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PAPER

PATHOLOGY/BIOLOGY

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Silicosis: Diagnosis and Medicolegal Implications*

ABSTRACT: Despite well-publicized sources of occupational hazard, silicosis continues to threaten industrial workers in the United States. We performed a retrospective search of the University of Wisconsin electronic pathology database to retrieve autopsy cases of silicosis and collaborated with the Wisconsin Department of Health Services to obtain statewide epidemiologic data regarding silicosis morbidity/mortality since 2003. Three silicosis autopsy cases were retrieved: all were men with ≥ 30 years of occupational crystalline silica exposure and similar histologic features of collagenous pulmonary nodules with admixed refractile particles. Overall, our state exceeds the national rate of silicosis-related hospitalizations and mortality, that is, 10.1 hospitalizations per million WI residents versus 1.2 nationally and 1.2 deaths per million WI residents versus 0.4 nationally. Surveillance is crucial to identify emerging occupational hazards and protect workers. A diagnosis of silicosis must be carefully considered at autopsy since it carries substantial implications for worker's compensation, compensatory losses, and employer liability.

KEYWORDS: forensic science, forensic pathology, silicosis, pneumoconiosis, occupational diseases, workers' compensation

Silicosis is a pneumoconiosis usually resulting from prolonged exposure to crystalline silica (SiO_2), an inorganic compound found in a number of natural and industrial products such as stone, granite, sand, quartz, and glass. It is estimated that approximately 2.3 million American workers are at occupational risk for exposure to respirable silica (1). Even after cessation of occupational exposure, chronic silicosis may develop or progress and there, currently, is no curative treatment other than potentially lung transplantation (2). In addition to silicosis, inhalation of crystalline silica dust may result in other sequelae such as chronic obstructive pulmonary disease, lung cancer, or renal disease (2). Despite stringent Occupational and Safety Health Administration (OSHA) regulations, silicosis continues to threaten industrial workers in the United States. Although overall there appears to be a recent trend of declining cases in which silicosis was certified as either a direct or contributing cause of death, it is suspected that many silicosis deaths remain unreported and that deaths from other silica-related diseases (e.g. lung carcinoma) are not specifically certified as such (2,3). Such certification may be critical in enabling a decedent's family to obtain workers' compensation benefits or compensatory damages as well as identifying which occupations place workers at greatest risk. The incidence of silicosis-related mortality in Wisconsin is approximately 3 times the national average (4). Wisconsin has had an occupational disease surveillance program since 1983, but did not have state reporting statutes that explicitly required reporting of silicosis until July 2018 (5). To provide a comprehensive analysis of silicosis in Wisconsin from an epidemiologic and pathologic perspective, we review Wisconsin silicosis incidence, mortality data, compensation regulations, and autopsy results from the prior 14 years. Silicosis mortality trends seen in our state are compared to those at the national level.

Methods

The University of Wisconsin Hospital and Clinics annually performs approximately 500-550 autopsies which include a mixture of medical and forensic cases. A retrospective search of the University of Wisconsin Hospital and Clinics electronic pathology databases PowerPath (Sunquest Informational Systems) and Beaker (Epic Systems Corporation) was conducted for autopsy cases in which silicosis was diagnosed. Cases were retrieved from years 2003-2018 utilizing the search term "silicosis." This study was exempt from UW Health Sciences Institutional Review Board (IRB) approval as it involved only specimens or associated data obtained from deceased individuals.

Four cases in which silicosis was diagnosed either before or at autopsy were retrieved from the University of Wisconsin Hospital and Clinics autopsy database. In three cases, autopsy gross and microscopic findings supported the diagnosis of silicosis. In one case, the antemortem diagnosis of silicosis was not confirmed. The decedent had reportedly undergone right lower lung lobe resection for silicosis many years prior to autopsy. Clinically, the diagnosis of silicosis was later questioned; also, no silicotic nodules were evident in any of the remaining lung lobes at autopsy. Given the questioned diagnosis, the case was excluded from further data analysis.

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Wisconsin statewide silicosis epidemiologic data were provided by the Wisconsin Department of Health Services (WI-DHS) from the years 2003 to 2017. Silicosis-related morbidity/mortality as defined by WI-DHS follows the national case definition of silicosis as either *probable* (i.e., based on death certificates, hospitalization records, workers' compensation claim with diagnosis of silicosis) or *confirmed* (i.e., verified with chest radiography or lung histopathology). State data were gathered by means of tracking death certifications and hospitalizations as silicosis reporting was not yet mandatory in Wisconsin at the time of this study.

Electronic WI-DHS, Centers for Disease Control and Prevention (CDC), and Occupational Safety and Health Administration (OSHA) silicosis publications were reviewed. A PubMed literature search utilizing terms "silicosis" AND "autopsy" was performed. Limitations included publication since January 1, 2000, human subject and English language-only (n = 27). Additional silicosis articles were sought and reviewed as necessary.

Results

Wisconsin Autopsy Silicosis Data

Key demographic and pathologic findings from the three autopsied silicosis-related fatalities are summarized below and tabulated (Table 1).

Autopsy Case 1—A 70-year-old man with a medical history significant for smoking, atrial fibrillation, silicosis, chronic obstructive pulmonary disease (COPD), and pneumonia presented to the hospital with shortness of breath, cough, fatigue, and recent weight loss. His occupational history was significant for 30-year employment in an industrial chemical plant where his job entailed mixing dry silica powders and pouring them into a vat. On admission, he was found to be severely hypoxic with acute exacerbation of his COPD. Despite treatment including levofloxacin, prednisone, and respiratory support on BiPAP, his respiratory status continued to worsen and he expired approximately 2 weeks after presentation. At autopsy, the thorax revealed a few calcified intrathoracic plaques, extensive fibrous pleural adhesions, and a right empyema (Fig. 1). The lungs were markedly anthracotic and heavy (right: 850 g; left: 820 g) with yellow fibrinopurulent material exuding from right lower lung microabscesses. Subpleural bullae were noted. Sectioning revealed hilar lymph nodes that appeared involved by fibrosis (Fig. 2*A*), while the pulmonary parenchyma revealed geographic areas of subpleural interstitial fibrosis with admixed anthracotic nodules ranging from 0.5 to 1.5 cm in maximal dimension (Fig. 2*B*). Histologic sections showed numerous collagenous nodules coalesced into masses with pigmented macrophages and birefringent ovoid to needle-shaped particles 1–3 μm in length evident on polarization (Fig. 3*A*–*C*). No asbestos bodies were evident. There were right lower lung abscesses with neutrophils and apoptotic debris (Fig. 4*A*, *B*). Postmortem empyema fluid culture showed polymicrobial growth but was negative for fungal or mycobacterial organisms; cultured bacteria including alpha hemolytic *Streptococcus*, group F beta hemolytic *Streptococcus*, coagulase negative *Staphylococcus*, and *Nocardia*. GMS stain highlighted a branching filamentous organism that morphologically appeared consistent with *Nocardia* (Fig. 4*C*). The death was attributed to complications of chronic obstructive pulmonary disease with chronic pulmonary silicosis. The manner of death was natural.

