Environment and Occupational effects on TB- Case Studies

Ige George MD MS

Asst Professor

Washington University St Louis

Tale of two construction workers

35 yr old and 32 yr old males , originally from India

Came to New Jersey in 2018 for work

2021- was given refugee status in the United states and was evaluated for TB

Chronic dry cough. Denies any sputum production , weight loss or systemic symptoms

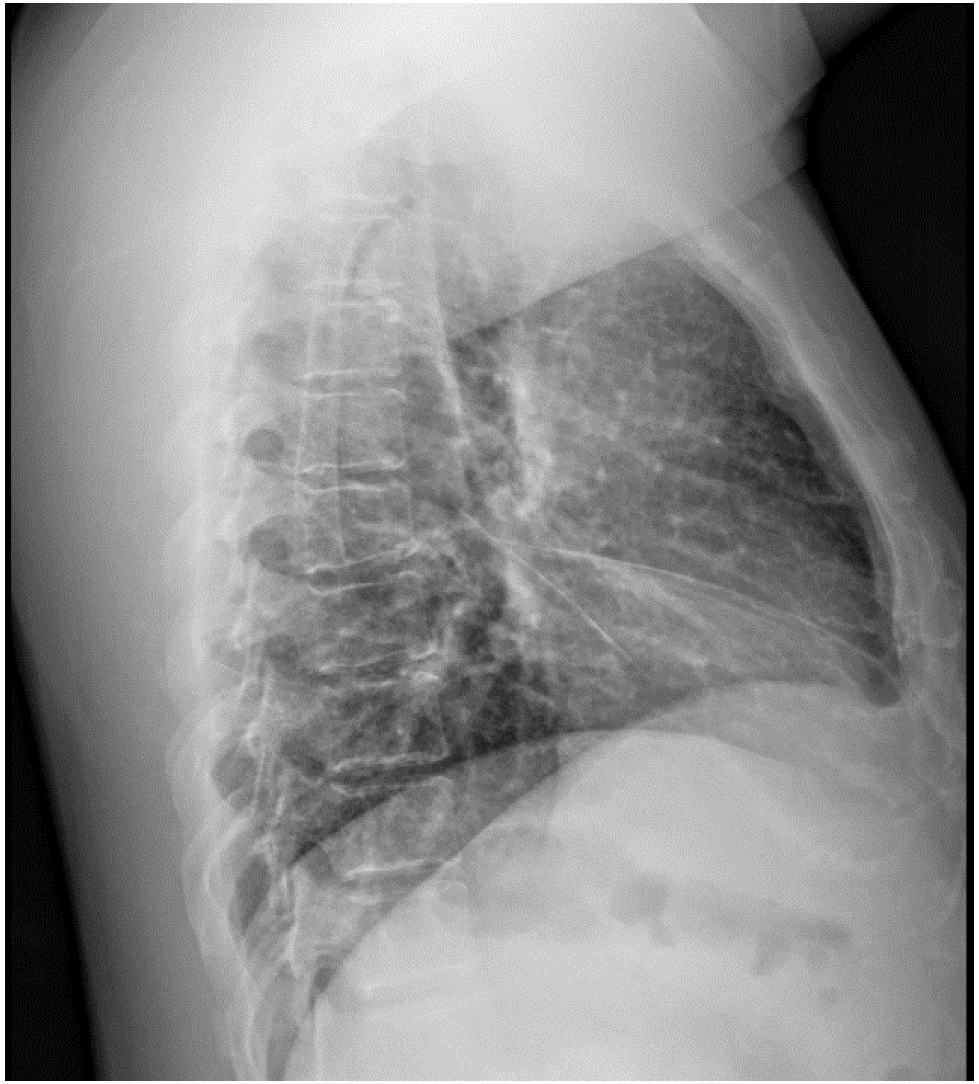
Exam : RS: normal. No clubbing. Healthy appearing

