Presented at the DOE/EPRI Annual Contractors Review Meeting, Savannah, GA, November 1993.

Kelsh MA, Sahl JD, Sorenson S. Sex differences in injury rates among electric utility workers. Presented at the American Public Health Association Annual Meeting, San Francisco, CA, October 1993.

Kelsh MA, Ke D, Morgenstern H. Shoulder, neck, and back pain among trade and office workers. Presented at the American Public Health Association Annual Meeting, San Francisco, CA, October 1993.

Kelsh MA, Ke D, Morgenstern H. The importance of non-occupational risk factors in the assessment of occupationally-related carpal tunnel syndrome. Presented at Society for Epidemiologic Research Annual Meeting, Keystone, CO, June 1993.

Kelsh MA, Sahl JD, Smith R. The next generation of work exposure assessments. Presented at Bioelectromagnetics Society Annual Meeting, Los Angeles, CA, June 1993.

Sahl JD, Scarfuto J, Pineo J, Kelsh MA, Aseltine D. Magnetic field exposures among electric utility workers: Consideration of occupation, job task and facility type. Presented at Bioelectromagnetics Society Annual Meeting, Los Angeles, CA, June 1993.

Kelsh MA and Sahl JD. Work related injuries among electric utility workers. Presented at the Soc. for Epidemiologic Research Annual Mtg., Minneapolis, MN, June 1992.

Sahl JD and Kelsh MA. Exposure assessment for power frequency magnetic fields among electrical utility workers. Presented at First World Congress for Electricity and Magnetism in Biology and Medicine, Orlando, FL, June 1992.

Kelsh MA, Sahl JD, Greenland S. Improving study design and exposure assessment procedures in the analyses of the health effects of occupational exposures to electromagnetic fields. Presented at 1st World Congress for Electricity and Magnetism in Biology and Medicine, Orlando, FL, June 1992.

Kelsh MA, Morgenstern H, Ke D. A cross-sectional study of carpal tunnel syndrome symptoms among trade and office workers. Presented at the Ninth International Symposium, Epidemiology in Occupational Health, Cincinnati, OH, September 1992.

Kelsh MA, Sahl JD, Greenland S, and Guggenheim DE. An analysis of cancer mortality among utility electrical workers. Presented at Bioelectromagnetics Society Annual Meeting, Salt Lake City, UT, June 1991.

Kelsh MA, Guggenheim DE, Sahl JD. Application of epidemiologic methods to occupational injury prevention. Presented at National Safety Congress, New Orleans, LA, October 1991.

Kelsh MA, Sahl JD, Greenland S, Guggenheim DE. Influence of study design, analytical decisions and data sources in occupational mortality. Presented at Bioelectro-magnetics Society Annual Meeting, Salt Lake City, UT, June 1991.

Rock AR, Kelsh MA, Faeder EJ. Information management approach for databases required for hazard assessment in the aerospace industry. Presented at Society for the Advancement of Material and Process Engineering, San Diego, CA, May 1991.

Sahl JD, Kelsh MA, Guggenheim DE. Characteristics of minor injuries that predict the occurrence of severe injury. Presented at Society for Epidemiologic Research Annual Meeting, Buffalo, NY, June 1991.

Sahl JD, Kelsh MA, Guggenheim DE. Injury coding for occupational injury surveillance. Presented at Society for Epidemiologic Research Annual Meeting, Salt Lake City, UT, June 1990.

Sahl JD and Kelsh MA. Exposure models in retrospective cohort studies. Presented at American Statistical Association Eighth Conference on Radiation and Health, Copper Mountain, CO, July 1989.

Morgenstern H, Kraus J, Kelsh MA, Margolis W. A cross-sectional study of carpal-tunnel syndrome in female grocery checkers. Presented at Society for Epidemiologic Research Annual Meeting, Vancouver, British Columbia, June 1988.

Kelsh MA. Health impacts of a latrine-sanitation project on rural villages of Michoacan, Mexico. Presented at American Public Health Association Annual Meeting, New Orleans, LA, October 1987.

Locke GE, Levy DA, Hauser WA, Lampert DI, Forsythe S, Kelsh MA, Wheeler NC, Kramer LD. Prevalence of epilepsy in an urban minority community. Presented at American Epilepsy Society Meeting, New York, NY, November 1986.

Lampert DI, Locke GE, Kelsh MA. Head injury in an urban minority community. Presented at American Public Health Association Annual Meeting, Washington, DC, November 1985.

Kelsh MA, Iverson E, Scrimshaw SW. Differences in perception and treatment of asthma and epilepsy among Latino and Anglo children and adolescents in Los Angeles. Presented at American Public Health Assoc. Annual Meeting, Dallas, TX, November 1983.

Technical Reports

Kelsh MA, Ramachandran K, Asuncion N. Occupational health and safety annual report 2000: Injury & illness in the electric energy workforce, 1995-1999, EPRI, Palo Alto, CA 2000. 1000740.

Kelsh MA, Chapman P, Bracken, TD, Sahl JD, Rankin R, Exuzides A. Female breast cancer feasibility study: A comparison of magnetic fields exposures in a garment manufacturing and electric utility work environment. EPRI, Palo Alto, CA 2000. TR-114845.

Kelsh MA and Mrad R. Pilot Study: Occupational health and safety surveillance database. EPRI, Palo Alto, CA 1999. TR-113884.

Bowman JD, Kelsh MA, Kaune WF. Manual for measuring occupational electric and magnetic field exposures. Prepared for the U.S. Department of Health and Human Services, Ojai, CA, and Richland, CA, 1998.

Michael A. Kelsh, Ph.D., M.P.H.

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Sahl JD and Kelsh MA. Codebook for work injuries—safety data management system for injury surveillance and prevention. Prepared for Southern California Edison Company, Health Research and Evaluation Division, Rosemead, CA, 1996.

Sahl JD and Kelsh MA. A report on the International Utility Symposium—Health effects of electric and magnetic fields: Research, communication, regulation. WEST Associates, ETF 86–12. Southern California Edison Company, Rosemead, CA, 1987.

Academic Appointments

- Adjunct Associate Professor, UCLA School of Public Health, Department of Epidemiology, 1999–present

Project Experience

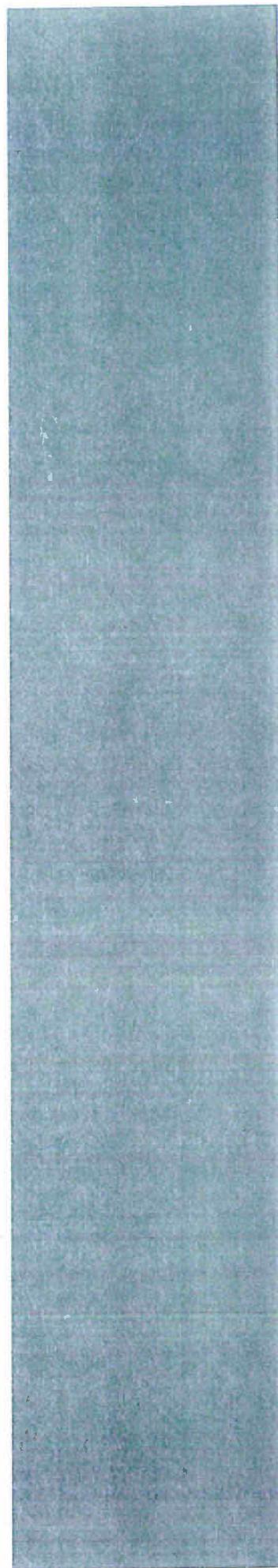
- Principal Investigator, Cell Phone Exposure Assessment, CTIA/CRADA, 2003–2006
- Co-Principal Investigator, EMF Exposure Assessment, NIOSH/NCI, 2005–2006
- Principal Investigator, EPRI Injury, Electric Power and Research Institute, 1999–2006
- Principal Investigator, TCE Meta-Analysis, TCE Issues Group, 2004–2005
- Co-Principal Investigator, Newborn Thyroid Study, Lockheed, 2000–2005
- Project Manager, Chevron Epidemiologic Study, University of California, Berkeley, 2003–2005
- Principal Investigator, EPRI Breast Cancer Exposure Assessment, Electric Power and Research Institute, 1999–2002
- Project Manager, Motorola Epidemiologic Study, Motorola, Inc., 1997–2001
- Co- Investigator, Childhood Leukemia – EMF Pooled Analysis, NIEHS, 1996–1999
- Project Manager, Aerospace Workers Epidemiologic Study, Hughes Aircraft, 1997–1998
- Co-Investigator, EMF Exposure and School Policy, California Department of Health Services, 1995–1996
- Project Manager, Electric Utility Worker Injury Surveillance Study, Southern California Edison, 1990–1995
- Project Manager, UCLA Study of Musculoskeletal Injury Among Trade and Office Workers, 1990–1993
- Project Manager, Electric Utility Worker Epidemiologic Study, Southern California Edison, 1985–1990

Professional Affiliations

- International Society of Pharmacoepidemiology (member)
- International Society for Environmental Epidemiology (member)
- Society for Epidemiologic Research (member)
- American College of Epidemiology (member)
- American College of Occupational and Environmental Medicine (associate member)
- Bioelectromagnetics Society (member)
- American Public Health Association (past member)
- American Industrial Hygiene Association (past member)

Attachment B

***Curriculum Vitae* for
Dr. Martha L. Doemland**



Martha L. Doemland, Ph.D.
Senior Managing Scientist

Professional Profile

Dr. Martha L. Doemland is a Senior Managing Scientist in Exponent's Health Sciences Center for Epidemiology, Biostatistics, and Computational Biology. Dr. Doemland has over 30 years of experience in the design, implementation, management, analysis, and interpretation of epidemiologic studies related to both chronic and infectious diseases. Prior to joining Exponent, Dr. Doemland was with Sanofi Pasteur, the vaccine division of Sanofi-Aventis, from 2003 to 2010, where she served as Director of Epidemiology, with responsibility for the epidemiologic research strategy for vaccines under development and in early clinical trials. The research strategy, developed through a comprehensive disease understanding, focused on assessing the current state of knowledge, including an assessment of potential clinical trial endpoints, potential pharmacoepidemiologic issues, and disease risk factors, and establishing profiles for the "at risk" population; as well as proposing and conducting studies to measure and monitor the global incidence/prevalence of the disease or infection. She designed studies to measure the incidence and prevalence of healthcare-acquired infections and sexually transmitted diseases using claims and administrative databases (e.g., Premier/i3/United Health). Dr. Doemland was also involved in monitoring the epidemiology of vaccine-preventable diseases to assess the impact of vaccination on the incidence and prevalence of disease, and to discern changes in circulating strains of the pathogen. While at Sanofi Pasteur, she developed a comprehensive understanding of the vaccine development process through the entire life cycle, and in particular the important role of observational studies in vaccine development in both the pre- and post-licensure phases.