TABLE 1—*Demographic features and pathologic findings in autopsied silicosis-related deaths at the University of Wisconsin Hospital and Clinics, 2003–2018.*

Features of Autopsied Silicosis-Related Deaths	
Demographics	
Male gender	3/3
Mean age at death (range)	69 years (67–70)
Caucasian	3/3
Known occupational exposure to crystalline silica	3/3
Duration of exposure ≥ 30 years	3/3
Comorbidities	
Tobacco smoking	1/3
Asthma	1/3
Systemic hypertension	1/3
Atherosclerosis	3/3
Chronic renal disease	2/3
Mycobacterium tuberculosis infection	0/3
Gross findings	
Bilateral firm anthracotic nodules	3/3
Hilar lymphadenopathy	3/3
Marked pulmonary fibrosis	2/3
Intrathoracic plaques	1/3
Empyema	1/3
Histologic findings	
Collagenous nodules	3/3
Increased interstitial fibrosis	3/3
Pneumonia with pulmonary abscesses	2/3
Birefringent foreign particles	3/3
Dark pigment-laden macrophages	3/3
Positive acid-fast stain	0/3
Silicosis causal or contributory to death	
Causal	1/3
Contributory	2/3

Autopsy Case 2—A 70-year-old man with a medical history significant for chronic interstitial lung disease, hypertension, hyperlipidemia, asthma, and chronic kidney disease presented to the emergency department (ED) with dyspnea, fever, and syncopal episodes over the preceding 2 days. His occupational history was significant for 40 + year employment in sand and gravel quarries. In the ED, he was found to be tachycardic, hypotensive, had elevated creatinine kinase and troponin, a new left bundle-branch block, and bilateral pulmonary edema. He developed worsening hypoxemia, for which he was later intubated and

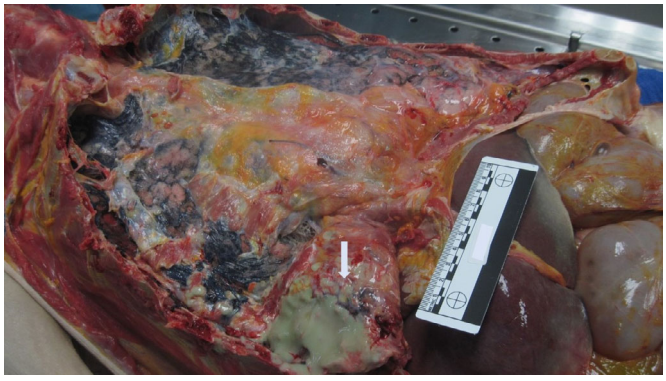

FIG. 1—*Case 1, specimen unfixed. On opening the thoracic cavity, lungs appear markedly anthracotic with extensive pleural fibrous adhesions. There was a right thoracic empyema (arrow) with subjacent right lower lung abscesses and acute bronchopneumonia. [Color figure can be viewed at wileyonlinelibrary.com]*

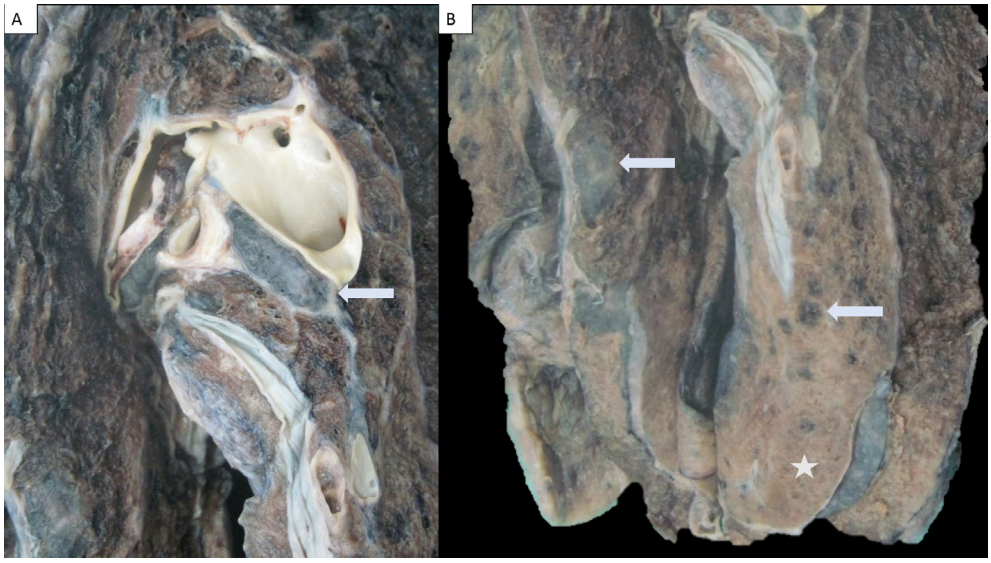

FIG. 2—*Case 1, specimen fixed in formalin. (A) On serial sectioning of lungs, hilar lymph nodes were firm/fibrotic and anthracotic (arrow). (B) Fibrosis was most prominent in the subpleural distribution (star) with admixed anthracotic nodules (arrows). [Color figure can be viewed at wileyonlinelibrary.com]*