TSPOT positive 26/16/P/P and 18/16/P/P

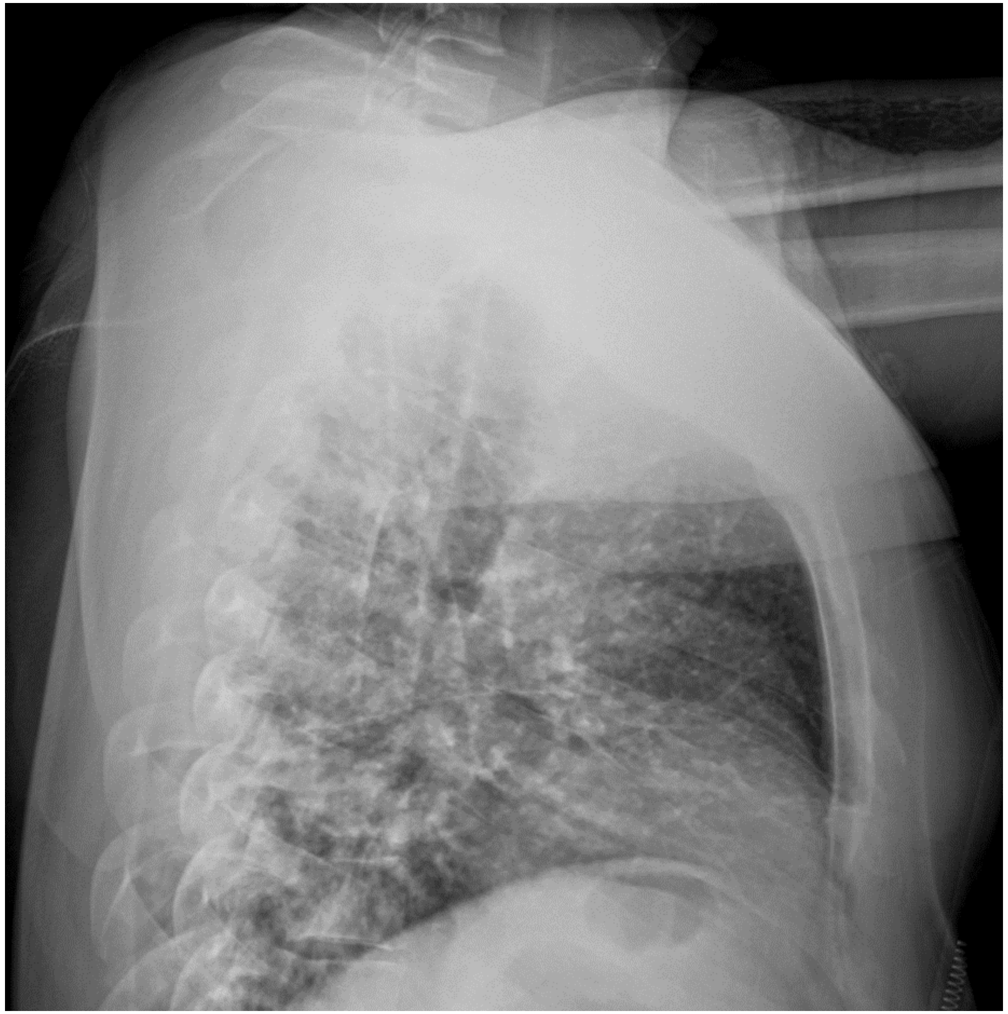
CXR : bilateral reticulonodular shadows.

Sputum AFB smears and cultures done

F/U in St Louis- Repeat AFB smears negative. No new symptoms


Acc: 05
Key Images



More history

The New York Times

Hindu Sect Is Accused of Using Forced Labor to Build N.J. Temple

Federal agents descended on the massive temple in Robbinsville, N.J., as a lawsuit charged that low-caste men had been lured from India to work for about $1 an hour.

Give this article 443

The BAPS temple opened in Robbinsville, N.J., in 2014 and is still under construction.
Annie Correal/The New York Times

By Annie Correal
Published May 11, 2021 Updated Nov. 10, 2021

The lawsuit says more than 200 workers — many or all of whom don't speak English — were coerced into signing employment agreements in India. They traveled to New Jersey under R-1 visas, which are meant for "those who minister, or work in religious vocations or occupations," according to the lawsuit.

When they arrived, the lawsuit says, their passports were taken away and they were forced to work at the temple from 6:30 a.m. to 7:30 p.m. with few days off, for about $450 per month a rate that the suit said came out to around $1.20 per hour. Of that, the workers allegedly only received $50 in cash per month, with the rest deposited into their accounts in India.