Dr. Doemland has wide-ranging experience managing and analyzing large data sets, ranging from occupational cohorts to large patient populations (patients undergoing coronary angiography or coronary bypass surgery at a large teaching hospital), including analyses of cohort mortality to survival, and calculating measures of incidence and prevalence using national databases (National Inpatient Survey, CDC Wonder).

Dr. Doemland has comprehensive knowledge and experience in assessing health effects from occupational and environmental exposures in both adults and children. Most notably, she was the co-principal investigator and project manager of a large occupational study of workers exposed to polychlorinated biphenyls in which follow-up spanned more than 60 years. As part of this epidemiologic research, she gained extensive experience conducting vital status determination using the National Death Index and other sources.

Academic Credentials and Professional Honors

Ph.D., Epidemiology and Community Health, School of Medicine and Biomedical Sciences,
State University of New York at Buffalo, 1994

M.S., Epidemiology, State University of New York at Buffalo, 1986

B.A., Psychology, Bard College, 1981

Fellowship, National Health Service Award, U.S. Public Health Service Cancer Training Grant,
1987–1990

Publications

Greenberg DP, Doemland M, Bettinger JA, Scheifele DW, Halperin SA; IMPACT Investigators, Waters V, Kandola K. Epidemiology of pertussis and Haemophilus influenzae type b disease in Canada with exclusive use of a diphtheria-tetanus-acellular pertussis-inactivated poliovirus-Haemophilus influenzae type b pediatric combination vaccine and an adolescent-adult tetanus-diphtheria-acellular pertussis vaccine: Implications for disease prevention in the United States. *Pediatric Infectious Disease Journal* 2009 Jun; 28(6):521–528.

Kimbrough RD, Doemland ML, Mandel JS. A mortality update of male and female capacitor workers exposed to polychlorinated biphenyls. *Journal of Occupational and Environmental Medicine* 2003; 45:3.

Kimbrough RD, Doemland ML, Krouskas CA. Analysis of research studying the effects of polychlorinated biphenyls and related chemicals on the neurobehavioral development in children. *Veterinary & Human Toxicology* 2001; 43(4)220–228.

Kimbrough RD, Doemland ML, LeVois ML. Mortality in male and female capacitor workers exposed to PCBs. *Journal of Occupational and Environmental Medicine* 1999; 41(3):161–171.

Freudenheim JL, Russell M, Trevisan M, Doemland ML. Calcium intake and blood pressure in blacks and whites. *Ethnicity and Disease* 1991; 1(2).

Rosenthal TC, Perrapato TH, Doemland ML, Fridorich JE, et al. Endometrial sampling: Analysis of 310 procedures performed by family physicians. *Journal of Family Practice* 1989; 29(3):249–256.

Book Chapters

Kimbrough RD, Doemland ML, LeVois ML. Mortality in male and female capacitor workers exposed to PCBs. In: *Standard Handbook of Environmental Science, Health, and Technology*. Lehr J (ed), McGraw-Hill, 2000.

Abstracts, Posters, and Oral Presentation

Doemland ML, Trevisan M, Krogh V, Winkelstein W. Sleep patterns and blood pressure results from the Buffalo Blood Pressure Study. Abstracts, American Journal of Hypertension 1989; 2(5): Part 2.

Htar MTT, Doemland M, Muros-Le Rouzic E. Global incidence and case fatality rates due to different *N. meningitides* serogroups. Poster, 17th International Pathogenic Neisseria Conference, Cairns, Australia, September 2007.

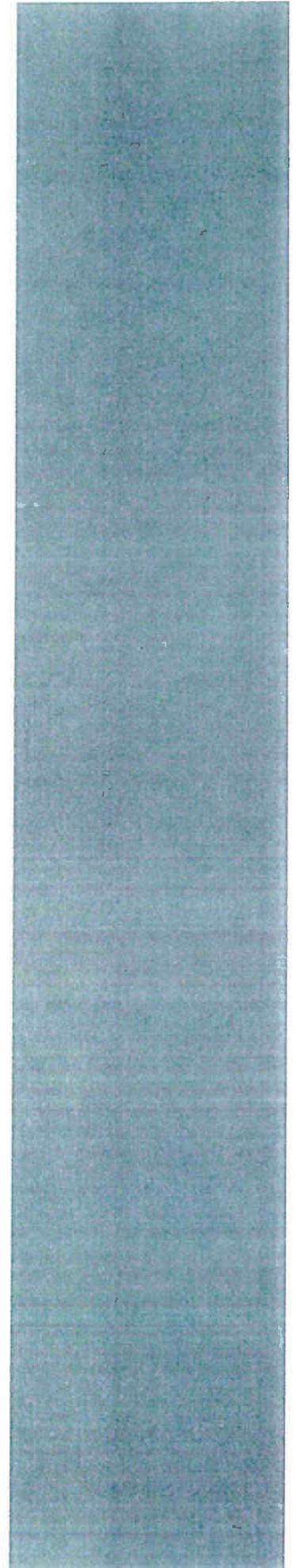
Greenberg DP, Doemland ML, Lavigne P, Galanis E, Kandola K, Bettinger J, Halperin SA, Scheifele DA, on behalf of the Immunization Monitoring Program. Active (IMPACT) Impact of Pentacel™ (DTaP-IPV//PRP-T) on the epidemiology of invasive Hib disease and pertussis in Canada. Poster, 5th Annual Pediatric Infectious Disease Society, Napa, CA, October 9–11, 2005.

Muros-Le Rouzic E, Doemland M, Teyssou R. Geographical differences in invasive meningococcal disease rates and serogroup distribution. Oral Presentation, Canadian Public Health Association Meeting, Ottawa, Ontario, September 2005.

Muros-Le Rouzic E, Doemland M, Teyssou R. Geographical differences in invasive meningococcal disease rates and serogroup distribution. Poster, 8th European Monitor Group for Meningococci Meeting Dublin, Ireland, September 7–9, 2005.

Attachment C

**Recently Published Studies
on Coal Miners**



Short report



Coal workers' pneumoconiosis and progressive massive fibrosis are increasingly more prevalent among workers in small underground coal mines in the United States

A Scott Laney, Michael D Attfield

Surveillance Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia, USA

Correspondence to

A Scott Laney, Surveillance Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, 1095 Willowdale Road, Mail Stop HG900.2, Morgantown, WV 26505-2888, USA; alaney@cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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ABSTRACT

Objective To determine whether the prevalence of coal workers' pneumoconiosis (CWP) or progressive massive fibrosis (PMF) among United States underground miners is associated with mine size.

Methods We examined chest radiographs from 1970 to 2009 of working miners who participated in the National Coal Workers Health Surveillance Program for the presence of small and large opacities consistent with pneumoconiosis, based upon the International Labour Organization classification system.

Results A total of 145 512 miners contributed 240 067 radiographs for analysis. From the 1990s to the 2000s, the prevalence of radiographic CWP increased among miners in mines of all sizes, while miners working in mines with fewer than 50 employees had a significantly higher prevalence of CWP compared to miners who worked in mines with 50 or more employees ($p < 0.0001$). When adjusted for age and within-miner correlation, the difference in prevalence of CWP by mine size was significant for all decades. Since 1999, miners from small mines were five times more likely to have radiographic evidence of PMF (1.0% of miners) compared to miners from larger mines (0.2% of miners) with a prevalence ratio of 5.0 and 95% CI 3.3 to 7.5.

Conclusion The prevalence of CWP among United States coal miners is increasing in mines of all sizes, while CWP and PMF are much more prevalent among workers from underground mines with fewer than 50 workers.

INTRODUCTION

Since 2000, pneumoconiosis among miners examined in the National Institute for Occupational Safety and Health (NIOSH)-administered Coal Workers' Health Surveillance Program (CWHSP) has increased markedly.¹ Additionally, recent findings suggest changes in the epidemiology and clinical features of pneumoconiosis among underground coal miners, characterised by an increase in severity and rapid disease progression.²⁻⁵ Excessive inhalation of coal dust is the only recognised cause of coal workers' pneumoconiosis (CWP), although multiple factors are likely responsible for the increased prevalence and severity. Hypothesised explanations include: over-exposure to silica dust, increased production and increasing hours worked.⁵ An additional risk factor may be employment size of the mine.

Data from the Mine Safety and Health Administration (MSHA) show that fatality rates of US miners are highest among workers in the smallest

What this paper adds

- ▶ There has been an increase in the occurrence and severity of coal workers' pneumoconiosis (CWP) and progressive massive fibrosis (PMF) in US coal miners since 2000.
- ▶ However, the factors driving these increases are not properly understood.
- ▶ This is the first study to directly examine underground miner respiratory health and mine size (as measured by the number of employed workers).
- ▶ CWP and PMF are significantly more prevalent among workers from underground mines with fewer than 50 workers compared to larger mines.

mines.⁶ Resources likely influence the mine size/fatality rate association. Smaller mining operations may have limited capital to upgrade safety equipment and dedicated safety and health personnel are less likely to be available to workers in smaller mines.⁷ Lack of resources may determine the effectiveness of dust monitoring and control, and thus have the potential to influence pneumoconiosis prevalence and severity.

To assess whether CWP prevalence and severity are associated with mine size, we examined chest radiographs from miners who participated in the NIOSH CWHSP for the presence of small and large opacities consistent with pneumoconiosis based upon the International Labour Organization (ILO) classification system.

METHODS

Data were derived from the CWHSP and the enhanced CWHSP (ECWHSP). Characteristics of the surveillance program, including data collection and historical perspectives, have been described elsewhere.⁸⁻¹⁰ In brief, all US underground coal miners are eligible for a chest radiograph prior to working underground, 3 years after the initiation of employment and then every 5 years thereafter. For the CWHSP, radiographs are obtained from NIOSH-approved health facilities. In 2006, NIOSH enhanced this program by collecting radiographs at or near mine sites with a mobile examination unit (ECWHSP). Additional information regarding this program including survey sites is publicly available.¹¹

The radiographs were classified by NIOSH certified readers for the presence, profusion and type of lung parenchymal abnormalities consistent with pneumoconiosis using the ILO Classification of Radiographs of Pneumoconioses.¹² A final determination of the classification of each radiograph was made using a standardised procedure, and required agreement between at least two NIOSH certified readers.⁸ For the present analysis, presence of CWP was defined as an ILO classification of 1/0 or greater for small pneumoconiotic opacities and/or progressive massive fibrosis (PMF). PMF was defined as the presence of any large opacity (category A, B or C).

Data were restricted to radiographs of underground coal miners acquired from 1 January 1970 to 15 May 2009. Complete information for mine location, employment size (ie, number of underground employees) and date of the radiograph was required for inclusion into the analytic dataset.

Approximately one third of miner participants contributed more than one radiograph over the 39-year study period. To account for within-miner correlation, we estimated prevalence ratios (PR) and 95% CIs using generalised estimating equations (GEE) employing a first order auto-regressive correlation structure. We adjusted all prevalence ratios in the GEE models for age at the time of radiograph acquisition.