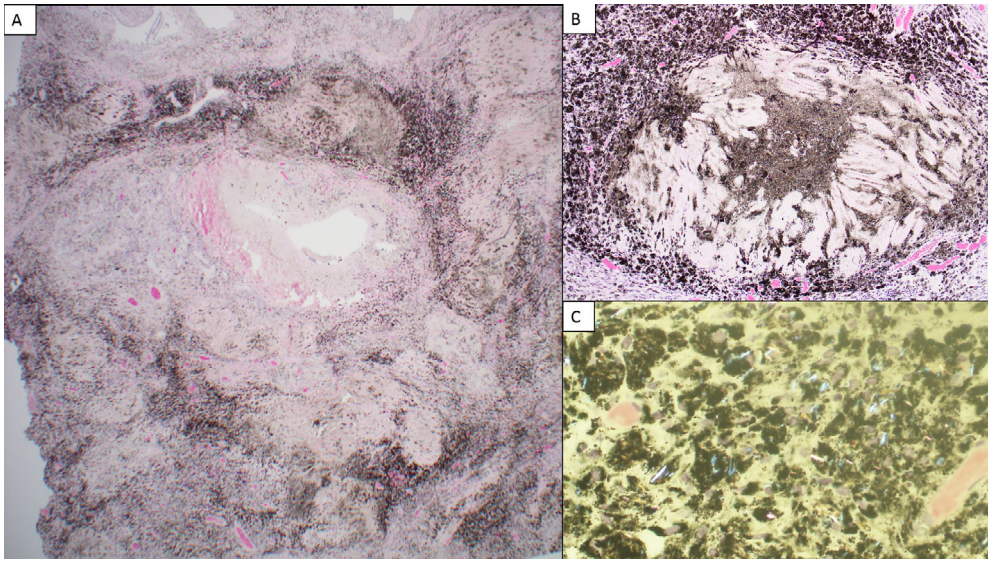

FIG. 3—*Case 1. (A) Confluent fibrotic nodules with extensive anthracosis centered around bronchovascular structure: H&E, 2x. (B) Higher power view of nodule showing whorled dense central collagenous fibrosis with peripheral dust-laden macrophages: H&E, 10x. (C) Polarized light demonstrating refractile birefringent particles admixed with fibrosis: H&E, 40x. [Color figure can be viewed at wileyonlinelibrary.com]*

ventilated. Despite being administered several pressors for persistent hypotension, his gas exchange, blood pressure, and pulmonary edema continued to worsen. Chest X-ray revealed extensive bilateral opacities that appeared consistent with diffuse alveolar damage superimposed on chronic interstitial pulmonary fibrosis (Fig. 5*A*). He died one day after admission. The family requested a lung-only autopsy to assess for pulmonary infection and the lung nodules. Grossly, the lungs were heavy (right: 1180 g; left: 1140 g) with a cobblestone appearance to the pleural surfaces. Histologic sections confirmed diffuse alveolar damage (DAD) characterized by hyaline membranes, desquamated type-II pneumocytes, and extravasated red blood cells (Fig. 5*B*). The DAD arose in a background of advanced chronic interstitial fibrosis (Fig. 6). Dense collagenous nodules were apparent within areas of interstitial fibrosis, and were also noted to involve the lymph nodes and pleura (Fig. 7*A*). Polarized microscopy revealed many associated 1–3 μm in length ovoid birefringent particles within the collagenous nodules (Fig. 7*B*). GMS and AFB stains were negative for fungal and mycobacterial organisms, respectively. While no acute pneumonia was evident, the patient had been recently treated for community-acquired pneumonia; it was suspected that exacerbation of chronic interstitial pulmonary disease by the community-acquired pneumonia (or potentially acute myocardial infarction) precipitated the DAD. The death was attributed to acute myocardial infarction arising due to hypertensive and atherosclerotic cardiovascular disease. Other significant contributory factors included chronic pulmonary silicosis with superimposed diffuse alveolar damage. The manner of death was natural.

Autopsy Case 3—A 67-year-old man with a medical history significant for coronary arterial disease, diabetes mellitus,

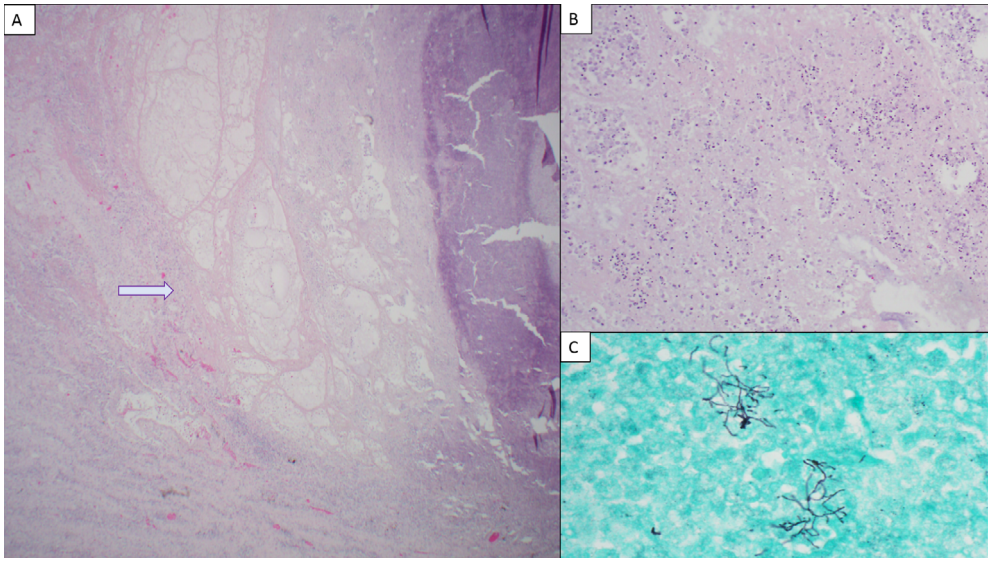

FIG. 4—*Case 1. (A) Abscess cavity within right lower lung lobe (arrow) with central necrosis and surrounding bronchopneumonia and fibrosis: H&E, 2x. (B) Higher power view of abscess showing neutrophils and copious apoptotic debris: H&E, 10x. (C) Filamentous organism morphologically consistent with Nocardia within abscess cavity: GMS, 100x oil immersion. [Color figure can be viewed at wileyonlinelibrary.com]*