WHYY

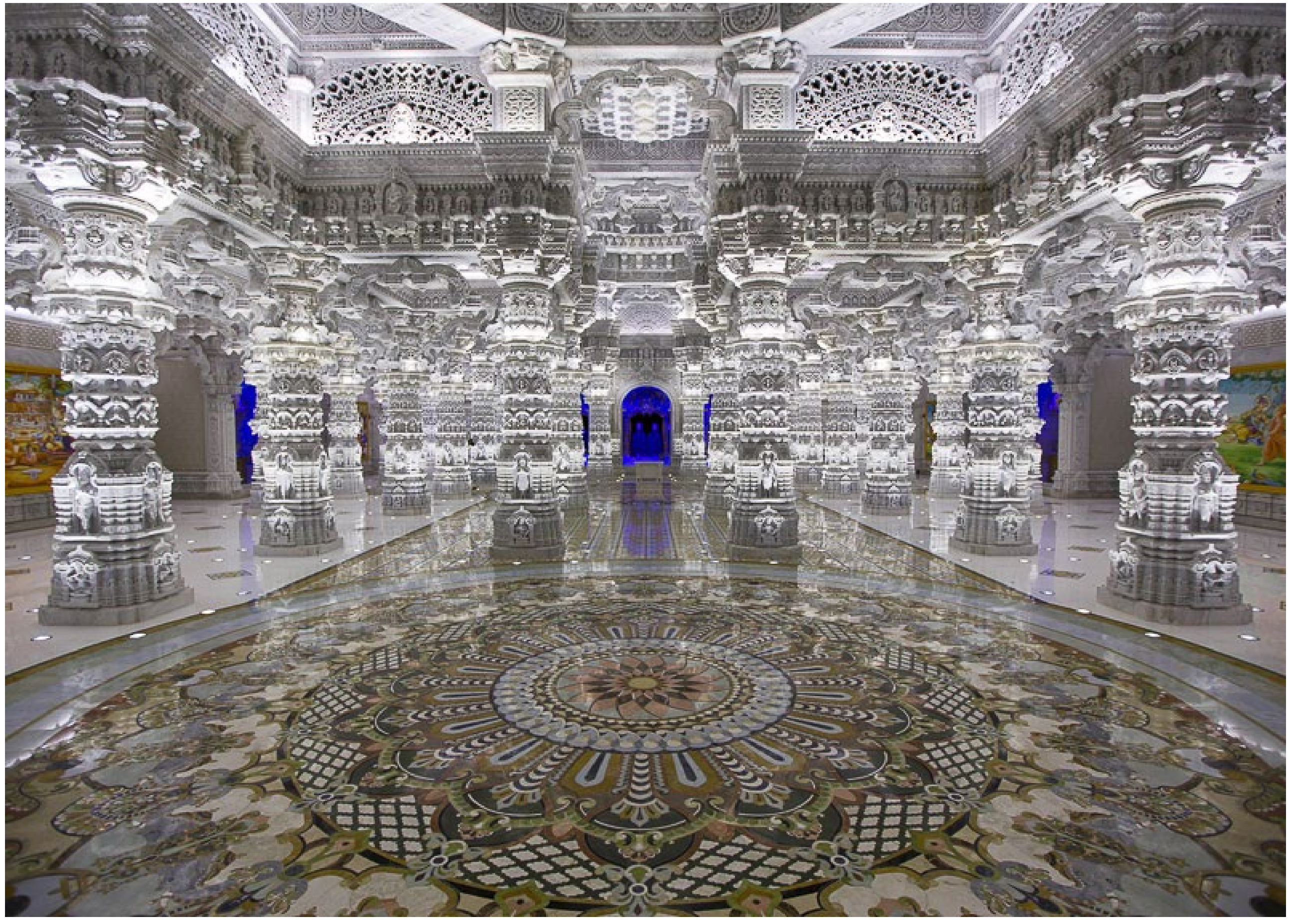
Suit: Workers lured to N.J. from India paid $1.20 per hour for years

Next steps ?

Rule out active TB disease ?

Treat for Latent TB ? Is an ‘intensified regimen’ useful?

Do CT chest ?



https://www.baps.org/Global-Network/North-America/Robbinsville.aspx

Silicosis and Tuberculosis – Silico-tuberculosis

What is Silica ?

- Respirable silica dust <7 microns
- SiO_2
- 6 natural forms of free crystalline silica-
  - Most common quartz (sands rocks & stones)

Diseases associated

Table 1 Diseases associated with respirable crystalline silica

Pneumoconiosis
Chronic silicosis
Accelerated silicosis
Alveolar lipoproteinosis
Progressive massive fibrosis (PMF)
Chronic bronchitis
Emphysema
Mineral dust airways disease (MDAD)
Mycobacterial disease
Pulmonary and extra-pulmonary tuberculosis
Non-tuberculous mycobacterial (NTM) disease
Lung cancer
Autoimmune diseases
Scleroderma
Systemic lupus erythromatosis
Rheumatoid arthritis
Renal disease

Adapted from *Murray and Nadel's Textbook of Respiratory Medicine* (Table 61.2), with kind permission from Elsevier Saunders.[6]