RESULTS

A total of 145 512 miners were included in the analysis. Study participants were predominantly white (96.3%) and male (97.5%) with an overall mean age of 35.8 years (range 16.1–83.1). Mean and median miner age significantly increased over time with mean age in the 1970s being 33.7 years compared to 41.4 years in the 2000s. Mines with 50 or more employees tended to have a slightly older workforce compared to mines with fewer than 50 miners. From 1970 to 2009 a total of 240 067 radiographs were eligible for analysis. Of the 145 512 miner participants, 86 915 (59.7%) contributed one radiograph, 36 164 (24.9%) two radiographs, 13 915 (9.6%) three radiographs, 5148 (3.5%) four radiographs and the remaining 3370 (2.3%) five or more.

A classification of CWP was present for 11 753 radiographs (4.9%) and 653 radiographs had a final determination of PMF. Prevalence of CWP was 6.5% in the 1970s, 2.5% in the 1980s, 2.1% in the 1990s and 3.2% in the 2000s. Within-decade prevalence of CWP differed by mine size (figure 1). In every decade examined, the prevalence of CWP was lowest among miners who worked in mines with 500 or more employees. Linear regression demonstrated a modest association between mine size and CWP prevalence in the 1970s and 1980s but a significant trend in the 1990s and 2000s (top panel, figure 1). In the 1990s and 2000s, miners from mines with fewer than 50 employees had a higher prevalence of CWP compared to radiographs from miners who worked in mines with 50 or more employees ($p<0.0001$). When adjusted for age and within-miner correlation, the difference in prevalence of CWP by mine size was significant for all decades (figure 2, white circles).

Although a regional analysis at the state level was not possible due to small numbers in some states, an aggregated regional analysis was conducted to assess whether the mine size association with CWP varied by region. The mine size effect was similar across all regions. For example, the adjusted prevalence ratio (aPR) for the states of Kentucky, Maryland, Pennsylvania, West Virginia and Virginia for the 2000s was 2.9 (95% CI 1.7 to 4.7), compared to the overall United States aPR of 3.5 (95% CI 3.1 to 4.0).

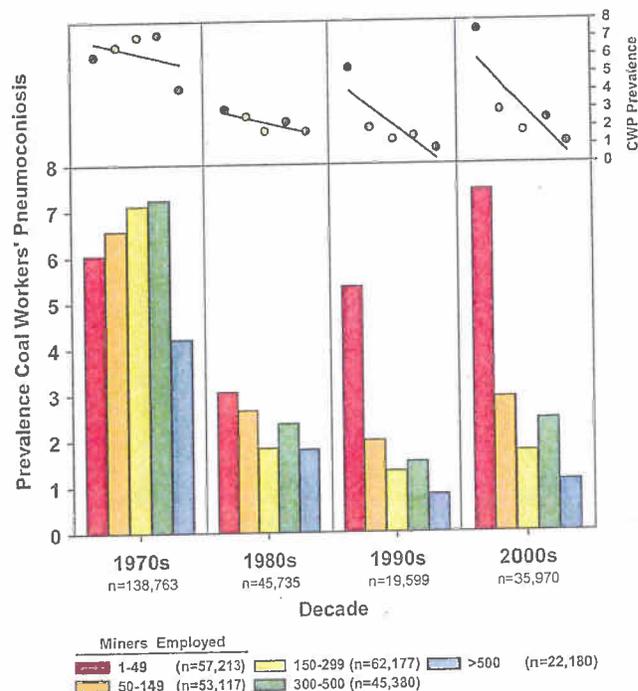


Figure 1 Coal workers' pneumoconiosis (CWP) prevalence by decade and mine size. Bars represent CWP prevalence among all radiographs. Totals (n) in the key are individual miners. Totals (n) on the x axis represent total number of radiographs by decade. Some miners contributed more than one radiograph. Top panel shows linear regression.

The 653 radiographs with PMF were contributed by 485 miners. The percentage of radiographs with a determination of PMF in the 1970s was 0.33%, 0.11% in the 1980s, 0.14% in the 1990s and 0.31% in the 2000s. In the 1970s and 1980s the prevalence of PMF was higher among miners in larger mines (figure 3). In the 1990s and 2000s PMF was more prevalent among miners working in mines with fewer than 50 workers ($p<0.0001$). When adjusted for miner age and accounting for within-miner correlation, miners from small mines were five times more likely to have radiographic evidence of PMF compared with miners from larger mines (figure 2, black circles).

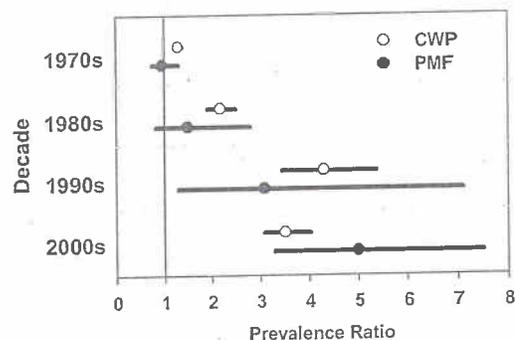


Figure 2 Coal workers' pneumoconiosis (CWP) and progressive massive fibrosis (PMF) prevalence ratios and 95% CIs for mines with fewer than 50 employees compared to mines with 50 or more employees in the United States (prevalence of CWP in small mines/prevalence CWP in larger mines). Generalised estimating equation models were used for calculation of values presented and adjusted for miner age at date of radiograph.

Short report

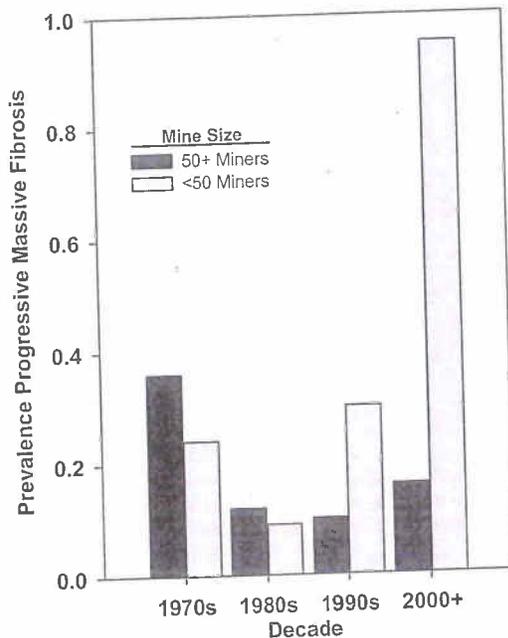


Figure 3 Prevalence of radiographs with progressive massive fibrosis in the National Institute for Occupational Safety and Health-administered Coal Workers' Health Surveillance Program by decade and mine size in US underground coal miners.

DISCUSSION

The increase in the occurrence and severity of CWP and PMF in United States coal miners since 2000 has been well documented. However, the factors driving these increases are not properly understood. We examined whether differences in prevalence existed between large and small mines. Our findings demonstrate increased prevalence and severity in mines of all sizes in the United States. However, CWP and PMF are more prevalent among workers from underground mines with fewer than 50 workers.

Previous reports have demonstrated that non-fatal disabling injuries and fatalities are more common in smaller mines.^{6 7 13–15} Why smaller mines have higher injury rates has not been thoroughly examined. One study suggested that smaller mines may have a younger, less experienced, workforce compared to larger mines.¹³ Our data confirm that mines with fewer than 50 employees have a younger workforce. This association was statistically significant for all decades examined; however, the actual mean age difference between small and large mines was relatively modest. In addition, the measure of effect was age-adjusted for the CWP/mine size comparisons. Therefore, we consider this finding to be robust, and discount age as an explanation for the results.

Geographical region is a surrogate for coal rank which is known to be associated with CWP. Had the small mines been concentrated in areas where the coal rank is higher, the findings might have been a reflection of confounding between mine size and coal rank. We were unable to undertake a complete analysis by geographical region (state) because of lack of sufficient data for some states. However, the findings we were able to derive showed the same pattern of findings across states for the CWP/mine size association. Overall, we do not believe that the small mine effect is due to confounding with coal rank or geographical region.

Other possible dust-related factors relate to excessive exposures to silica and mixed-mine dust. It may be that small mines

work thinner seams of coal, in which there is greater risk of silica exposure from cutting the mine roof or floor to gain adequate access. In part, this hypothesis is not supported because thin seam mines are primarily concentrated in Kentucky, Virginia and West Virginia; however, the small mine effect was evident in other states.

With respect to mixed-mine dust, the results from a sampling exercise undertaken in the 1990s by MSHA are informative.¹⁶ MSHA inspectors made unannounced visits to coal mines and sampled the airborne dust levels at the mine faces. These data were compared with operator-sampled dust levels which showed a decreasing trend in dust levels with decreasing mine size. In contrast, the unannounced operator samples showed an increasing trend in dust levels with decreasing mine size. While for large mines the inspector samples were less or about the same level as the operator samples, the inspector samples in small mines were about twice the level of those from operator samples. The findings of the MSHA study may provide an explanation for our results, as these data suggest that dust levels in small mines may be substantially higher than in larger mines. However, a limitation of this study is that consistent reliable information regarding the cumulative dust exposures for those with CWP and PMF was not available.

To our knowledge, this is the first study to directly examine miner respiratory health and mine size. There are distinct differences between large and small mines which potentially influence the amount and type of exposures experienced in these different environments. Our observation that miners working in smaller underground mines have a greater risk of CWP and PMF is a first step towards targeted prevention efforts. The next step is to systematically identify the factors most likely responsible for the increases in CWP and PMF in small mines through exposure assessments and observation of workforce practices.

Although the focus of this report has been on mine size, it is important to highlight that CWP and PMF prevalence increased between the 1990s and 2000s for mines of all sizes. The ultimate goal must be to return to and surpass the historic reductions in CWP prevalence seen in the 1980s and 1990s, regardless of mine size.

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Competing interests None.

Ethics approval This study was conducted with the approval of the National Institute for Occupational Safety and Health.

Provenance and peer review Not commissioned; externally peer reviewed.

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Pneumoconiosis among underground bituminous coal miners in the United States: is silicosis becoming more frequent?

A Scott Laney, Edward L Petsonk, Michael D Attfield

Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia, USA

Correspondence to

A Scott Laney, Surveillance Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, 1095 Willowdale Road, Mail Stop HG900.2, Morgantown, W V 26505-2888, USA; alaney@cdc.gov

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ABSTRACT

Objectives Epidemiological reports since 2000 have documented increased prevalence and rapid progression of pneumoconiosis among underground coal miners in the United States. To investigate a possible role of silica exposure in the increase, we examined chest x-rays (CXRs) for specific abnormalities (r-type small opacities) known to be associated with silicosis lung pathology.

Methods Underground coal miners are offered CXRs every 5 years. Abnormalities consistent with pneumoconiosis are recorded by National Institute for Occupational Safety and Health (NIOSH) B Readers using the International Labour Organization Classification of Radiographs of Pneumoconioses. CXRs from 1980 to 2008 of 90 973 participating miners were studied, focussing on reporting of r-type opacities (small rounded opacities 3–10 mm in diameter). Log binomial regression was used to calculate prevalence ratios adjusted for miner age and profusion category.