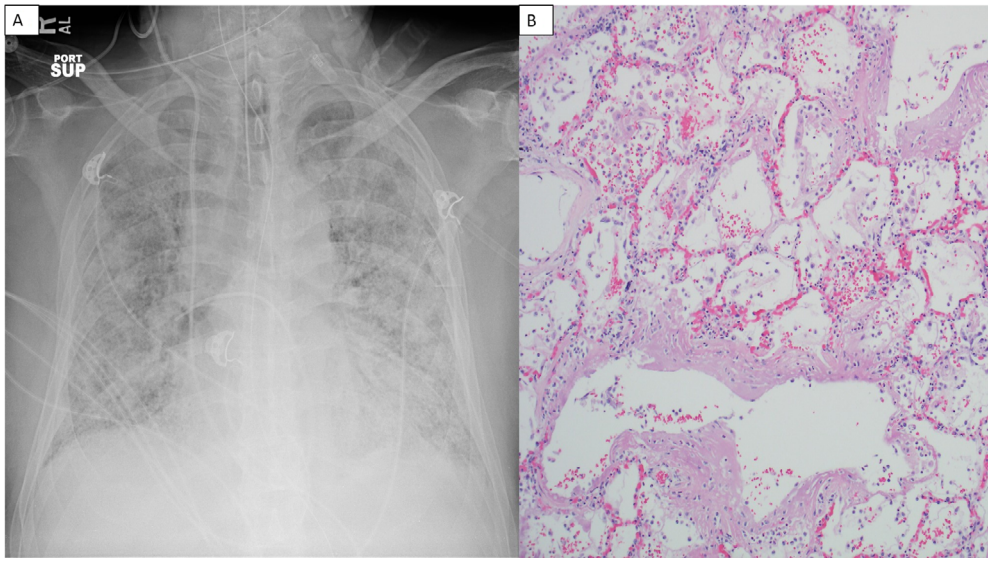

FIG. 5—*Case 2. (A) Anteroposterior chest radiography demonstrating extensive bilateral opacities that appeared consistent with diffuse alveolar damage superimposed on chronic interstitial pulmonary fibrosis. (B) Diffuse alveolar damage characterized by hyaline membranes, desquamated Type-II pneumocytes, and extravasated red blood cells: H&E, 10x. [Color figure can be viewed at wileyonlinelibrary.com]*

silicosis, and peripheral neuropathy presented with severe back pain. He had a military history significant for exposure to Agent Orange and an occupational history of working in a foundry from high school until retirement. Radiologic studies revealed numerous bone metastases and he was ultimately diagnosed with metastatic high-grade urothelial carcinoma. He underwent radiation therapy and was discharged. Two months later, he was readmitted for drowsiness and lethargy during his cryoablation treatment. His condition declined, and he was transferred to hospice care where he expired 1 week later. At autopsy, tumor was grossly evident in the urinary bladder and microscopically confirmed to be urothelial carcinoma. The lungs were heavy (right: 980 g; left: 830 g) with innumerable firm anthracotic parenchymal nodules (Fig. 8). There was hilar lymphadenopathy. Histologic sections revealed collagenous nodules with pigment-laden macrophages (Fig. 9) and rare ovoid birefringent particles. Also, acute bacterial bronchopneumonia with focal microabscess formation was seen (Fig. 10). Undoubtedly his underlying chronic pulmonary disease—in conjunction with immunocompromise arising due to type-II diabetes mellitus and metastatic cancer—predisposed him to developing such severe pneumonia. The death was attributed to metastatic high-grade urothelial carcinoma of the urinary bladder. Other significant contributory diseases included chronic silicotic pulmonary disease with superimposed acute bronchopneumonia, atherosclerotic cardiovascular disease, and type-II diabetes mellitus. The manner of death was natural.

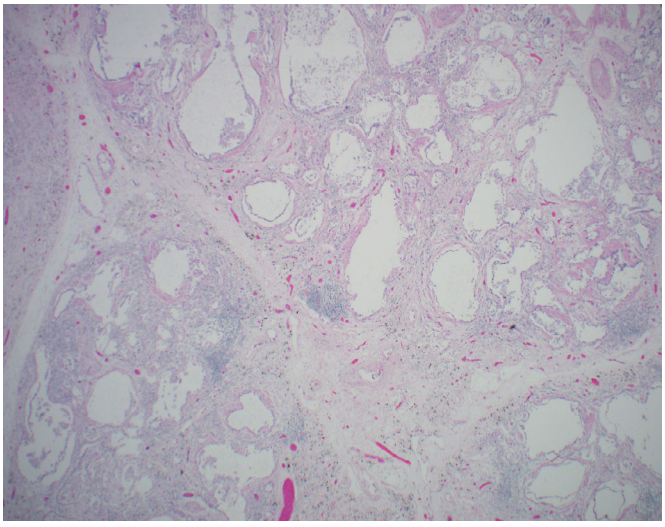

FIG. 6—*Case 2. Dense interstitial fibrosis with smooth muscle proliferation and cystically dilated airspaces (i.e., "honeycomb lung"): H&E, 2x. [Color figure can be viewed at wileyonlinelibrary.com]*

FIG. 8—*Case 3, specimen unfixed. In both lungs firm, anthracotic nodules measuring < 1 cm in maximal dimension and centered around bronchovascular structures were seen (arrows). [Color figure can be viewed at wileyonlinelibrary.com]*

Wisconsin Epidemiologic Silicosis Data

Although not a reportable disease in Wisconsin until July 1, 2018, morbidity and mortality associated with silicosis have been tracked by WI-DHS since 1983 using hospitalization records and death certificates. Overall in Wisconsin, the age-adjusted rate of hospitalizations attributable to silicosis steadily declined between 2003 and 2012, but remained substantially higher than the national average (10.1 hospitalizations per million Wisconsin residents in 2010 versus 1.2 hospitalizations per million residents nationally in 2010—the most recent year in which official reports are comparable) (4). The total number of silicosis-related inpatient hospitalizations in Wisconsin declined from 81 in 2003 to 17 in 2017 (Fig. 11). Silicosis-related mortality in Wisconsin also decreased gradually during 2003 to 2017, but with year-to-year variability (Fig. 12). The age-adjusted death rate from silicosis per million residents was also higher in Wisconsin (1.1 deaths per million residents in 2009) than the national average (0.4 deaths) (4).

