Silica Exposure, Disease, and Prevention: Old and New
Updates in Occupational and Environmental Medicine – San Francisco March 9, 2017

Robert Cohen, MD, FCCP
Professor of Medicine
Northwestern University Feinberg School of Medicine
Clinical Professor - EOHS, University of Illinois School of Public Health
Chicago, Illinois

Goals For Today’s Talk
- Describe recent trends in silica dust lung disease
- Describe spectrum of disease
  - Silicosis
  - Lung cancer
  - NMRD
  - Renal and autoimmune disease
- Review the new OSHA standard to prevent disease

Disclosure of Financial Interest
- Funded by the Alpha Foundation for the Improvement of Mine Safety and Health
- Funded by HHS/HRSA/ORHP/BLCP & BLCE
- Employee of NIOSH/DRDS
- Funded Contractor for USDOL/OWCP & MSHA
- Provide IME’s for Occupational Lung Disease

Case 1
- PG 44 year old male with symptoms for more than 3 years.
  - Cough, sputum production, DOE
  - Multiple exacerbations with increased symptoms
- Social History – Lifelong non-smoker
- Occupational History – Makes steel parts for elevators.
- Referred for evaluation to r/o Miliary TB
Case 1 - Occupational History

- Mr. Gonzalez was born in Celeya, Guanajuato, Mexico. He came to US at age 16, at 1986
- He came to Rockford where he has lived ever since. His got his first job at age 16:
  - 2 years - Eckland Metal - Rockford – Manufactured metal screws. No significant exposures.
  - Ingersoll, Inc. - Painting pieces of engines - with brushes - no sprays - 3 months

- At age 22 until the present he worked for State Line Foundries in Roscoe Illinois
  - Manufacture parts out of steel for elevators, engines, and cars.
  - Worked a grinder, grinding off residual particles of sand from the steel products.

He describes the process as molten steel placed into a sand mold which was then cooled and placed in a cleaning machine which uses steel shot to remove the sand mold material. He reports that this process produces a lot of dust. Then the steel is then cut and ground into final product.

Case 1 - Diagnosis

- Used a paper dust mask 16 years and a half face elastomeric respirator for 6 years.
- There was local exhaust ventilation but he reports that he feels it did not remove all of the dust.

- Diagnosis – Simple Silicosis – Category 3
Lung Disease from Silica Exposure

- Results from inhalation of silicon dioxide (SiO₂) or silica in the crystalline form.
- Chronic simple silicosis
  - Usually requires 10 years of exposure
- Subacute/accelerated form
- Acute form
- PMF

Occupations where there is risk for silicosis

<table>
<thead>
<tr>
<th>Industry/Activity</th>
<th>Operations/Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agriculture</td>
<td>Plowing, harvesting, processing</td>
</tr>
<tr>
<td>Mining</td>
<td>Bagging, crusher operator, cleanup, bullgang</td>
</tr>
<tr>
<td>Road</td>
<td>Tunneling, excavation, demolition, construction maintenance</td>
</tr>
<tr>
<td>Glass</td>
<td>Raw material processing, refractory installation and repair</td>
</tr>
<tr>
<td>Ceramics</td>
<td>Bricks, tile, pottery, porcelain, dental</td>
</tr>
<tr>
<td>Foundries</td>
<td>Sand molder, shake out, core knock-out</td>
</tr>
<tr>
<td>Construction</td>
<td>Excavation, blasting, sandblasting, concrete and brick work, roofing</td>
</tr>
<tr>
<td>Fracking</td>
<td>Harvesting sand, hydraulic fracturing</td>
</tr>
</tbody>
</table>

Exposure factors in prevalence & severity of silicosis

- 3 important forms of “free” crystalline silica:
  - Quartz
  - Cristobalite
  - Tridymite

- Toxicity is greater with freshly fractured, more highly reactive particles
- Intensity and duration of exposure:
  - Prevalence of silicosis increases with increasing exposure.
- Host factors: Race - (SENSOR data showed 7 x rate in African Americans; foundry worker study showed 2 x rate of silicosis in AA compared with whites)