Results Among miners from Kentucky, Virginia and West Virginia, the proportion of radiographs showing r-type opacities increased during the 1990s (prevalence ratio (PR) 2.5; 95% CI 1.7 to 3.7) and after 1999 (PR 4.1; 95% CI 3.0 to 5.6), compared to the 1980s (adjusted for profusion category and miner age). The prevalence of progressive massive fibrosis in 2000–2008 was also elevated compared to the 1980s (PR 4.4; 95% CI 3.1 to 6.3) and 1990s (PR 3.8; 95% CI 2.1 to 6.8) in miners from Kentucky, Virginia and West Virginia.

Conclusions The increasing prevalence of pneumoconiosis over the past decade and the change in the epidemiology and disease profile documented in this and other recent studies imply that US coal miners are being exposed to excessive amounts of respirable crystalline silica.

INTRODUCTION

Underground coal miners are at risk of developing coal workers' pneumoconiosis (CWP), and to a lesser extent, silicosis, both being progressive and potentially fatal interstitial lung diseases.^{1 2} The prevalence of pneumoconiosis among working underground coal miners in the United States declined progressively from 1970 to 2000 as a result of federal restrictions on respirable dust concentrations in underground coal mines enacted in 1969.^{3–5} However, since 2000 the decreasing trend appears to have reversed and the prevalence of pneumoconiosis among examined miners with 15 or more years of coal-mining tenure has increased markedly.⁶ In addition to the increasing prevalence, recent reports suggest changes in the epidemiology and clinical features of pneumoconiosis among

What this paper adds

- ▶ Epidemiologic reports since 2000 have documented increased prevalence and rapid progression of pneumoconiosis among underground coal miners in the United States.
- ▶ This study found an increase in a specific type of radiographic abnormality that has been shown to be associated with silicosis lung pathology.
- ▶ The increasing prevalence of r-type opacities, and greater number of cases of severe disease found in this study within the Appalachian coal fields point to excessive exposures to crystalline silica, a long recognized cause of rapid disease progression and severe pneumoconiosis in coal miners.
- ▶ These findings stress the need for a timely, comprehensive, accurate, and ongoing evaluation of crystalline silica exposures and control strategies in underground coal mines throughout the United States.

underground coal miners, characterised by an increase in severity, geographical clustering, rapid disease progression and advanced disease in younger miners.^{7–9}

Since 1980, national mean exposure levels of respirable mixed coal mine dust reported for enforcement purposes have been consistently below federal permissible exposure limits and relatively unchanged on an annual basis. In the face of the established aetiological association of CWP with coal mine dust, and the reported stability in miners' exposures to respirable mine dust over the last three decades, we sought additional explanations for the current increasing disease trend and changing clinical pattern.

One potential explanation is that the toxicity of the dust generated during coal mining has changed, resulting in an increased inflammatory response and more potent induction of pneumoconiosis. An increased proportion of crystalline silica in coal mine dust provides a plausible explanation for an increase in dust toxicity.¹⁰ Some underground coal mining jobs are known to be associated with silica exposure, and the lungs of a minority of coal miners have been demonstrated to show typical pathological lesions of silicosis.^{2 10 11} Additionally, rapid progression⁹ and progressive massive fibrosis (PMF)^{10 12} are more likely with silicosis than with CWP.¹¹

To investigate the potential role of dusts containing free silica in the increasing prevalence and severity of dust-related lung disease in coal miners, we examined radiographs from underground coal miners for the presence of a specific type of abnormality that has been shown to be associated with silicosis lung pathology (rounded pneumoconiotic opacities exceeding 3 mm—r-type). Using data from miners who participated from 1980 to 2008 in the National Institute for Occupational Safety and Health (NIOSH)-administered Coal Workers' X-ray Surveillance Program (CWXSP), we report the time trends and geographical distribution of these radiographic abnormalities.

METHODS

Data were derived from the CWXSP. Characteristics of the surveillance program, including data collection, historical perspectives, institutional review board approval and patient consent, have been extensively described elsewhere.^{4 13 14} In brief, all US underground coal miners are eligible, and those that participate complete a standardised questionnaire documenting age, sex and employment history, and undergo a chest radiograph approximately every 5 years. The radiographs are classified by NIOSH B Readers for the presence, profusion and type of lung parenchymal abnormalities consistent with pneumoconiosis, according to the International Labour Organization Classification of Radiographs of Pneumoconioses (ILO Classification)¹⁵ and results are recorded in a standardised format.¹⁶ Under the ILO Classification, small pneumoconiotic opacities are scored as category 0 (absent) or categories 1, 2 or 3 profusion as the disease severity increases. In addition, the opacities are categorised by their shape and size (type) under the ILO Classification.¹⁵ Large opacities are similarly recorded as categories A, B and C. PMF was defined as the presence of any large opacity.

Data for the present analysis were restricted to radiographs of underground coal miners acquired from 1 January 1980 to 15 September 2008. For inclusion in the analytical dataset, an ILO Classification complying with NIOSH program procedures, as well as complete information regarding mine location, date of birth and date of the radiograph, were required. Because the CWXSP is an ongoing health surveillance program, many miners had multiple radiographic readings recorded over time. For the present analysis, data were restricted to the most recent classification of the most recent radiograph available for each individual.

The presence of r-type opacities on a miner's radiograph was determined from the primary and secondary shape and size of small pneumoconiotic opacities designated by the NIOSH B Reader on the standard Roentgenographic Interpretation Form.¹⁶ A radiograph was determined to show r-type opacities when the classification indicated r-type for either the primary or secondary opacity type. Mining tenure was not available for all miners, however a date of birth for each miner was provided. Sub-analyses indicated mining tenure was correlated with miner age. Prevalence ratios (PR) were adjusted for profusion category and median age using log binomial regression. The SAS statistical software package V9.1 (SAS Institute, Cary, North Carolina, USA) was used for all analyses.

In total, 31 different B Readers contributed 98% of the total readings from 1980 to 2008. However, different readers participated in the CWXSP for various time periods, with 14 readers participating in more than one decade and four reading for the full period of this investigation. To understand any time-dependent reader effects on the results, we examined the findings after grouping readers by the decade or decades during which they classified study radiographs.

RESULTS

Mining population

Classifications for 90 973 miners from 1980 to 2008 (any mining tenure) were included in the analysis. The majority were male (97%) and white (96%), and 50.7% were mining in Kentucky, Virginia or West Virginia at the time the radiograph was obtained. Of the 90 973 radiographs, 2868 (3.2%) had a profusion determination of ILO category 1 or greater. Median miner age (in years) at the time of the radiograph was 32.5 for 1980–1989 compared to 42.8 and 44.3 for the 1990–1999 and 2000–2008 time periods, respectively.

Radiographic small opacity profusion

Of the 2868 radiographs taken in 1980–2008 and showing ILO category 1 or greater small opacities, 85.7% showed category 1, 12.3% showed category 2 and 2.0% category 3. The distribution of small opacity profusion classifications for the study population is presented in table 1 by decade. The proportion of radiographs showing category 0 or 1 varied little over the study period. In contrast, since 2000 there has been a 28% increase in category 2, and a greater than twofold increase in category 3 classifications compared to 1980–1999 (prevalence ratio (PR) 2.4; 95% CI 1.4 to 4.0; Fisher $p=0.001$) (table 1).

When stratified by region, a marked increase over time in the proportion of small opacity profusion categories 2 and 3 is apparent among miners in Kentucky, Virginia and West Virginia, although not in the remainder of the United States (figure 1). Specifically, since 1999, radiographs showing opacity profusion categories 2 and 3 have become over twice as common compared to 1980–1999 (PR 2.3; 95% CI 1.8 to 2.9) in Kentucky, Virginia and West Virginia. In contrast, in the remainder of the USA, the proportion of radiographs with categories 2 and 3 opacity profusion appears to have decreased over time (PR 0.66; 95% CI 0.42 to 1.0).

Progressive massive fibrosis

The prevalence of PMF in the USA has increased since 1999 compared to 1980–1999 (PR 2.2; 95% CI 1.6 to 3.0; Fisher $p<0.0001$). However, similar to the trend observed for small opacity profusion category, outside of Kentucky, Virginia and West Virginia, PMF has declined in the last three decades (figure 2). The prevalence of PMF between the 1980s and 1990s did not significantly differ. However, in Kentucky, Virginia and West Virginia the prevalence of PMF in 2000–2008 was elevated compared to the 1980s (PR 4.4; 95% CI 3.1 to 6.3) and 1990s (PR 3.8; 95% CI 2.1 to 6.8).

r-Type opacities

r-Type opacities were noted as the primary shape/size for 201 radiographs, representing 0.22% of the total radiographs. A similar finding was observed for the secondary r-type opacities,

Table 1 Small opacity profusion and progressive massive fibrosis among participants in the NIOSH Coal Workers' X-ray Surveillance Program, 1980–2008

Year	Small opacity profusion category				Large opacity PMF
	0	1	2	3	
1980–1989 (n=46928)	45437 (96.8)	1303 (2.8)	168 (0.36)	20 (0.04)	68 (0.14)
1990–1999 (n=15564)	15100 (97.0)	402 (2.6)	55 (0.35)	7 (0.04)	21 (0.13)
2000–2008 (n=28481)	27568 (96.8)	754 (2.7)	130 (0.46)	29 (0.10)	91 (0.32)

Data are numbers (%). PMF includes category A, B and C opacities.

NIOSH, National Institute for Occupational Safety and Health; PMF, progressive massive fibrosis.

Original article

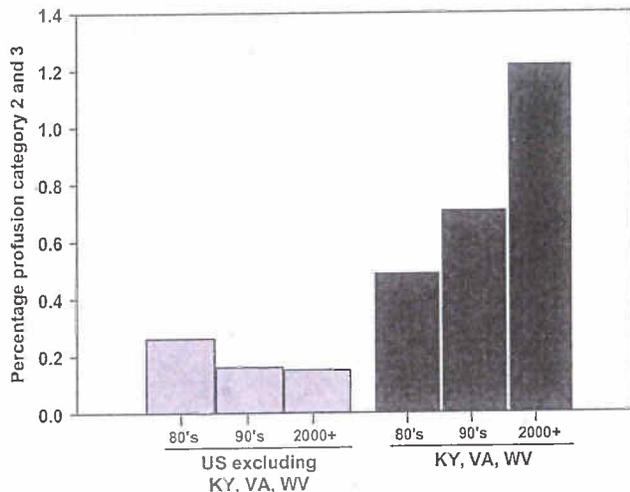


Figure 1 Pneumoconiosis small opacity category 2 and 3 by region and decade, 1980–2008.

which comprised 0.21% of the total radiographs. The 321 radiographs (0.35%) classified as showing r-type opacities (primary and/or secondary type) are the focus of the subsequent analyses.