Deaths were primarily attributable to chronic rather than acute or accelerated silicosis and arose predominantly in older individuals. From 2003 to 2017, there were a total of 89 silicosis deaths reported in Wisconsin. The vast majority of patients were ≥ 65 years of age at the time of death (83/89: 93.2%). Of these, the overwhelming majority of decedents were male (87/89: 97.7%). The race/ethnicity in the majority of cases was Caucasian (71/89: 79.8%); however, lesser numbers of African–American (14/89: 15.7%) and Hispanic (4/89: 4.5%) silicosis deaths were also reported (4).

Discussion

Silicosis is characterized as acute, accelerated, or chronic based on the disease time course and pattern. Acute silicosis (also known as silicoproteinosis) arises within a few weeks to 5 years of exposure to high concentrations of respirable silica (6,7). It is characterized by periodic acid-Schiff (PAS) positive proteinaceous secretions distending alveolar airspaces and is

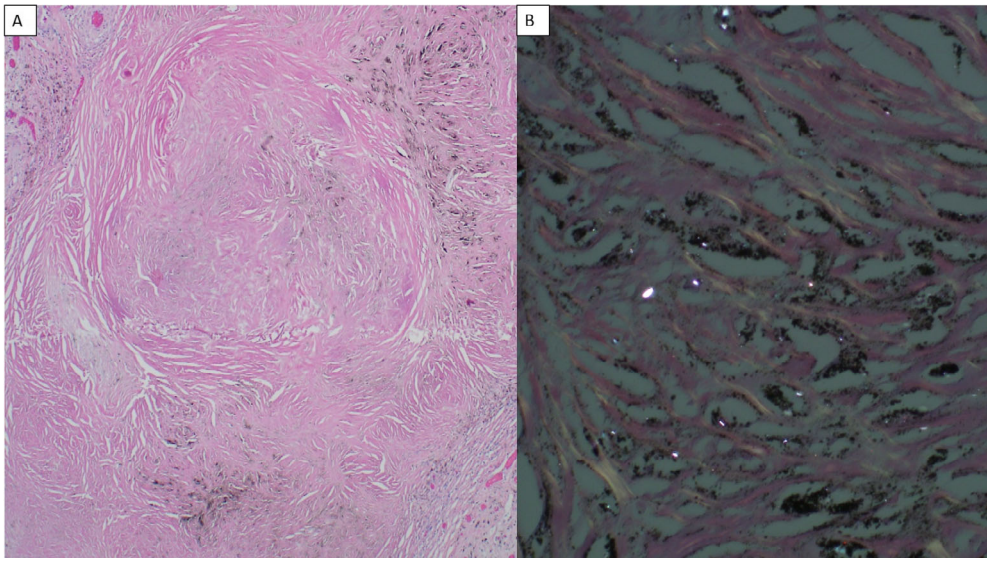

FIG. 7—*Case 2. (A) Dense collagenous nodule with peripheral dust-laden macrophages: H&E, 4x. (B) Polarized light revealing multiple minute birefringent particles within the collagenous nodule: H&E, 40x. [Color figure can be viewed at wileyonlinelibrary.com]*

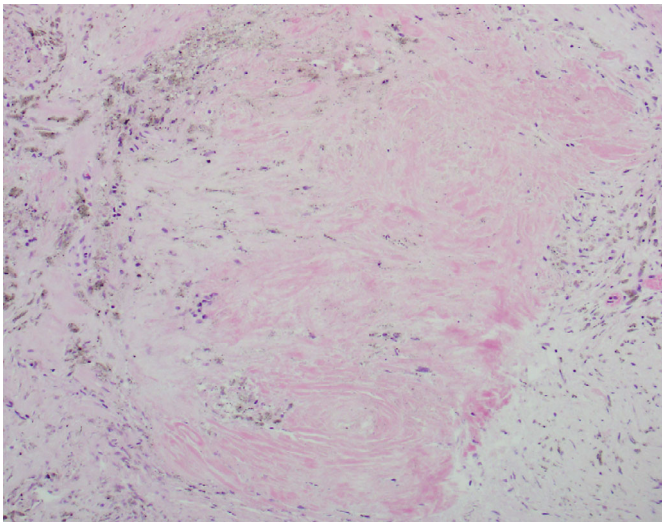

FIG. 9—*Case 3. Dense whorled collagen with peripheral dust-laden macrophages: H&E, 10x. [Color figure can be viewed at wileyonlinelibrary.com]*

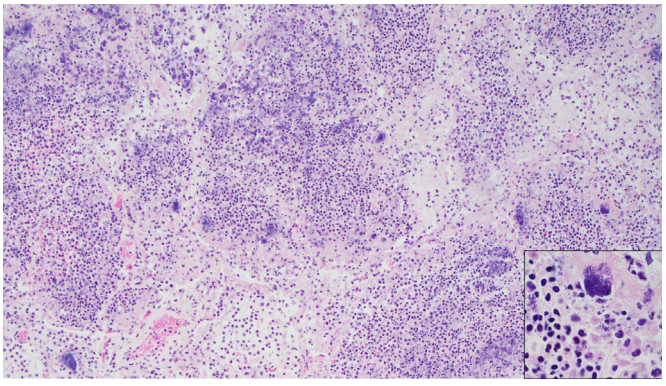

FIG. 10—*Case 3. Acute bronchopneumonia with intra-alveolar neutrophils, fibrin, and associated bacterial colonies: H&E, 10x. Inset showing bacterial cocci: oil immersion 100x. [Color figure can be viewed at wileyonlinelibrary.com]*

considered a form of secondary pulmonary alveolar proteinosis (PAP) (8,9). Accelerated silicosis and chronic silicosis develop within 5–10 years and 10–30 years of exposure, respectively (6,7). Both are characterized by nodular fibrosis (i.e., "simple silicosis") that may progressively become more confluent (i.e., "progressive massive fibrosis"). Accelerated silicosis is characterized by immature and mature nodules, however, while chronic silicosis features predominantly mature nodules (6,7). In progressive massive fibrosis, nodules conglomerate are often bilateral, may be irregularly-shaped, and measure > 1 cm in at least one dimension (10–12). Silicosis tends to have a long latency; acute and accelerated silicosis are reportedly far less common than chronic silicosis (1–6). In cases in which the patient has predominantly irregular fibrotic lesions rather than well-defined silicotic nodules, a diagnosis of mixed-dust pneumoconiosis may be more appropriate. Mixed-dust pneumoconiosis arises due to inhalation of mixed silica, silicates, and other dusts. As opposed to the typical well-defined whorled collagenous silicotic nodule, mixed-dust lesions tend to be stellate, with haphazardly arranged central collagen, numerous dust-laden macrophages, and prominent birefringent particles (11,13,14).