Sources of respirable silica

Table 2 Sources of exposure to respirable crystalline silica

Sources of exposure	Comment
General	
Moving, drilling, working, processing, crushing or mining sand, stones or rocks	Free silica content in respirable fraction of dust determines risk
Mining and related activities	
Mining and milling	Country rock* an important determinant of risk. Gold, coal, tin, copper, mica, uranium, crocidolite, iron, important in some regions
Small-scale mining	Under-researched, but exposure may be high
Mining related	Quarrying, tunnelling, excavating, digging wells and boreholes. Country rock and mineral determines risk. Quarrying granite, sandstone, flint, quartzite, shale and slate may produce high levels of quartz. Potency of silica may be reduced in some clays
Major industrial sources	
Foundry	
Ceramics	Pottery, tiles, brick and refractory articles
Glass manufacture	
Furnace masonry	Cutting, grinding, etc., refractory articles
Construction	Cutting, grinding, etc., concrete, tiles or bricks. Digging foundations
Stoneworking and monumental masonry	Making, cutting, abrasive polishing, etc., of tombstones, billiard tables, slate pencils, cladding and surfaces, including granite counter tops
Abrasive blasting with sand (sandblasting) or siliceous material	Very high exposures common. Usually cleaning or preparation for coating of metal pieces, but also unusual applications, e.g., sandblasting jeans
Minor industrial sources	
Fillers and scourers	Fine silica may be used for fillers in paints, coatings, plastics, rubber, explosives, dental supplies, etc., or in scouring materials (such as cleaning agents and those used for polishing flour) or grinding materials
Jewellery	Cutting, buffing, etc., semi-precious gems
Diatomaceous earth	Calcined material contains cristobalite
Craft work	Stone carvers, sculpture, pottery. Cases unusual unless frequent exposure, e.g., most working days
Less well established sources	
Agriculture	High levels of quartz exposure possible in farming sandy soils but silica-associated disease rare
Non-occupational	Frequent exposure to sand storms

* Country rock = rock hosting the mineral or being mined. Silica content varies from location to location, even within a mine.

INT J TUBERC LUNG DIS 11(5):474–484

Risk of silica and tuberculosis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Low or intermediate tuberculosis burden countries				
Chang 2001	0	0		Not estimable
Yarahmadi 2013	1.40609	0.22307	18.3%	4.08 [2.63, 6.32]
Li 2011	1.76	0.5	8.0%	5.81 [2.18, 15.49]
Sherson 1990	2.3	0.57	6.6%	9.97 [3.26, 30.48]
Westerholm 1986	3.49620448	1.015526	2.5%	32.99 [4.51, 241.43]
Subtotal (95% CI)			**35.4%**	**6.59 [3.36, 12.94]**
Heterogeneity: Tau² = 0.22; Chi² = 5.83, df = 3 (P = 0.12); I² = 49%				
Test for overall effect: Z = 5.49 (P < 0.00001)				
1.1.2 High tuberculosis burden countries				
Corbett 2000	0.788	0.266	16.1%	2.20 [1.31, 3.70]
Cowie 1994	1.0152	0.2133	18.8%	2.76 [1.82, 4.19]
Hnizdo 1998	1.376	0.216	18.6%	3.96 [2.59, 6.05]
Corbett 1999	1.59	0.39	11.0%	4.90 [2.28, 10.53]
Subtotal (95% CI)			**64.6%**	**3.16 [2.31, 4.32]**
Heterogeneity: Tau² = 0.04; Chi² = 4.62, df = 3 (P = 0.20); I² = 35%				
Test for overall effect: Z = 7.21 (P < 0.00001)				
Total (95% CI)			**100.0%**	**4.01 [2.88, 5.58]**
Heterogeneity: Tau² = 0.11; Chi² = 14.99, df = 7 (P = 0.04); I² = 53%				
Test for overall effect: Z = 8.21 (P < 0.00001)				
Test for subgroup differences: Chi² = 3.77, df = 1 (P = 0.05), I² = 73.4%				

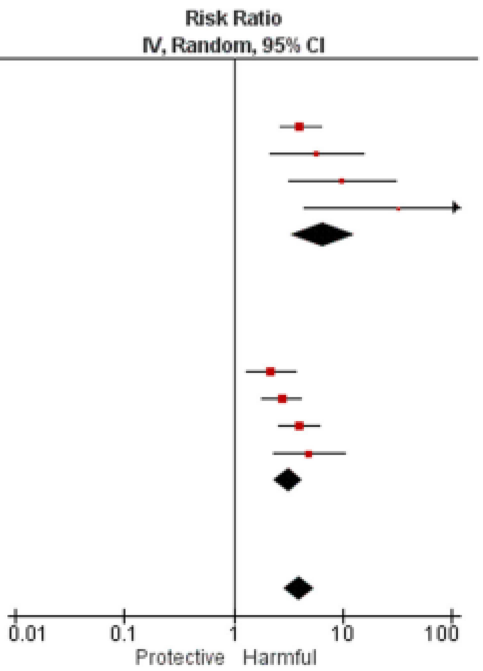


Fig. 3 Forest plot: Studies of the association between silicosis and tuberculosis