The proportion of radiographs showing r-type opacities increased over time since 1980. Simple linear regression of the percentage of radiographs showing r-type opacities per year between 1980 and 2008 yielded a regression coefficient of 0.02 and p value of <0.0001. For the United States overall, there has been a 3.7-fold increase in r-type opacities among miners with radiographs taken after 1999, compared to 1980–1989 (PR 3.7; 95% CI 2.8 to 4.7), and a twofold increase compared to 1990–1999 (PR 2.0; 95% CI 1.5 to 2.7).

When stratified by region, the overall national increase observed in r-type opacities is diminished when data from Kentucky, Virginia and West Virginia are excluded. This suggests that a substantial portion of the effect observed at the national level is driven by the regional contribution of Kentucky, Virginia and West Virginia. In fact, for the three-state region, there has

been a 7.6-fold increase (95% CI 5.5 to 10.2) in the proportion of r-type opacities observed in 2000–2008 compared to the 1980s (figure 3). We found no statistical difference among any other specific opacity type (p, q, s, t, u) over time.

Adjustment for small opacity profusion and reader

It may be that the likelihood of reporting r-type opacities increases with increasing small opacity profusion category, independent of the presence of silicosis. When all the study radiographs were analysed together, increasing small opacity profusion category was associated with progressively greater percentage of the radiographs showing r-type opacities (table 2). However, increasing profusion over time in the three-state region does not fully account for the overall increase observed in r-type opacities. Since 1999, the proportion of r-type opacities increased within every profusion category among all participating US coal miners (table 2).

In fact, r-type opacities increased significantly over time, even accounting for the effect of profusion category and region. Overall, the proportion of radiographs showing r-type opacities increased nearly twofold in the 1990s (PR 1.7; 95% CI 1.2 to 2.3) and threefold after 1999 (PR 3.1; 95% CI 2.4 to 4.1), compared to the 1980s, after adjusting for profusion category and miner age (table 3). A significant increase was observed in the proportion of r-type opacities between the 1980s and 1990s and between the 1990s and 2000–2008 in Kentucky, Virginia and West Virginia (table 3). Since 1999, a greater than 1.5-fold increase has occurred both regionally and nationally (table 3).

An apparent increase in reporting of r-type opacities could have arisen because different readers were employed over time in the CWXSP. If the readers employed at different times differed systematically in their predilections for reporting r-type opacities, it could have given rise to an artifactual temporal increase. This was explored by analysing the data by groups of readers corresponding to the decade or decades during which they read for the CWXSP. Importantly, the overall observed trend was evident in the sub-group of readers who read during all three decades. Here the PRs were 2.1 for the 1990s to 2000–2008 and 3.6 for 1980s to 2000–2008, virtually identical to those reported earlier of 2.2 and 3.7 for the whole dataset.

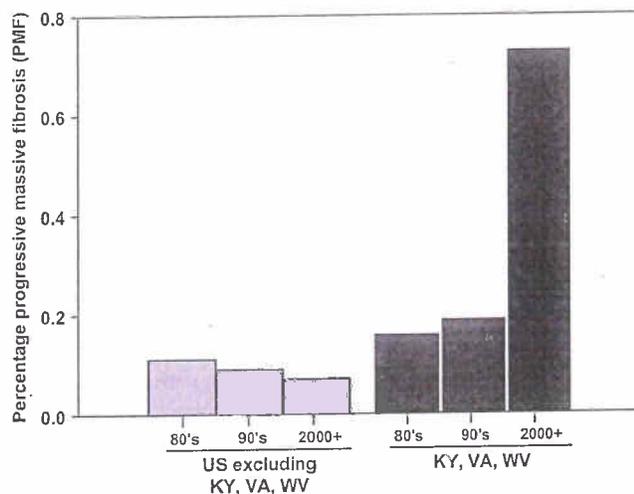


Figure 2 Progressive massive fibrosis by region and decade, 1980–2008.

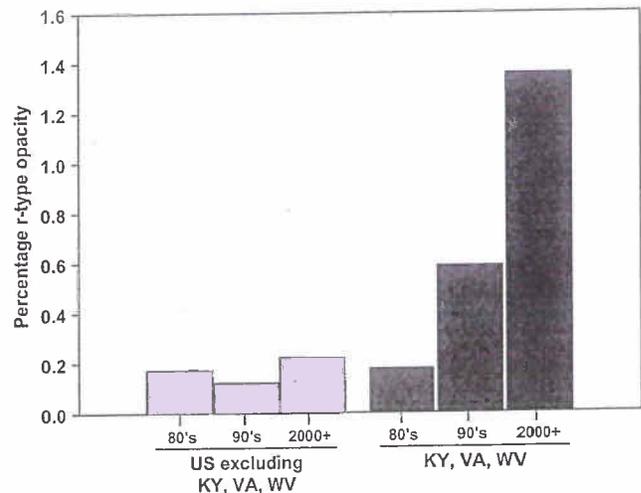


Figure 3 Percentage of r-type opacities by region and decade, 1980–2008.

Table 2 Prevalence of r-type opacities among participants in the NIOSH Coal Workers' X-ray Surveillance Program by small opacity profusion category, 1980–2008, any tenure

Year	Small opacity profusion category		
	0	1	2 or 3
1980–1989	0.02% (8/45444)	3.5% (45/1303)	16.5% (31/188)
1990–1999	0.02% (3/15106)	7.2% (29/403)	30.6% (19/62)
2000–2008	0.08% (23/27493)	12.4% (95/765)	43.0% (68/158)

Category 0 includes borderline abnormality (ie, 0/1).
NIOSH, National Institute for Occupational Safety and Health.

DISCUSSION

The prevalence of r-type pneumoconiotic opacities on the radiographs of US underground coal miners has increased markedly since 1999. This is most apparent among miners in Kentucky, Virginia and West Virginia. This finding is not explained by any changes in the readers employed over time, nor by the concurrent reported increase in pneumoconiosis severity.

Miners with r-type opacities often demonstrate classical silicotic nodules on lung pathology,¹ and autopsy studies have shown that the lungs of coal workers with r-type opacities contain the highest levels of non-combustible ash consistent with silica.^{17–18} Because the latency for pneumoconiosis is generally 10 or more years after the onset of exposure, the study results suggest a marked increase in the exposure of coal miners to respirable silica during the last 30–40 years.

Based upon the data available, we were unable to establish a specific exposure mechanism to account for our observations. However, over the last four decades there have been changes in coal demand, accessibility and mining technology that could potentially explain increasing respirable silica exposure in coal mines. US coal consumption has increased 62% since 1980, reaching 1129 million short tons consumed in 2007.¹⁹ The continuous rise in the demand for coal, coupled with increasingly productive mining equipment, has led to the depletion of the largest, most easily accessible North American underground coal seams.²⁰ These factors, and the increasing price of energy sources, have made mining thinner seams of coal more economically feasible. US thin seam coal mines (less than 43 inches) are almost exclusively located in the Appalachian bituminous coal fields. In fact, 96% of US thin seam mines are located in Kentucky, Virginia and West Virginia.²¹

Crystalline silica is commonly found in the rock strata surrounding coal seams, in concentrations much higher than within the coal seam itself.²² The risk of breaching the coal/rock interface is greater in thin coal seams and is likely associated with greater waste rock mined. However, from the economic perspective, the increased mining of waste rock has been offset by improved coal cleaning technologies, allowing

Table 3 Prevalence ratios and 95% CIs of r-type opacities among participants in the NIOSH Coal Workers' X-Ray Surveillance program, 1980–2008, any tenure

	Prevalence ratios and 95% CI		
	1990s vs 1980s	2000+ vs 1990s	2000+ vs 1980s
USA except Kentucky, Virginia, West Virginia	1.0 (0.49 to 1.8)	1.6 (0.86 to 3.0)	1.5 (1.0 to 2.4)
Kentucky, Virginia, West Virginia	2.5 (1.7 to 3.7)	1.6 (1.2 to 2.2)	4.1 (3.0 to 5.6)
All USA	1.9 (1.3 to 2.7)	1.7 (1.2 to 2.3)	3.1 (2.4 to 4.1)

Log binomial regression was used for miner age and small opacity profusion adjustments. Prevalence ratios were calculated separately for each region. Models were of the form: r-type opacity = $\alpha + \beta_1(1990s) + \beta_2(2000+) + \beta_3(\text{Profusion category } 0) + \beta_4(\text{Profusion category } 1) + \beta_5(\text{Profusion category } 2) + \beta_6(\text{Age})$.

for more cost-efficient removal of non-combustible by-products (particularly siliceous rock) in lower quality run-of-the-mine coal. The trends in mining practices and the geographical location of thin seam mining provide a plausible explanation for an increasing exposure to silica dust implied by the results of this study.

To explain the study findings, we would anticipate that the mean exposure to respirable silica would have increased since 1980. Paradoxically, the mean levels of respirable crystalline silica reported for compliance purposes do not demonstrate an increasing trend over that time.⁶ However, the compliance method for controlling silica exposure in coal mining has been criticised.^{23–24} Instead of monitoring silica levels directly and ensuring enforcement on that basis, the procedure is indirect and complicated, involving a reduction in the overall coal mine dust compliance standard depending on past measurements of the quartz percentage. This has been said to result in inadequate enforcement.^{23–24} Others have criticised the enforcement approach for coal mine dust, upon which the current silica compliance approach is based.^{25–28} Currently, NIOSH recommends that exposure to respirable quartz dust be limited to 0.05 mg/m³, measured and enforced directly during the work shift.

This study has focused specifically on silica exposure and its possible role in the increase in extent and severity of pneumoconiosis in the USA and selected states. However, other factors, such as increased production (implying an increase in general coal mine dust exposures) and increasing hours worked, may have contributed to the observed increases in disease. However, it does seem likely that the previous reports of geographical clustering of rapidly progressing CWP in younger miners,^{7–9} the increasing prevalence of r-type opacities, and the greater number of cases of severe disease found in this study within the Appalachian coal fields point to excessive exposures to crystalline silica, a long recognised cause of rapid disease progression¹¹ and severe pneumoconiosis in coal miners.^{10–12} Taken together, these findings stress the need for a timely, comprehensive, accurate and ongoing evaluation of crystalline silica exposures and control strategies in underground coal mines throughout the United States.

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The OEM Blog

We are pleased to announce the initiation of the Occupational & Environmental Medicine blog, available at <http://blogs.bmj.com/oem/>. The OEM blog is edited by Dr. Leslie Elliott. It's our hope that the blog will serve the occupational and environmental health community as a forum for discussion and debate of current issues in the field. We welcome a wide range of relevant contributions, including comments on articles published in the Journal, discussion of developments of interest to researchers and practitioners, novel observations and ideas for research, news, and announcements. Contributions to the OEM blog are not peer reviewed, but are screened for relevance and appropriateness and may be edited before posting. As with other correspondence with the Journal, we reserve the right to decline contributions, and we cannot publish material that is offensive, libelous or illegal. As this is a new medium for OEM, we expect that the blog will develop in its own way as the community begins to use it.