Silicosis Epidemiology

Both within our state as well as nationally, silicosis is predominantly diagnosed in men, typically over age 45 (1). This gender predisposition is likely a reflection of the fact that men are more likely to be engaged in occupations with high likelihood of respirable silica particle exposure such as mining, sandblasting, quarrying or foundry work. In general, any occupation in which rocks or stones containing free crystalline silica are mechanically broken down, or particulate matter is handled, increases the risk of silicosis (6,7). Crystalline silica is also a component used to make brick, concrete, artificial stone, ceramics, pottery, and glass (3). Both the age-adjusted rate of hospitalizations and age-adjusted death rate from silicosis per million residents in Wisconsin are above the national averages (4). It is suspected that this is a reflection of the fact that, historically, Wisconsin has many workers employed in industrial machinery, masonry, construction, and foundry work where occupational exposure to silica dust is high (15). The increasing petroleum industry demand for "frac sand" may also be a contributing factor (16,17). Among our autopsy series, all decedents had at least a 30-year occupational history of respirable silicosis exposure.

As of July 2018, silicosis became a reportable disease in the state of Wisconsin (5). This has significant epidemiologic implications for tracking cases of silicotic disease, and will almost certainly improve prior limitations in obtaining demographic/occupational data; for instance, nonhospitalized patients with silicosis were previously notoriously difficult to identify. In addition to Wisconsin, pathologists and clinicians making the diagnosis of silicosis in the following states are also required to notify their respective health departments: Arkansas, Connecticut, Delaware, Iowa, Kentucky, Louisiana, Massachusetts, Michigan, Missouri, New Jersey, New York, Rhode Island, South Dakota, Texas, and Virginia (18). Obtaining a thorough occupational history is critical to making the diagnosis of silicosis; reportedly, occupational pneumoconioses are missed in up to 25% of lungs biopsied to rule out idiopathic pulmonary fibrosis (IPF) (6). Participation in occupational surveillance programs can assist not only in tracking incidence of silicosis, but also aid in identifying outbreaks and newly emerging sources. For instance, in 2004, nine confirmed cases of silicosis were diagnosed among U.S. dental laboratory technicians; among the dental procedures potentially resulting in respirable silica particles are removing castings from teeth molds, grinding/polishing castings and porcelain, and using silica sand for abrasive blasting (19). More recently, silicosis has been associated with the fabrication and installation of quartz-containing countertops, as well as transporting, moving, and refilling of silica sand during hydraulic fracturing (2,20,21).

In 2012, WI-DHS released a publication regarding respirable crystalline silica and sand mining in Wisconsin (16). Due to high quality sand resources, the state has received progressively more requests for industrial sand mining and processing plants. The quartz sand is utilized by the petroleum industry for hydraulic fracturing (i.e., "fracking"), a technique used to extract oil and natural gas from rock in states such as Texas, North Dakota, and Pennsylvania (16,17). Currently, 128 industrial sand facilities are present in Wisconsin (17). Both the sand mining process as well as subsequent sorting and washing process may generate silica dust, including respirable crystalline silica particles less than four microns in size that can penetrate deeply in the lungs increasing the risk of silicosis (16). While the new U.S. Occupational Safety and Health Administration (OSHA) silica standard

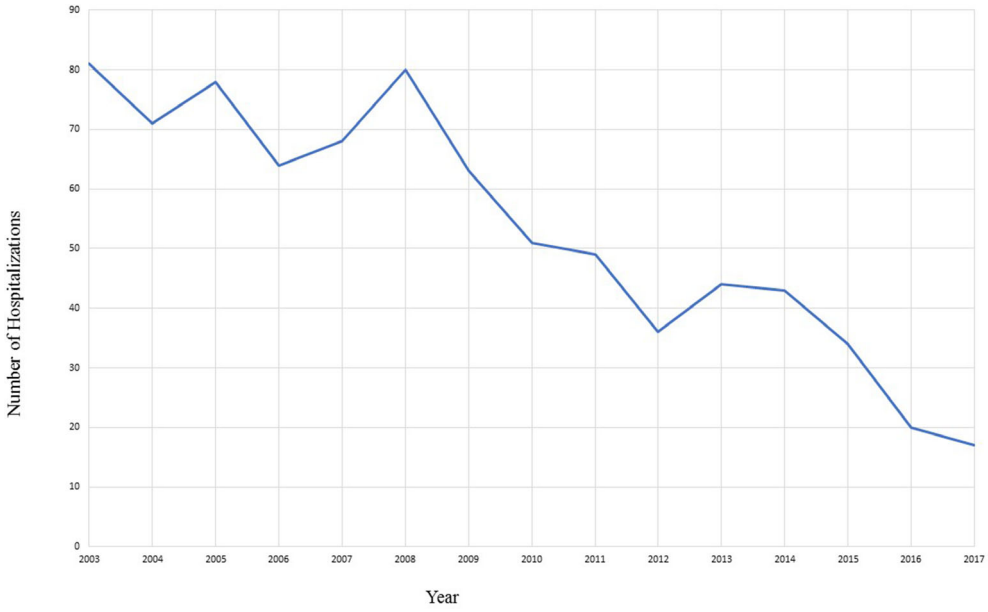

FIG. 11—*Silicosis-related hospitalizations in Wisconsin, 2003–2017 (4). [Color figure can be viewed at wileyonlinelibrary.com]*