Table 3 Risk or odds of tuberculosis by severity of silicosis

Study by date of publication (effect measure)	Cowie 1994 (IR) [48]	Hnizdo 1998 (RR) [49] (*Autopsy grading*)	Corbett 1999 (OR) [50]	Corbett 2000 (RR) [51]	Chang 2001 (RR) [52]
Adjusted/controlled for. N	Age, date of CXR. *N* = 1153	Age, smoking. *N* = 2255	Age, HIV, duration employed, dusty job. *N* = 561	Age, HIV, duration employed, underground/surface job. *N* = 4022	Age, sex, smoking. *N* = 707
Grades or markers of extent of silicosis	None (*n* = 335): 1.0 (0, 2.0) ILO 1 (*n* = 418): 2.2 (0.7, 3.6) ILO 2 (*n* = 355): 2.9 (1.1, 4.6) ILO 3 (*n* = 45): 6.3 (0, 13.4)	None (*n* = 577): 1.00 Negligible (*n* = 310): 1.86 (0.97, 3.58) Slight (*n* = 196): 2.62 (1.36, 5.03) Moderate/ marked (*n* = 213): 2.71 (1.41, 5.20)	None (*n* = 340): 1.00 ILO 0/1 (*n* = 69): 1.6 (0.86, 2.90) ILO 1/0 (*n* = 48): 2.8 (1.24, 6.46) ILO > 1/1 (*n* = 90): 4.9 (2.32, 10.58)	None (*n* = 2924): 1.00 ILO 0/1 (*n* = 460): 1.4 (1.0, 2.2) ILO 1/0 (*n* = 212): 1.8 (1.0, 3.0) ILO 1/1 (*n* = 156): 2.2 (1.3, 3.7) ILO > 1/1 (*n* = 197): 2.5 (1.6, 4.0)	PMF (*n* = 141) vs no PMF (*n* = 566): 3.78 (2.24, 6.35)

95% confidence intervals in parentheses. *IR* incidence rate (annual), *RR* relative risk, rate ratio or risk ratio (see Table 1), *OR* odds ratio; *CXR* chest x-ray, *ILO* International Labour Organization, *PMF* progressive massive fibrosis

Pooled relative risk of 4.01 (only surpassed by HIV)

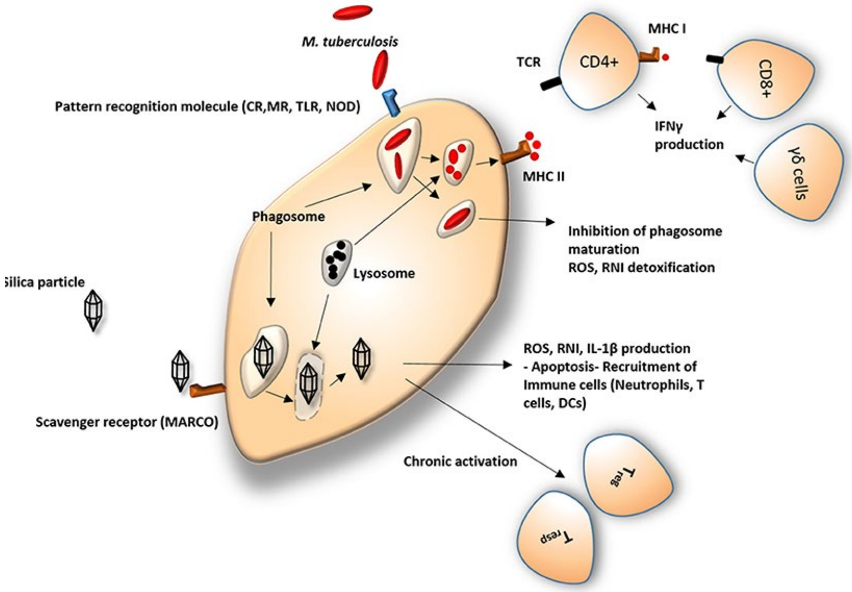
Risk even evident in ‘sub radiological’ categories – ‘radiological silicosis should not be required for attribution of the excess risk of tuberculosis to silica exposure in silica exposed workforce’

Increased risk in ‘accelerated silicosis’