Dana Loomis
Leslie Elliott

What Component of Coal Causes Coal Workers' Pneumoconiosis?

Robert J. McCunney, MD, MPH
Peter Morfeld, PhD
Stephen Payne, BS

Objective: To evaluate the component of coal responsible for coal workers' pneumoconiosis (CWP). **Methods:** A literature search of PubMed was conducted to address studies that have evaluated the risk of CWP based on the components of coal. **Results:** The risk of CWP (CWP) depends on the concentration and duration of exposure to coal dust. Epidemiology studies have shown inverse links between CWP and quartz content. Coal from the USA and Germany has demonstrated links between iron content and CWP; these same studies indicate virtually no role for quartz. *In vitro* studies indicate strong mechanistic links between iron content in coal and reactive oxygen species, which play a major role in the inflammatory response associated with CWP. **Conclusions:** The active agent within coal appears to be iron, not quartz. By identifying components of coal before mining activities, the risk of developing CWP may be reduced. (J Occup Environ Med. 2009;51:462-471)

The growing world economy will increase demand for energy on the order of a 100% by 2050, with coal combustion playing a major role, in particular in Asia and Africa.¹ This trend has already challenged occupational medicine in economically developing countries for many years.^{2,3} The extraction, transportation and use of coal, however, carry certain risks, most notably of injury in the extraction of coal and illness in the form of coal workers' pneumoconiosis (CWP), among those who extract the coal.⁴ Over many years of research, epidemiological studies have shown that decreasing dust exposure will lead to decreased risks of CWP.⁵⁻⁸ Questions remain, however, as to the active agent responsible for causing lung disease due to inhalation of coal. At this point, it is unclear as to the precise component(s) of coal that leads to this potentially disabling illness, although for many years quartz was considered the active agent.

Regulations for occupational exposure to coal have often focused on quartz content.⁹ Epidemiological studies, however, are conflicting about the level of quartz in coal in terms of its potential to cause pneumoconiosis. In fact, "dust dose and composition (of quartz) do not appear to account wholly for changes in the prevalence of CWP."¹⁰

The purpose of this report is to assess the scientific literature related to studies that have investigated the active agent(s) within coal responsible for causing CWP. By understanding such risks, preventive efforts can be improved.

From the Department of Biological Engineering (Dr McCunney, Mr Payne), Massachusetts Institute of Technology, Cambridge, Mass; Institute for Occupational Epidemiology and Risk Assessment (Dr Morfeld), Evonik Industries, Essen; and Institute for Occupational Medicine (Dr Morfeld), Cologne University, North Rhine—Westphalia, Germany.

There are no conflicts of interest.

Address correspondence to: Robert J. McCunney, MD, MPH, MS, Department of Biological Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Room 16-771, Cambridge, MA 02139; E-mail: mccunney@mit.edu.

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Methods

To address the fundamental question as to the active agent within coal, an updated literature search was conducted through PubMed, a national search mechanism of the National Library of Medicine. References to other reports in the articles thus identified were examined in an effort to supplement the initial search.

Results

Coal Workers' Pneumoconiosis

CWP, which was originally thought to be a variant of silicosis, results from the inhalation of coal mine dust that usually contains relatively small amounts of free crystalline silica (quartz).^{11,12} This potentially disabling lung disease results from exposure to coal mine dust and its deposition in the lungs; the dust and resultant inflammatory reactions lead to the formation of coal macules and in some cases, coal nodules and progressive massive fibrosis (PMF).

People with CWP can experience symptoms such as cough and shortness of breath on exertion. The diagnosis is usually made based on a chest film; however, more recent diagnostic studies such as chest tomography can aid in the assessment of this disease. Treatment is usually symptomatic once the person is removed from exposure. Risk factors are primarily related to coal dust concentration, although genetics.¹³⁻¹⁶ and the characteristics of the coal mined (ie, rank and iron content) play a role.¹⁷

Numerous epidemiological studies in a variety of countries have consistently shown that the development of CWP is related to exposure to respirable mixed coalmine dust. Coal rank (age and hardness of the coal) has also been found to play a role because the risk of CWP increases with the carbon content of the coal. Quartz (silica) was found to be a minor contributor to CWP.^{18,19} The "main environmental factor involved in the development of simple CWP is

mixed coal dust exposure. Coal rank, age, and quartz exposure and dust residence time probably also play a role, although these effects appear to have secondary importance unless the silica levels are high."¹⁹

CWP is usually diagnosed based on findings on a chest film, in the context of occupational exposure to coal mine dust. Chronic interstitial fibrosis can develop. The degree of CWP (main parameters: profusion of small opacities and occurrence of large opacities) is assessed by using the International Classification of Radiographs.²⁰ If only small opacities (diameter <2 cm) are detected, CWP is called simple (coal workers' simple pneumoconiosis [CWSP]). Pathological findings usually consist of nodules, but CWSP can also result in mixed nodular and irregular opacities. A chest film with mostly irregular opacities in a coal miner, however, should raise concern about exposures to other occupational hazards, such as asbestos.

The differential diagnosis of CWP includes other diseases that can produce acute nodular lesions, such as miliary tuberculosis and viral pneumonia, as well as conditions that result in chronic nodular patterns, such as metastatic disease and tuberculosis. Silicosis can present with similar radiographic patterns as CWP, which can only usually be differentiated by occupational history or tissue examination. The characteristic pathological lesion of CWP, however, is distinct from silicosis. The primary lesion of CWP is the coal macule, which occurs specifically among workers who have been exposed to coal mine dust. This lesion has been defined by the Pneumoconiosis Committee of the College of American Pathologists as follows: "The focal collection of coal dust laden macrophages, at the division of the respiratory bronchioles that may exist within alveoli and extend into the peribronchiolar interstitium with associated reticular deposits and focal emphysema."²¹ The coal macule can be similar in appear-

ance to macules found in urban dwellers and smokers, but coal macules tend to be more profuse; macules range in size from 1 to 5 mm. Macules may be rounded, irregular or stellate. Because the macule can be associated with other occupational and environmental exposures, the nature of the dust particle should be identified. Bituminous and anthracite coal can usually be identified through light microscopy of lung tissue.

PMF is a more severe form of CWP, which can also occur secondary to coal exposure. This condition is defined based on the diameter of the lung lesions. For example, macules with a minimal diameter of 2 cm are necessary for the diagnosis of PMF. These PMF-related lesions can be unilateral or bilateral. However, there are discussions whether PMF should be considered a different disease entity with a different mechanistic background than CWSP.²² Coal miners may also show signs of silicotic nodules that can arise from free silica exposure, which is often a reflection of siliceous rock in the vicinity of coal seams. These nodules, which tend to be incidental in association with coal macules, include collagen fibers around a hyalinized center. Despite the potential for a significant percentage of quartz in coalmine dust and its potential for accumulation in the lungs, no excess mortality from lung cancer in coal miners has been noted.²³

Coal has been described as "able to mask the fibrogenic activity of quartz" and that there are "distinct pathological differences between simple pneumoconiosis of CWP and silicosis."¹¹

Mechanism. The manner in which coal dust induces pulmonary disease has been investigated by in vitro evaluations and appears to be based on inflammatory mechanisms, most notably by formation of reactive oxygen species. According to some authors, the following mechanism of initiation and progression of CWP occurs in coal miners: coal dust stimulates the production of reactive ox-

xygen species, which not only cause lung injury, but can also activate transcription factors, such as nuclear factor, kappa-B, and activator Protein 1, which induce messenger RNA to produce of a host of chemokines, inflammatory cytokines, and growth factors associated with the formation of lung lesions and fibrosis.²⁴

Castranova and Valyathan¹² have proposed that the development and progression of CWP and PMF as well as silicosis occur with four fundamental molecular mechanisms:

1. Coal dust or silica react with epithelial and macrophage cells, resulting in the per oxidation of membrane lipids. This process damages the cell membrane, leading to the release of intracellular enzymes. These enzymes scar, or even destroy, the alveolar septa of the lung tissue.
2. Alveolar macrophages or alveolar epithelial cells interact with dust particles, resulting in the secretion of fibrogenic factors that induce fibroblast proliferation or collagen synthesis, causing fibrosis.
3. The interaction of dust particles with alveolar macrophages or alveolar epithelial cells stimulates the secretion of inflammatory chemokines and cytokines, leading to the displacement of macrophages and polymorphonuclear leukocytes from the pulmonary capillaries to the air spaces. These mediators can also activate pulmonary phagocytic production of oxidant species, which causes damage to lung tissue.
4. Coal dust or silica that becomes engulfed by alveolar macrophages can lead to the generation of reactive oxidant species, which overwhelms antioxidant defenses, resulting in lipid per oxidation and lung scarring.

Clinical Care. Shortness of breath is usually the symptom that most often prompts an evaluation for CWP. The shortness of breath can be evaluated based on standard questions of the American Thoracic Society²⁵

with the physical examination focusing on the lung fields. Initial laboratory studies include spirometry and a chest film. Clinical care of coal miners with lung impairment is similar to other patients with interstitial lung disease.

Prevention. The major means of controlling CWP is through reduction in exposure to coal dust. The occupational exposure to coal is 2 mg/m³ (and 0.1 mg/m³ for coal dust containing greater than 5% quartz).⁹ These levels were established to limit the progression of simple CWP to PMF. Recommendations for prevention of CWP have been proposed by the National Institute for Occupational Safety and Health.²⁶

In light of the continued hazards of exposure to coal dust, despite dust reduction methods, increased attention has focused on the role of prevention. It is important to note, however, that much of these measures are aimed at limiting (not preventing) simple CWP and PMF. A World Health Organization study group also made recommendations for prevention, which focused on dust control.²⁷

Other approaches used modeling of CWSP data to estimate threshold values for developing profusion category 1/1²⁰ while applying dosimetric models to take latency and internal dose accumulation into account.²⁸ A long-term limit for respirable coal mine dust of 1.5 mg/m³ to 6 mg/m³ was derived by this procedure. The range reflects uncertainties of data and model assumptions. This kind of approach was preferred by the German MAK committee to identify threshold limit values for coal mine dust. However, the committee did not recommend a limit value because of the suspicion that coal mine dust exposure may be linked to stomach cancer risk in coal miners.²⁹

Silicosis

In light of the potential role of quartz in CWP, a review of silicosis is appropriate. Silicosis refers to pulmonary diseases that can occur secondary to inhalation of various types

of free crystalline silica and silica-dioxide. Workers at risk of silicosis include sand blasters, miners, millers, pottery workers, glassmakers, foundry workers, and people who work in quarries or with abrasives. Pathological features associated with silicosis have been described by a special committee of the National Institute for Occupational Safety and Health.³⁰ The earliest parenchymal lesion in silicosis is a collection of dust-laden macrophages. Eventually, these lesions may become organized and lead to the silicotic nodule, which is the pathological hallmark of silicosis. The key pathological event in the onset of silicosis is the interaction between the silica particle and the alveolar macrophage and the resulting inflammatory process.