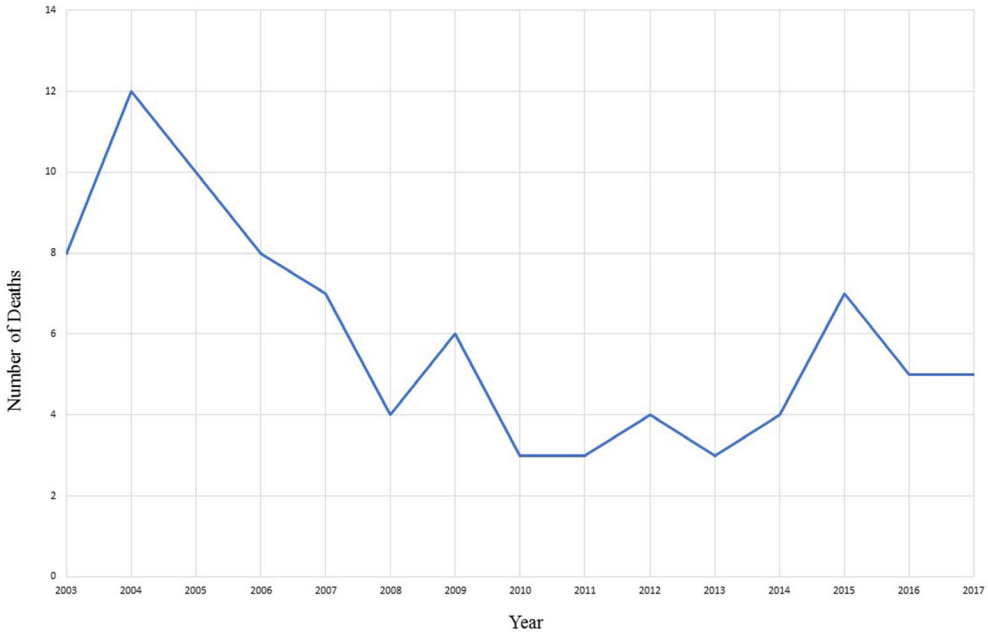

FIG. 12—*Silicosis-related fatalities in Wisconsin, 2003–2017 (4). [Color figure can be viewed at wileyonlinelibrary.com]*

lowering the silica permissible exposure limit and requiring medical monitoring to identify workers with silicosis will undoubtedly help reduce the true incidence of silicosis, it is suspected that the measured incidence in our state may actually increase due to underrecognition and underreporting arising under the "passive surveillance" system employed prior to 2018 (3,22).

Silicosis Pathophysiology

Inhaled crystalline silica particles are ultimately ingested by alveolar macrophages. The pathogenicity of silicosis is believed to result from the generation of free radicals that damages alveolar macrophages, triggering a cascade of inflammation and release of cytokines (especially IL-1 and TNF-β); the resulting alveolitis can culminate in pulmonary fibrosis (12). In simple nodular silicosis, discrete fibrotic nodules up to 1 cm in diameter form; they are often centered on bronchovascular structures and more typically located in the upper lung lobes (6,11,12). They are generally multiple and bilateral; hilar lymph nodes are almost always involved by silicosis as well (12,23). In our autopsy series, all cases showed bilateral pulmonary nodules and hilar lymph node involvement. Histologically, nodules were characterized by a central collagenous region that often had a whorled appearance surrounded by aggregates of dark dust-laden macrophages. Under polarized light, admixed birefringent particles were seen in all cases. Silica particles reportedly appear weakly birefringent and

are typically 1–3 μm in length, while silicates (inhaled along with silica dust) appear brightly birefringent and are often platy or needle-shaped; birefringent silica may be present intracellularly or extracellularly (6,10,12). While the weakly birefringent silica particles may be seen throughout the nodule, the more brightly birefringent silicate particles are reportedly more prevalent at the nodule periphery (14). Eventually, nodules may coalesce forming confluent fibrotic areas (i.e., progressive massive fibrosis) as occurred in the first two autopsy cases.

The time between exposure and onset of symptoms is influenced by the concentration of inhaled silica, form of silica (i.e., vitreous silica is relatively nontoxic compared to crystalline silica), and duration of exposure. In one study of 94 Colorado miners, workers exposed to dust levels of ≤ 0.4 mg/m^3 (corresponding to ≤ 0.05 mg/m^3 silica) had a silicosis rate of 10%; whereas, those exposed to levels > 0.8 mg/m^3 (corresponding to > 0.1 mg/m^3 silica) had a silicosis rate of 48.6%. Similarly, the prevalence of silicosis increased with exposure duration from 15.4% for workers exposed to silica for < 20 years to 47.1% for those exposed > 30 years (24). Tobacco smoking may potentiate the severity of the disease; in one recent study of Chinese iron miners, tobacco smoking and silica exposure among workers were found to have an additive joint effect on mortality from lung cancer and pneumoconiosis, and a multiplicative effect on mortality from all causes (25).

Silicosis Autopsy Protocol

In cases of suspected occupational lung disease at autopsy, the Royal College of Pathologists recommends that a minimum of 5 tissue blocks per lung be submitted with one section taken from each of the following lung regions: upper lobe apex, upper lobe base, mid zone/middle lobe, lower lobe upper aspect, and lower lobe base (26). Formalin-infusing lungs for at least 1 h prior to sectioning may optimize appreciation of subtle histologic features (27). Placing the formalin fixative container above the lung and running a tube from the container spigot to the main bronchus allows for simple gravity perfusion—though other means are possible (27). A modified College of American Pathologists 4-point grading system may be of utility in histologically assessing the extent and severity of occupational lung disease fibrosis (26,28). In addition to silicotic fibrosis, silica exposure has been associated with multiple other disorders including autoimmune diseases (e.g. scleroderma/systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, ANCA-associated vasculitis), chronic kidney disease attributable both to glomerular and tubular dysfunction, and chronic obstructive pulmonary disease (6,29,30). Thus, a full-autopsy rather than chest-only should be encouraged in order to fully assess for other silica-related diseases as well as extrathoracic silicotic lesions; in cases of prolonged silica exposure, silicotic nodules may also be found in the liver, spleen, abdominal lymph nodes, and/or bone marrow (13).

Respirable crystalline silica has been classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC) with multiple studies showing an increased risk of lung cancer (31). While some authors argue that the evidence is inconclusive, the U.S. Occupational Safety and Health Administration (OSHA) as well as National Toxicology Program (NTP) agree with the IARC, asserting there is ample evidence that exposure to respirable crystalline silica increases the risk of lung cancer (11,22,32). A variety of small and nonsmall cell lung cancers have been reported in association with silicosis. In one autopsy-based study of 450 silicosis-related deaths, lung carcinoma was found in 48 cases (10.7%); the predominant histologic subtype was squamous cell carcinoma (54.2%), followed by small cell carcinoma (22.9%), adenocarcinoma (14.6%), and large cell carcinoma (8.3%) (33). While lung cancer was not detected in any of our autopsy cases, pulmonary infection was common. In the majority of cases (2/3), necrotizing bronchopneumonia with parenchymal abscess formation was found. While silicosis can generally increase the predisposition to bacterial or fungal lung infection, the association with *Mycobacterium tuberculosis* infection has been particularly well-established. It is thought that this largely arises as a result of alveolar macrophage functional impairment by inhaled silica particles. Less commonly, chronic necrotizing pulmonary aspergillosis may develop (34). Thus, lung tissue or abscess aspirate cultures and/or special stains such as acid-fast (AFB) or silver (GMS) may be of utility in decedents with a history of respiratory dysfunction and silica exposure.