Ehrlich et al. BMC Public Health (2021) 21:953

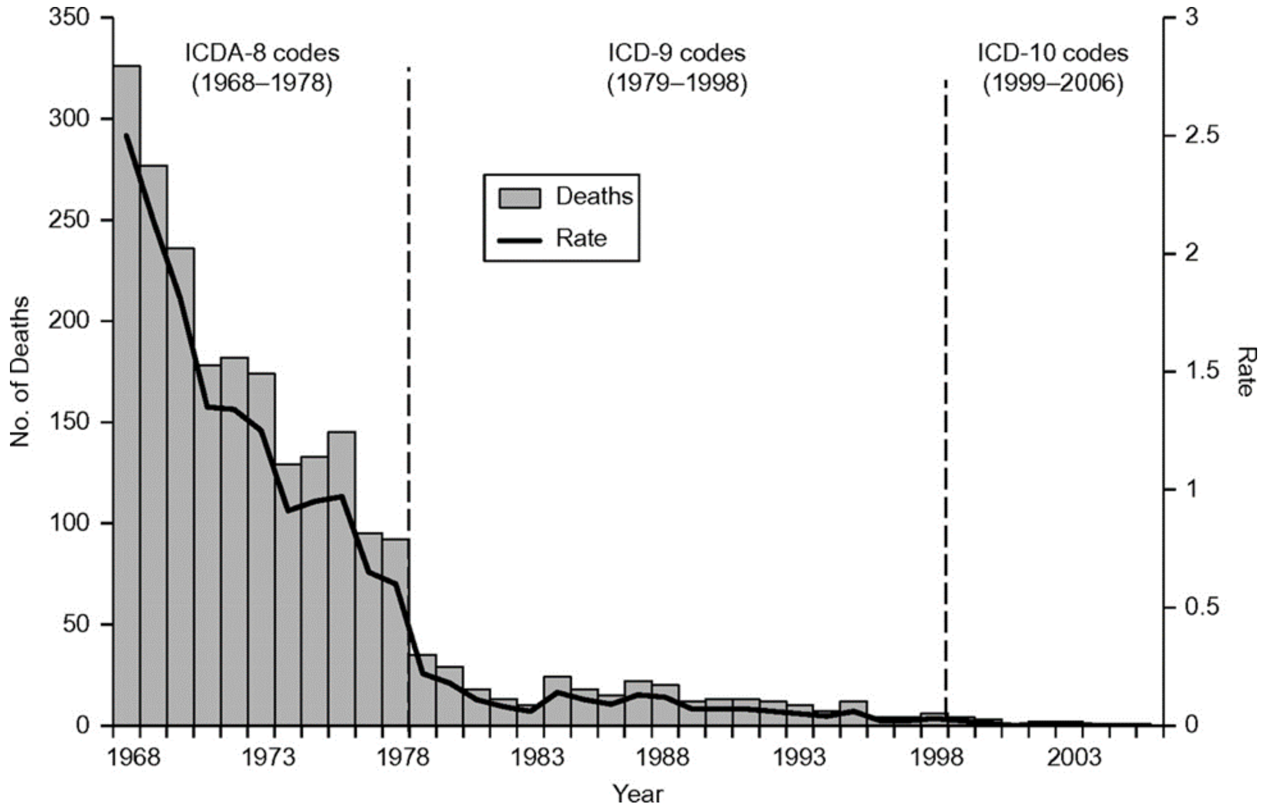
Silica decreases cellular function, capacity of dendritic cell activation and leads to a non-specific, impaired inflammatory response

	Silica	Mtb	Silica + Mtb
Macrophages	Dose-dependent Induction of apoptosis, fibrotic nodule formation, chronic activation of inflammatory and anti-inflammatory pathways, ROS, and RNI production (6)	Granuloma formation, chronic inflammation, survival mechanisms: ROS and RNI detoxification, blockade of phagosome maturation, granuloma formation (70)	Increase in Mtb uptake (71); impairment of adhesion and migration (72, 73)
Dendritic cells	Lower viability (74)	Cells with the highest bacterial burden in lymph nodes (75); increase in antigen presentation and secretion of pro-inflammatory cytokines (76); activation of adaptive immunity (77)	Yet to be investigated
Neutrophils	Decreased phagocytosis and viability (78, 79)	Control of Mtb replication, prolonged activation—tissue damage (80); trapping of bacilli (81); facilitation of disease progression (82)	Yet be investigated
NKs	Decrease in NKs (83, 84); silica nanoparticles cause increase in NKs (85)	Protective role of NKs—production of IFNγ (86)	Yet to be investigated
Antigens	Inconsistent evidence, increase in antigen-presenting properties of AMs (87)	CD1 mediated T cell activation (88, 89); signaling for APCs (90)	Yet to be investigated
T cells CD4+, CD8+, γδ T cells	Increase in FAS ligand—higher rate of apoptosis (91); shift between Th1/Th2 response (92–96); Tregs and Tresps activation (97); reduced inhibitory activity of T cells (98)	Bacteriostatic and bactericidal effect (77); IFNγ production—phagocytic properties of macrophages, Th2 response activation and Tregs production (99, 100)	Sporadic and contradictory evidence
Antibody-mediated immunity (B cells)	Increase and decrease in B cell activity (101); increase in autoantibodies (97)	B cells are the producers of antibodies, modulators of T cell activity and T cell memory, influencing function of dendritic cells (102); association with containment of Mtb (103); CD4+ T cell regulation (104)	Yet to be investigated