Chronic silicosis results from low to moderate exposure to silica dust for 20 years or more. Patients may experience cough and shortness of breath and have a predisposition to tuberculosis, as well as PMF, which can cause respiratory impairment.

The characteristic radiographic appearance of silicosis is rounded opacities that range in size from 1 to 10 mm. When these nodules coalesce into a larger mass, the diagnosis of PMF can be made. In approximately 10% of the cases, the hilar lymph nodes can calcify and produce the so-called eggshell calcification pattern, a condition can also occur in Hodgkin's disease, scleroderma and histoplasmosis. The presence of eggshell calcification, along with nodular parenchymal opacities, in light of exposure to silica, reinforces the diagnosis of silicosis.

Epidemiology of CWP and Findings From Animal Experiments

The active agent in coal responsible for CWP has attracted scientific inquiry for many years. Attention initially focused on quartz, a well known fibrogenic agent, as the component of respirable coalmine dust responsible for causing CWP. In two

of the earliest reports to address the role of quartz in CWP, a poor correlation was noted between radiological evidence of CWP and quartz concentration in the corresponding coal dusts.^{31,32} No pattern was noted between the quartz content of mixed dust and the probability of developing simple pneumoconiosis at quartz levels, averaging 5%.³² A case-control study reaffirmed the absence of an effect of quartz in causing CWP.³³

Studies in British coal mines showed that the risk of developing simple pneumoconiosis (ILO 2/1 categories) was primarily dependent on the mean concentration of dust and the duration of exposure. One colliery with high quartz content, had a prevalence of CWP 1/5th that of predicted, whereas another colliery with low quartz content had almost twice the prevalence of CWP.³⁴ The results of the British coal miners led critical observers to question the role of quartz in coal on the risk of CWP. For example, British collieries with low progression of simple CWP to PMF had the highest quartz concentration, whereas workers with a high progression of CWP to PMF had worked with coal that had the lowest quartz concentration.³⁵ In an analysis of 2600 British coal miners, a clear impact of coalmine dust exposure but no influence of quartz dust exposure was found.³⁴ The role of quartz in causing CWP to progress to PMF was evaluated in additional British studies. Coal mine dust exposure and degree of CWSP were clearly linked with PMF, but no definite effect of quartz could be identified.³⁶⁻³⁸

Studies in other countries have also noted inverse links between risk of CWP and quartz concentrations in coal. Epidemiological studies from Germany, for example, indicated that the risk of CWP varied from 2% to 40%, although the miners had comparable levels of dust exposure.³⁹ In these studies, differences in the mineral content of respirable dust, such as quartz, did not explain the wide

range of the risk of developing CWP; moreover, it was clear that the hazard of CWP was not affected by quartz content. In fact, as in the British studies noted above, a lower prevalence of pneumoconiosis was noted in German coalmines with higher concentrations of quartz. Similar observations have been made among French miners.⁴⁰ In studies of Welsh miners, the quartz content averaged 2.8% of total lung dust with a range of 0.5% to 10.5%; the highest levels of quartz did not lead to silicotic responses.⁴¹ "Further evidence against the quartz hypothesis (as a cause of CWP) came from cases of massive fibrosis indistinguishable pathologically from the changes in coal workers who have been exposed to purified carbon, and from whose lungs quartz was only isolated in traces." These studies led one author to conclude: "This component of the dust (quartz) does not play a specific or overriding role in the genesis of massive fibrosis in CWP."¹⁰

In a summary of animal studies conducted at the time of the preparation of his report in 1988, Heppleston noted that "inhaled mixtures of anthracite and quartz in proportions ranging from 5% to 40% led to distinct fibrosis, (assessed histological and biochemically) only when the quartz level reached 20% and became severe at 40%."⁴² In other animal studies, a fibrogenic role for quartz at concentrations noted in coal mine dust was not apparent. A working group of the German MAK committee (threshold limit value committee) summarized rat experiments with coal mine dust; experiments showed far lower fibrogenic risks than expected from the experiments with pure quartz of the same mass concentration; there was almost no correlation of fibrogenicity indices with varying quartz contents of coal mine dusts; the high variability of coal mine dust fibrogenicity suggest unidentified factors different from quartz.⁴³

Heppleston concluded that "dust concentration and duration of expo-

sure remain the major determinants of disease prevalence in coal workers, but within the overall pattern exist anomalies that require explanation. Continued emphasis on the role of quartz is evident at all levels of inquiry, but without emergence of a consensus. The proportion of quartz in respirable coalmine dust varies considerably among British and German collieries."¹⁰ "A specific role for quartz inhaled at the customarily low levels by coal workers' is difficult to sustain and sometimes can be excluded."¹⁰

In a study of coal miners exposed to unusually high concentrations of quartz at one specific mine (about 10% quartz in coalmine dust), high CWP rates were attributed to a misdiagnosis of silicosis.⁴⁴ The authors suggested that the rapid progression in radiological abnormalities, their relationship with quartz exposure estimates, and the strength of their relationship with lung function resembled classical silicosis rather than CWP.⁴⁴ Thus, the notion that the progression of CWP to PMF is caused by high concentrations of quartz in coal may be the result of a misdiagnosis of silicosis. Similar findings were reported in a case-control study with British coal miners: an effect of quartz on rapid CWSP-progression was noted when exposure to quartz was unusually high.⁴⁵

Subsequent to an IARC working group meeting that classified crystalline silica (quartz) as an IARC group I carcinogen,²³ a review attempted to shed light on the divergent results of lung cancer incidence in industries in which quartz exposure can occur.⁴⁶ The authors noted that the deposition of quartz in the lungs leading to silicosis was critically dependant on the surface reactivity of the crystalline silica. They proposed that the hazard posed by quartz is not a constant entity, but one that may vary dramatically depending on the origin of the silica sample or its contact with other chemicals and minerals within its complex constitution. Ac-

According to their review, the risk of quartz exposure from coal is subject to considerable variation. In pointing out some of the epidemiological results of risks of CWP associated with different types of coal, the authors described a German study: although miners had comparable levels of exposure to coal, neither mineral content nor percentage of quartz accounted for differences in rates of CWP; in fact, a low prevalence of simple CWP occurred in collieries with high gravimetric concentrations of quartz. Similar findings were made in France.⁴⁶ In an American study, higher ranked coals were more fibrogenic. "The slope of the dose-response curve between cumulative exposure to coal and incidence of CWP (response) is different despite similar quartz content."⁵

To address some of these uncertainties, a variety of investigations have assessed quartz content, biological activity of the coal dust, and incidence of CWP. Some authors have noted that "quartz can be relatively easily modified in its ability to cause biological effects."⁴⁶ They also pointed out that "modification of the surface (quartz) could occur when substances such as iron or aluminum are present." They referred to studies in which clear differences in the slope of the dose-response curve relating incidence of CWP to years

of exposure in groups of miners can be profoundly different—despite minor differences in quartz content of the coal to which the miners were exposed.

In a review of mechanisms and mediators of coal dust-induced lung disease, inhaled coal dust particles were described as sources of reactive oxygen species in the lungs.⁴⁷

The Role of Coal Rank in Causing CWP

In addition to quartz, the "coal rank" (based primarily on the carbon content of the coal) has long been recognized as associated with risk of CWP. Coal rank is defined by the U.S. Department of Energy as "the classification of coals according to their degree of progressive alteration from lignite. In the United States, the standard ranks of coal include lignite, sub bituminous coal, bituminous coal, and anthracite are based on fixed carbon, volatile matter, heating value, and agglomerating (or caking) properties" (<http://www.eia.doe.gov/cneaf/coal/page/gloss.html>). Coal rank is linked to the stratigraphic horizon of coal deposits: the older the horizon, the higher the carbon content and the lower the quartz content.¹⁷

Several studies have focused on the effect of coal rank on CWP.^{5,48,49} Due to the wide range of coal types

naturally present in the United States, the nation is a desirable study subject for extrapolating a relationship between the rank of coal mines and the pneumoconiosis rates of coal workers. Table 1 illustrates the trend relating coal rank and the prevalence of pneumoconiosis as obtained from data collected between 1969 and 1971 as part of the U.S. National Study of CWP.⁵ The table notes the strong correlation between exposure to higher ranked coal and a higher prevalence of pneumoconiosis. The prevalence of pneumoconiosis spans an order of magnitude from anthracite to low volatile coal.

From these data, Attfield⁵ formulated graphs relating cumulative dust exposure to CWP and PMF (Fig. 1A–C). Such graphs demonstrate the correlation between cumulative dust exposure and pneumoconiosis. Perhaps, the most significant finding, however, is the highly influential effect of the rank of coal on the prevalence of pneumoconiosis. An approximate 6- to 10-fold increase in pneumoconiosis rates occurred for anthracite (~93% carbon) workers when compared with high volatile bituminous coal (generally <80% carbon) workers of the Western and Midwestern United States. These data demonstrate a gradual decrease in pneumoconiosis rates corresponding to decreases in coal rank. Anthra-

TABLE 1

Summary of the Distribution of the Rank of Coal Mined in the Particular Mines Which Participated in the NSCWP and the Corresponding Pneumoconiosis Rates Among the Workers in Those Mines

Variable	Coal Rank Region					All Coal Rank Regions
	Anthracite	Medium/Low Volatile	High Volatile "A"	High Volatile Midwest	High Volatile West	
Number of observations	521	1362	4934	1225	981	9023
Age (yr)	52 (9)	43 (11)	44 (13)	44 (12)	44 (13)	44 (12)
Tenure underground (yr)	29 (12)	20 (13)	18 (13)	21 (13)	19 (14)	21 (13)
Estimated dust concentration (mg/m ³)	3.2 (0.7)	3.1 (1.0)	3.0 (0.9)	3.0 (1.0)	2.8 (1.1)	3.0 (1.0)
Estimated dust exposure (g-hr/m ³)	158 (70)	109 (76)	98 (81)	113 (81)	101 (83)	112 (81)
Overall prevalence of category 1 or greater (%)	41	21	9	5	4	12
Overall prevalence of category 2 or greater (%)	24	10	3	1	1	5
Overall prevalence of PMF (%)	14.2	4.6	1.0	0.5	0.4	2.1

Adapted from *Am Ind Hyg Assoc J.* 1992;53:486–449.

Estimated Dust Exposure (g-hr/m³)

Fig. 1. A, The dose-response relationship between the prevalence of CWP category 1 or greater to the estimated dust exposure levels for various coal ranks. B, The dose-response relationship between the prevalence of CWP category 2 or greater to the estimated dust exposure levels for various coal ranks. C, The dose-response relationship between the prevalence of PMF to the estimated dust exposure levels for various coal ranks. Adapted from *Am Ind Hyg Assoc J.* 1992;53:486–449.

centrations in the lungs of autopsied anthracite miners than in the lungs of autopsied lower ranked coal miners.⁵⁶ Lastly, it has also been suggested that the larger relative surface area among higher ranked coals may cause greater irritation to lung tissue.⁵⁷ Some combinations of the above characteristics of higher ranked coal likely contribute to the varying prevalence of CWP among miners.

