Addressing the Resurgence of Silicosis: Key Themes from ATS 2026

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Disclosure:	The author has declared no conflicts of interest.
Keywords:	Countertops, end-stage lung disease, engineered stone, lung transplantation, occupational lung disease, silicosis, surveillance.
Citation:	Respir AMJ. 2026;4[1]:34-37. https://doi.org/10.33590/respiramj/2QFDAP13

AT THE 2026 American Thoracic Society (ATS) International Conference, held in Orlando, Florida, USA, numerous presentations highlighted advances in research on silicosis. The ongoing resurgence of rapidly progressive silicosis, particularly among engineered stone countertop fabricators, with no existing treatments outside of lung transplantation, underscores the urgent need for continued investigation into this preventable yet fatal occupational lung disease. The wide range of work environments and exposure patterns complicate efforts to characterize disease pathogenesis, evaluate potential therapies, and develop effective prevention and screening strategies. Collectively, the studies presented at ATS 2026 demonstrated the continuum of silicosis research, spanning the identification of disease mechanisms, characterization of clinical manifestations and disease outcomes, and the enhancement of surveillance and screening approaches aimed at reducing disease burden.

TRANSLATIONAL STUDIES REVEAL POTENTIAL THERAPEUTIC TARGETS FOR DELAYING SILICOSIS DISEASE PROGRESSION

Studies in both humans and rodents identified molecular pathways and novel cell populations and characterized their roles in the pathogenesis of silicosis. Miao et al.[1] demonstrated that the expression and activity of histone deacetylase 6 (HDAC6), a cytoplasmic regulator of TANK-binding kinase 1 and interferon regulatory factor 3 (TBK1-IRF3), were increased in human and mouse silicosis lung tissue; thus, the expression of downstream proinflammatory and profibrotic genes were also increased. In addition, silica-exposed HDAC6 knockout mice had decreased activity of alveolar macrophages, cytokine production, and collagen deposition. In normal human precision cut lung slices (PCLS) cultured with silica particles, Liebler et al.[2] found an increase in the expression of mesenchymal

markers associated with lung injury and collagen deposition, including α-smooth muscle actin (α-SMA), vimentin, fibroblast specific protein 1 (FSP1 or S100A4), ER stress marker activated transcription factor 6 (CI-ATF6), mTOR effector eIF4E-BP1 phosphorylation, C/EBP homologous protein (CHOP), keratin 5 (KRT5), and KRT8. PCLS is evidently an emerging *ex vivo* model that can be used to study the different stages of silicosis pathogenesis. For example, Papagianis et al.[3] developed a novel PCLS model for studying mechanisms that drive macrophage uptake in early silicosis in both human and lung tissue.

Furthermore, using single-nuclei mRNA sequencing and spatial transcriptomics methods, Hussein et al.[4] identified different macrophage phenotypes, including osteoclast-like macrophages, associated with different stages of granuloma and fibrotic progression in lung tissue from patients with silicosis who fabricate engineered stone countertops. Through bulk RNA sequencing, Gaboyan et al.[5] identified an increased expression of genes associated with plasma cell differentiation and immunoglobulin secretion, including marginal zone B and B1 cell specific (Mzb1), joining (J) chain, and immunoglobulin heavy constant mu (Ighm) among many others, in silica-exposed rats from 6–18 months post-exposure. Emerging data provide new insights on potential pharmacologic targets.

> **The wide range of work environments and exposure patterns complicate efforts to characterize disease pathogenesis**

CLINICAL PRESENTATIONS AND COHORT-LEVEL FINDINGS AMONG PATIENTS WITH SILICOSIS

Several case reports showcased silicosis presenting concomitantly with infection, as demonstrated by Castillo-Morales et al.,[6] who described a case of silicosis with relapsing tuberculosis and aspergillosis, and by Moyer et al.,[7] who described a rare case of a stone fabricator with silicosis and concomitant cryptococcosis and rheumatoid arthritis. While silicosis has been well documented to be associated with tuberculous and non-tuberculous mycobacteria infections, the

connection between silicosis and fungal infections is less well characterized. Moyer et al.[7] theorized that increased susceptibility to fungal infection may be due to the impaired function of alveolar macrophages from exposure to silica dust. These cases further demonstrate the importance of routine and comprehensive monitoring with microbiologic testing for patients with silicosis to provide adequate treatment and avoid relapse of opportunistic infections.

Additionally, while parenchymal nodules are the hallmark radiographic finding of silicosis, a subset of patients present with predominant mediastinal and hilar lymph node involvement, as described in a case by Karakaya et al.[8] Such presentations may closely resemble sarcoidosis, lymphoma, or tuberculosis, and thus, obtaining occupational exposure history is a crucial step to avoid misclassification.

Moreover, few studies have examined the outcomes of patients with silicosis and concomitant pulmonary hypertension (PH). Among a cohort of 16 engineered stone countertop fabricators with silicosis who were referred for lung transplantation at the University of California Los Angeles, USA, Saggar et al.[9] reported a greater prevalence of precapillary PH (100%) and severe Group 3 PH (38%) when compared to patients with idiopathic pulmonary fibrosis (50% and 24%, respectively). These observations underscore the importance for further investigation, given the shortage of data on PH in silicosis and the potential for complications during lung transplantation.

Furthermore, among a cohort of 63 cassiterite miners in the Kayonza District of Rwanda, Surya et al.[10] uncovered that the nine miners with silicosis (chest radiograph profusion score cut-off of 1/1) had significantly decreased absolute forced vital capacity (-447 mL; 95% CI: -806–-89) over 8 months after adjusting for age. There was no significant change estimated in age-adjusted forced expiratory volume in one second (-125 mL; 95% CI: -313–63). Additional longitudinal cohort studies are warranted to further assess the effect of occupational exposure to silica dust on lung function.

EFFORTS FOR ADVANCING OCCUPATIONAL LUNG DISEASE SURVEILLANCE AND SCREENING MEASURES

While vulnerable workers continue to be exposed to alarmingly high levels of respirable crystalline silica dust, ongoing efforts to enhance surveillance and screening measures led by national experts in occupational respiratory health are encouraging.

Laura Reynolds, National Institute for Occupational Safety and Health, West Virginia, USA, emphasized the importance of standardized chest radiograph interpretation through the International Labor Organization (ILO) classification system and certified B readers, which serve as foundational components of screening and surveillance programs for pneumoconiosis, including silicosis, allowing for earlier disease detection and more consistent case identification.

David J. Blackley, National Institute for Occupational Safety and Health, highlighted the growing potential of AI in chest radiograph screening for pneumoconiosis to enhance surveillance efficiency and accessibility.

CLOSING REMARKS

The studies and presentations highlighted above represent only a portion of the large body of translational, clinical, and surveillance work focused on silicosis and occupational lung disease presented at ATS 2026. Silicosis remains a devastating yet preventable disease that continues to disproportionately affect vulnerable workers worldwide. Lessons learned from both unique clinical presentations and cohort-level investigations can help to improve the management and risk stratification of silicosis. Continued research is essential to better understand the mechanism driving disease progression and perpetuation, identify novel therapeutic targets, and improve outcomes for affected individuals.

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