In the event an occupational or exposure history is not available, special analytic techniques such as scanning or transmission electron microscopy (SEM/TEM) coupled with energy-dispersive X-ray analysis (EDXA) may be performed to identify and quantify inorganic particles (11). Whereas electron microscopy may provide helpful surface contour, quantification, and cross-sectional particle information, EDXA identifies the particle's elemental composition. The studies are often used in a complementary fashion and both can be performed on formalin-fixed paraffin-embedded tissue (35). Other analytic techniques include electron and X-ray diffraction, and mass spectrometry (11). Such specialized techniques, however, are generally unnecessary to make the diagnosis of silicosis in otherwise typical cases.

Clinicoradiologic Diagnosis of Silicosis

Not uncommonly, decedents may have a prior clinical diagnosis of silicosis, as occurred in all 3 of our autopsied cases. While a postmortem diagnosis of silicosis can be made on the basis of typical silicosis histopathologic features alone, antemortem diagnosis requires three criteria: an occupational history of crystalline silica exposure, characteristic radiologic findings, and the absence of an alternate more likely diagnosis (36). Radiologically, chest radiographs in simple silicosis generally show bilateral well-defined nodular opacities less than 1 cm in diameter. While these opacities may be found throughout the lungs, they tend to predominantly involve the upper and posterior lungs. In approximately 10–20% of cases there is nodular calcification. Hilar and/or mediastinal lymphadenopathy with peripheral calcification (i.e., "egg-shell" pattern) is considered highly supportive of the diagnosis of silicosis (10,11). Clinically, patients with simple silicosis may be asymptomatic (10,36). Complicated silicosis is characterized by larger bilateral radiologic opacities (i.e., diameter > 1 cm) with irregular margins, most commonly located in the upper and mid lung zones. Over time, opacities tend to extend toward the hilar region and are surrounded by emphysematous parenchyma. There may be central cavitation of opacities due to ischemic necrosis and/or superimposed infection such as tuberculosis (10,11,36). Patients typically manifest with dyspnea or cough and have abnormalities on pulmonary function testing. Silicosis may more rarely manifest as diffuse interstitial pulmonary fibrosis; in these cases, radiologic findings are similar to those seen in idiopathic pulmonary fibrosis (36). While lymph node involvement by silicosis may precede parenchymal involvement, patients should not be formally diagnosed with silicosis until there is demonstrated pulmonary parenchymal involvement (11,14).

Certification and Compensation

A diagnosis of silicosis carries significant medical and legal ramifications for the patient, the patient's family, the patient's employer, and physicians. It typically entitles the recipient to specific benefits, notably worker's compensation to cover medical costs associated with their condition. In cases in which the employer or insurance company disputes the worker's compensation claim, court proceedings in Wisconsin are adjudicated by an administrative law judge rather than a trial by jury (37). While the time frame within which a claim must be filed following a work-related injury in our state is typically 12 years, for occupational lung disease claims, there is no such statute of limitations for when a claim may be filed (however, there are still fixed caps that limit *how much* an employee may receive in benefits) (37).

Additionally, product liability may be filed against the manufacturer or distributor of safety equipment or products containing silica (38). A liability case may be filed for exposure that occurred decades ago when the risk of silica exposure was not well understood. Since product liability claims are filed against a third-party, such lawsuits entail a trial by jury (38). Product liability claims are not subject to the same fixed caps that limit employer's compensation claims.

In Wisconsin, the pathologist or clinician making the diagnosis of occupational silicotic lung disease is requested to complete a form entitled the "Practitioner's Report on Accident or Industrial Disease in Lieu of Testimony" (i.e., the WKC-16-B form); this form summarizes the condition of the patient and nature of the work exposure as a causative or contributory cause of death or disability (39,40). Similar to death certification, the degree of certainty required of the physician reporting the occupational lung disease is "to a reasonable degree of medical probability" (40). If the employer or insurer disputes the claim, medical experts may be called upon to provide testimony during court proceedings, including National Institute of Occupational Safety and Health (NIOSH)-certified B readers, clinicians, and pathologists. Physicians may be required to provide evidence relevant to the case including slides, gross photographs, medical records, and radiologic images. For this reason, surveys suggest that some physicians in recent years have hesitated to officially diagnose silicosis (3).

In any case of suspected occupational silicotic lung disease, it is recommended that the family authorize an autopsy in order to provide confirmation for medical claim purposes. If an occupational lung disease is found to have caused death, Wisconsin law provides for the payment of compensation to a spouse, parent or other relative, and extra benefits are paid to dependent children (37). Thus, the diagnosis can have significant financial implications for the next-of-kin. Establishing the correct diagnosis and identifying the source of exposure are all that matters for compensation purposes. If the decedent's work exposure was either the sole cause of the occupational silicotic lung disease—or at least a material contributory causative factor in the condition's onset or progression—then the worker is entitled to compensation, regardless of whether silicosis ultimately directly causes death (39).

It is worth noting that the burden of proof regarding exposure to silicosis has changed in the last several decades. Formerly, the burden of proof rested on the employee to prove that their employer was responsible for exposure to silica. Currently, however, a diagnosis of silicosis with plausible occupational exposure history places the burden of proof on the most recent employer (39).

Conclusion

Although state and federal OSHA regulations designed to minimize exposure to respirable silica in at-risk workers have led to an overall decline in incidence of pneumoconioses, silicosis remains a significant cause of disability in the United States. Surveillance is crucial to quickly manage outbreaks of acute silicosis, adequately protect workers, and identify new emerging occupational hazards. A diagnosis of silicosis must be carefully weighed in any patient with pulmonary fibrosis and suspicious occupational history, since it carries substantial implications for worker's compensation, compensatory losses, and employer liability.

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