A Role for Iron in Causing CWP?

After Heppleston's report in 1988, Ghio and Quigley⁵⁸ addressed the role of iron in CWP. After noting that the characteristics of coal dust responsible for CWP are not known, they pointed out that certain types of transition metals, such as iron, tend to be concentrated in the lungs of miners with CWP. "The accumulation of iron could result in part from its coordination by humic-like substances (HLS), which comprise up to 30% of dust weight in certain coals."⁵⁸ They suggested that HLS in coal dust with iron clad-ions which subsequently catalyze oxidant generation and the accumulation of this metal in the lungs. They noted the accumulation of iron in the tissue of CWP.

Ghio and Quigley⁵⁸ also pointed out that differences in mineral content of coals, including quartz, do not account for the variation in the onset of pneumoconiosis. The relevance of iron coordination by HLS in lung injury after exposure to coal dust can assist in the understanding of certain clinical features of CWP. Occurrence of massive fibrosis after inhalation of coal dust can occur without quartz in the lungs. They concluded: "it is likely that ionizable and chelatable iron in the dust and the consequent capacity to catalyze oxidant production approximate the toxic effects of coal."⁵⁸

To address the hypothesis that different levels of bioavailable iron (BAI) in coal account for regional

differences in both the prevalence and severity of CWP, coal samples in Utah, West Virginia, and Pennsylvania were analyzed; these areas had a prevalence of CWP of 4%, 10%, and 26%, respectively.⁵⁹ The results suggested that BAI in West Virginia and Utah Coal is the main metal species that induced ferritin and lipid peroxidation. The authors claimed that their results provided further evidence that "metals, particularly iron, play important roles in coal dust induced cellular damage ultimately leading to the development of CWP and contributing to the regional differences in the prevalence of the disease." In assessing their results, the authors noted studies (described earlier in this report) in the United States, the United Kingdom, France, and Germany, in which the prevalence and severity of CWP varied markedly among different coal regions; the results varied despite controlling for confounders, such as dust concentration, years of exposure, smoking status, job titles, mining techniques and variations among the radiologists in assessing the quality of the films. The authors noted: "average levels of low molecular weight iron, ferritin and lipids for oxidation induced by the coal samples from each region correlated well with the prevalence of CWP, indicating that BAI in the coals contributes to the regional differences in the prevalence and severity of CWP."⁵⁹ Such links between these agents and CWP is consistent with a "cause-effect relationship." The authors suggested that they suggested that "levels of ferritin in coal miners resulting from alterations due to coal dust inhalation may be used as a biomarker of exposure to coal dust."⁵⁹

Further efforts to understand the active agent responsible for coal-induced lung disease followed. To evaluate the potential link between iron in coal and risk of CWP, Zhang and Huang⁶⁰ showed that the prevalence of CWP in seven coal-mine regions correlated with levels of BAI in the coals from that particular re-

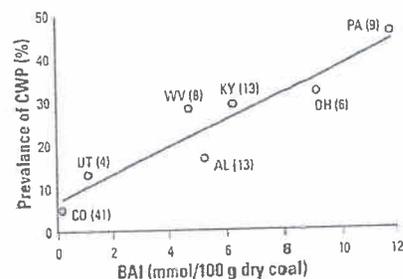


Fig. 2. Correlation between prevalence of CWP and BAI in seven U.S. states' coal mine regions. Numbers in parentheses indicate the number of coal samples per state for which analytical data were available. The expected prevalence of CWP (%) = 3.11 BAI + 7.04. Adapted from *Environ Health Perspect*. 2005;113:964-968.

gion (correlation coefficient $R = 0.94$; $P < 0.0015$). The prevalence of CWP was also correlated with pyretic sulfur or total iron, but not coal rank or silica content ($R = 0.28$; $P < 0.54$). They noted that iron in coal can become bioavailable by a process known as pyrite oxidation. Using a linear fit of CWP and BAI in the seven coal mining regions, they mapped pneumoconiotic potencies of 7000 coal samples and concluded: "Levels of BAI in the coals may be used to predict coal's toxicity, even before large scale mining."⁶¹ The relationship between CWP and BAI was well described by a linear model (Fig. 2).

In an in vitro comparison of coal from Pennsylvania and Utah, BAI in the coal played a major role in activation of factors associated with the pulmonary inflammatory response associated with CWP.⁶¹ The authors claimed their findings supported the hypothesis that "the prevalence of CWP correlates well with levels of BAI in coals from various mining regions." (Table 2 and Fig. 2 in this report have been abstracted from the Huang et al. study.⁶¹)

Commentary from the Huang et al⁶¹ article follows: "CWP, which was originally thought to be a variant of silicosis, results from the inhalation of coal mine dust that usually contains relatively small amounts of free crystalline silica (quartz) . . . It has

TABLE 2

Average Levels (mmol/100 g Dry Coal) of Total H_2SO_4 ($1/2 \text{S}_{\text{py}} + \text{SO}_4$), Available Amount of Acid ($1/2 \text{S}_{\text{py}} + \text{SO}_4 - \text{CaO}$), Total Iron, and Predicted BAI*

State	No. of Mines	CWP (%)	$1/2 \text{S}_{\text{py}} + \text{SO}_4$	$1/2 \text{S}_{\text{py}} + \text{SO}_4 - \text{CaO}^\dagger$	Fe_2O_3	BAI ‡
PA	9	45.35	18.61	14.63	12.48	11.82
OH	6	31.80	19.91	14.69	12.86	9.07
KY	13	29.00	13.17	7.49	9.78	6.25
WV	8	28.25	9.15	4.57	7.27	4.77
AL	13	16.70	9.65	6.77	8.85	5.29
UT	4	13.10	4.14	-3.19	2.69	1.09
CO	41	4.60	1.92	-2.69	3.68	0.15

*Levels of S_{py} , SO_4 , CaO , and Fe_2O_3 were obtained from the USGS database for each coal mine.

† CaO was presented as percentage of high-temperature ashes in the USGS database and was converted to percentage of dry coal based on the ash yield. Because 1 mol CaCO_3 produces 1 mol CaO in the ashes, the molar amount of CaO per 100 g coal was used as a measure of CaCO_3 levels in the coals.

‡ Values in the individual coal samples were calculated first and then averaged for the coal mine region for each of physicochemical parameters listed.

\S BAI was calculated as follows: if the difference in ($1/2 \text{S}_{\text{py}} + \text{SO}_4 - \text{CaO}$) is ≤ 0 for the individual coal mine, the BAI is given as 0. If the difference in ($1/2 \text{S}_{\text{py}} + \text{SO}_4 - \text{CaO}$) is > 0 , a lesser value between ($1/2 \text{S}_{\text{py}} + \text{SO}_4 - \text{CaO}$) or total iron (Fe_2O_3) is given for BAI (see text for details).

Adapted from *Environ Health Perspect.* 2005;113:964–968.

been suggested that higher rank coals with a higher electrostatic charge on breakage may contribute to the increased incidence of CWP in the high-rank coal regions. However, a correlation between coal rank and cell cytotoxicity has not yet been established in biologic studies. In the present study, no significant correlation between CWP prevalence and coal rank or silica was observed ($r = 0.59$, $P < 0.16$ for coal rank and $r = 0.28$, $P < 0.54$ for silica).⁶¹

Huang et al further discuss their results: "Based on the present study using the calculated model of BAI, we believe that it may be possible to predict which coal is likely to be toxic, even before large-scale mining. However, this study is far from concluding the cause-and-effect relationship between BAI and CWP and the associated COPD development. Further studies on the role of BAI in cell and lung injury, as well as the protective role of CaCO_3 in inhibiting BAI and the associated injuries, are still needed."⁶¹ The authors also referred to some of their earlier studies in which coal appeared responsible for oxidant formation and subsequent cytokine (inflammatory mediators) release in the lung after inhalation (of coal).^{62–64} These in vitro evalu-

ations support the epidemiological findings that associate different risks of CWP with different types of coal; moreover, different types of coal have various levels of metals, such as iron.

The same investigators assessed how reactive oxygen species formed by BAI in coal function. Using human lung epithelial cells, they noted that levels of interleukin-6 (IL 6), a key inflammatory protein varied between the Pennsylvania and Utah coal. They noted that BAI in the Pennsylvania Coal may induce interleukin, a key inflammatory mediator, via peroxidation and formation of hydroxyl radicals.⁶⁰

Further in vitro studies provided additional support for the role of iron in the development of CWP. One particular inorganic component in coal, pyrite (FeS_2), has been shown to spontaneously form reactive oxygen species, a key component in the inflammatory response associated with CWP. In experiments to evaluate the role of pyrite and coal dust reactivity, investigators concluded that "the prevalence of CWP can be correlated with the amount of FeS_2 in the coals."⁶⁵ The authors pointed out that coal is a variable mixture of organic carbon and inorganic mate-

rials, such as quartz, clays, carbonates, pyrite, kaolin, and mica; the iron in coal is associated predominantly with sulfur (FeS_2). The results indicated that "formation of reactive oxygen species from coal samples that contain pyrite is consistent with previous findings and that the pyrite content of coal may be a factor that contributes to the difference in the prevalence of lung disease among coal miners in different mining regions."⁶⁵ They further hypothesized that "the pyrite content of coal is a significant factor in determining the prevalence of lung disease among coal miners."

Support of the iron hypothesis was found in a German investigation that analyzed coal mine dust particles with Laser Microprobe Mass Spectroscopy and correlated the findings with cytotoxicity indices from in vitro experiments.⁶⁶ Iron and heavy-metal containing mineral particles were identified as possible toxic determinants but no clear quartz effect was shown.

SUMMARY

In summary, it can be stated with some scientific certainty based on human epidemiology studies, animal investigations and in vitro evalua-

tions—that quartz is not the predominant factor in the development of CWP. To the contrary, large scale epidemiological studies in Germany, the United Kingdom, France, and the United States indicate varying levels of risk of CWP, based on the type of coal regardless of silica content. Epidemiological studies, however, have confirmed that the rank of coal mined greatly influences CWP rates among coal workers, suggesting that coal's carbon content is a critical factor in assessing CWP risk. In addition, coal from regions with lower rates of CWP (while considering similar levels of exposure to coal, both in concentration and duration) show that coal high in BAI is associated with the highest risk of CWP. The link between quartz and the development of CWP is minimal, aside from circumstances associated with high concentrations of quartz (usually >10%) in which the pulmonary response is more typical of silicosis as opposed to CWP. Results of in vitro studies with human and animal cell lines are consistent with the epidemiological data that suggest that risk of CWP is not based on quartz, but most likely due to the concentration of BAI. In vitro studies provide further support for the role of iron in the inflammatory process associated with CWP. Although CWP and silicosis may have some similar clinical patterns, their etiology is different. However, without knowing the disease mechanism of CWP in greater detail, coal mine dust concentration should continue to be controlled by appropriate limit values to minimize disease risks.

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