Front. Immunol., 09 January 2019
| https://doi.org/10.3389/fimmu.2018.03069

Significant decline in silicosis-respiratory TB mortality in the United States during 1968–2006



Among 16,648 silicosis deaths, 2,278 (13.7%) had respiratory TB listed on the death certificate

95 silicosis-respiratory TB deaths reported during 1990–2006

Probably reflects prevention and control measures for both diseases.

Prevention


CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

A-Z Index
Search NIOSH
Advanced Search

The National Institute for Occupational Safety and Health (NIOSH)

NIOSH Publications & Products > NIOSH-Issued Publications

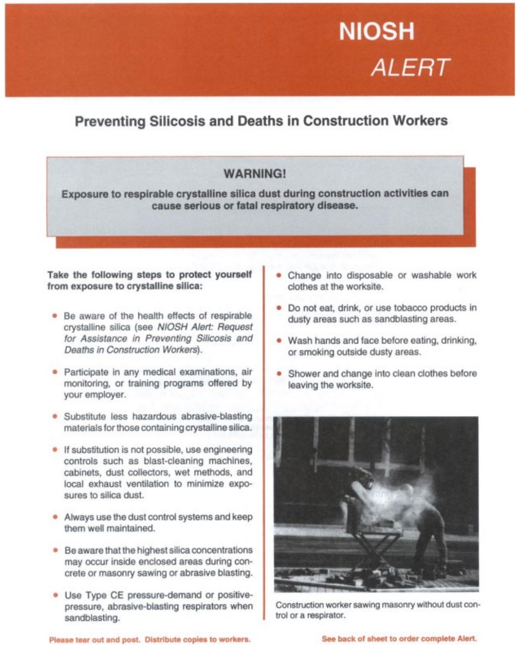
NIOSH Publications & Products
NIOSH-Issued Publications
Preventing Silicosis and Deaths in Construction Workers

Promoting productive workplaces through safety and health research / NIOSH

Preventing Silicosis and Deaths in Construction Workers

- Silicosis – incurable
- Recognize activities that generate silica dust and Plan for prevention
- OSHA and NIOSH have Permissible Exposure Limits (PEL's) 0.05 mg/m3 (50 µg/m3) as a TWA for up to 10 hours/day
- Engineering controls and containment methods

  (wet drilling)
- Air monitoring & Respirators
- Annual evaluation for TB


NIOSH
ALERT

Preventing Silicosis and Deaths in Construction Workers

WARNING!
Exposure to respirable crystalline silica dust during construction activities can cause serious or fatal respiratory disease.

Take the following steps to protect yourself from exposure to crystalline silica:

- Be aware of the health effects of respirable crystalline silica (see *NIOSH Alert: Request for Assistance in Preventing Silicosis and Deaths in Construction Workers*).
- Participate in any medical examinations, air monitoring, or training programs offered by your employer.
- Substitute less hazardous abrasive-blasting materials for those containing crystalline silica.
- If substitution is not possible, use engineering controls such as blast-cleaning machines, cabinets, dust collectors, wet methods, and local exhaust ventilation to minimize exposures to silica dust.
- Always use the dust control systems and keep them well maintained.
- Be aware that the highest silica concentrations may occur inside enclosed areas during concrete or masonry sawing or abrasive blasting.
- Use Type CE pressure-demand or positive-pressure, abrasive-blasting respirators when sandblasting.
- Change into disposable or washable work clothes at the worksite.
- Do not eat, drink, or use tobacco products in dusty areas such as sandblasting areas.
- Wash hands and face before eating, drinking, or smoking outside dusty areas.
- Shower and change into clean clothes before leaving the worksite.

Construction worker sawing masonry without dust control or a respirator.

Please tear out and post. Distribute copies to workers.

See back of sheet to order complete Alert.

Choice of treatment for LTBI in silicosis ?

Clinical Trial > Am Rev Respir Dis. 1992 Jan;145(1):36-41. doi: 10.1164/ajrccm/145.1.36.

A double-blind placebo-controlled clinical trial of three antituberculosis chemoprophylaxis regimens in patients with silicosis in Hong Kong. Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council

1981 to 1987; 679 Chinese men with silicosis
No prior TB Rx or active TB (not screened for LTBI)
4 treatment groups rifampin for 12 wk (R3), isoniazid and rifampin for 12 wk (HR3), INH alone for 24 wk (H6), or placebo (Pl)
No significant difference in outcome between 3 arms / adverse effects

Active Pulm TB (%)	2 yr	3 yr	4yr	5 yr
Placebo	9	15	20	27
Combined Rx arm	5	8	10	13

$p < 0.01$, log-rank test

Short course chemoprophylaxis with rifampicin, isoniazid and pyrazinamide for tuberculosis evaluated in gold miners with chronic silicosis: a double-blind placebo controlled trial

Tubercle and Lung Disease (1996) **77**, 239–243

R. L. Cowie
Department of Medicine, University of Calgary, Canada

Table 1. Comparison of treatment and placebo groups

	Treatment $n = 191$	Placebo $n = 191$
Age (SD) years	47.0 (5.99)	47.3 (6.11)
X-ray nodule Profusion* (SD)	7.2 (1.49)	7.1 (1.15)
Non-compliance	53	42
Tuberculosis	11	15

There are no significant differences between the two groups.
*The X-ray nodule profusion was expressed as a continuous variable from 1 to 10 with 1 equivalent to International Labour Office nodule profusion category 0/0 and 10 as 3/3.

? High rate of re-infection among mine workers?

Results still appear somewhat inferior to the generally recognized efficacy of treatment of latent TB infection of about 60–90% *

*WHO guidelines for low tuberculosis burden countries. Eur Respir J 2015;46:1563-76

Our patients

Sputum cultures – finalized negative.

CXR reviewed with radiology- consistent with silicosis

Rifampin x 4 months

Followed up after 6 months- continues to do well

Repeat CXR after 4 months – no changes

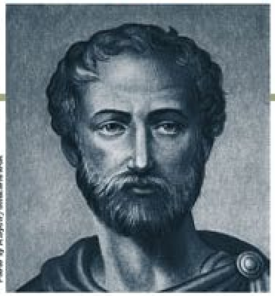
Conclusions

- Occupational exposure to silica dust (respirable crystalline silica) leading to the development of silicosis still occurs in many parts of the world
- Increased risk of developing active TB (Rates in US are declining)
- Chemoprophylaxis for latent TB infection should be considered with prolonged silica exposure, irrespective of development of silicosis
- Lack of dedicated studies on current TB preventive therapy regimen(s) for this specific population
- Better preventative strategies globally

MILESTONES IN RESPIRATORY PROTECTION

- Pliny the Elder (**23–79 AD**) used animal bladder skins to filter dust while crushing cinnabar
- Leonardo da Vinci (**1452–1519**) recommended the use of wet cloths over the mouth and nose

Pre-1800s



1800s–1919

- In **1877**, the English invented and patented the Nealy Smoke Mask
- United States Bureau of Mines (USBM) was established in **1910**
- USBM produced Schedule 13, "Procedure for Establishing a List of Permissible Self-Contained Mine Rescue Breathing Apparatus" in **1919**

- In **1920**, MSA Safety Company manufactured the Gibbs respirator, the first respirator approved by the USBM for industrial use
- The Hawk's Nest Tunnel Disaster in the early **1930s** expedited Schedule 21's standards for filter-type dust/fume/mist respirators

1920–1949

1950–1969

- Schedule 21B's expansion in **1965** provided further regulation and protection for industrial workers
- The **1969** Federal Coal Mine Health and Safety Act resulted in regulations governing the certification and use of approved respirators in the mining industry

- The Occupational Safety and Health Act of **1970** established both NIOSH and OSHA to protect the health and safety of American workers
- In **July 1995**, the respirator certification regulation, 30 CFR 11, was replaced by 42 CFR 84
- The necessity for respirators in healthcare became apparent with the outbreak of TB in the **1990s**

1970–1999

2000–2019

- Congress created the NIOSH National Personal Protective Technology Laboratory in **2001**
- The focus of respiratory protection for first responders shifted after the 9/11 terrorist attacks
- Public health emergencies like the **2009** H1N1 pandemic brought attention to the importance of respirators for healthcare workers

CDC NIOSH
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

100 Years of Respiratory Protection History, https://www.cdc.gov/niosh/npptl/Respiratory-Protection-history.html
September 2019

Is this an occupationally acquired ?

- 60 yr old mortician . US born, No travel. HIV negative
- Diagnosed with with Hodgkins Lymphoma 1 yr ago
- 4 months into chemotherapy developed skin lesions over the right scapula



The path revealed necrotizing granulomatous inflammation and rare acid-fast bacilli in the dermis
Cultures subsequent grew Mycobacterium tuberculosis complex (pan susceptible) and later MAC (clarithro susceptible)
Immune work up including CD4 , IFN-Gamma receptor-STAT1 and IL-12-STAT4 assays all normal