Chronic simple silicosis

- Usually recognized first by abnormal radiograph: upper lobe nodules
- Latency period 20-30 years
- Few symptoms and normal PFTs in early disease
- May slowly progress
Silica Exposed Population in US

- OSHA Estimates 2.2 million workers are currently exposed to silica*
  - 1.85 million in construction
  - 320,000 in general industry – fracking, foundry, brick, concrete, pottery, mining, tunneling, sandblasting
  - > 100,000 exposed to levels more than 2 times the NIOSH REL of 0.05 mg/m³ (PEL is 0.1 mg/m³)
  - Lifetime risk of silicosis after 2 mg/m³-years (20 years at 0.1 mg/m³) is 0.4% to 11%

*(Occupational Exposure to Respirable Crystalline Silica. Federal Register. 81 FR 16285)

Estimates of over-exposure

- 1.3-1.9% of construction, foundry and metal service workers estimated to be exposed to silica levels 10 time OSHA guidelines
- 6% of stone workers exposed to levels above OSHA standards


Enforcement

- Workplace may be tested voluntarily by management or by regulatory agencies
- Agency inspection may occur due to
  - routine evaluations
  - worker complaint
  - detection of sentinel cases

Case 2

- RJ was a 47 year old male admitted with a 3 week history of increasing cough and sputum production.
- PMH: Negative except for prior episodes of chest colds. No meds, NKA. No pets, no travel
- ROS: No fevers, chills, weight loss.
- Social: Positive 30 pack year tobacco exposure. ETOH occasionally. No drugs
Case 2 – Continued

- Occupational History: Worked in “construction”
- Physical exam: Afebrile Pulse 92, RR 18, BP 137/84
  - Remarkable for coarse breath sounds otherwise normal
- CXR and CT scan

Case 2 – Continued

- Real Occupational History:
  - Left high school and began working at age 17
  - Began working for demolition companies as an independent contractor – now 30 years.
  - Tearing down buildings – specialized in taking down concrete walls, floors, and ceilings.
    - He drilled into concrete walls, inserted hooks, and pulled down walls
    - Frequently used a jackhammer
    - Worked on demolition in CTA tunnels, drilling and jackhammering

Case 2 – Continued

- Work in Tunnels in Chicago
  - CTA and Deep Tunnel Project – Total 9 years
  - Never used respiratory protection
  - Worked 45 minutes underground and went up for air for 15 minutes each hour.
  - Noted he could barely see co-workers working 25 feet away
  - Had frequent cough productive of dusty sputum while on the job.
- PPD Negative, AFB X 3 negative, cultures negative –
- Diagnosis – Silicosis with Progressive Massive Fibrosis

Progressive massive fibrosis (PMF)

- Mass > 1 cm in diameter
- Mixed pattern of restriction and obstruction on PFTs
- Cicatricial emphysema may be seen.
- Usually symmetric, occasionally R>L
- Asymmetry, rapid growth, and cavitation possible, but should prompt search for mycobacterial disease or cancer
Other silica-related health effects

- Lung cancer
- Industrial bronchitis & COPD
- Lung Function Impairment
- Autoimmune Disorders
  - Systemic Sclerosis – Erasmus Syndrome
  - Lupus
  - Rheumatoid Arthritis
  - Caplan’s syndrome
  - Granulomatosis with Polyangiitis - GPA
- Pleural abnormalities
- Renal Disease
- Mycobacterial infections: Tb and NTM

Mechanism

- Silicon (Si) 28% earths crust
- Silica (SiO₂)= quartz, flint, sand (crystobalite, tridymite)
- Silicates (SiO₄)= numerous and various
- Silicic acid (H₄SiO₄)= soil water
- Adjuvant immune response (Animal models)
- Activate monocytes and macrophages to release cytokines, oxygen radicals, and lysosomal enzymes (e.g. PR3 and MPO)

Silica and Lung Cancer

- In 1987 The International Agency for Research on Cancer (IARC), based on animal experiments, came to the conclusion that there was sufficient evidence that crystalline silica was a carcinogen in experimental animals.
- Classified as Group 2A carcinogen i.e. probably carcinogenic to humans

Lung cancer and silica exposure

- IARC 1996, 2012: Silica classified as a Group 1 substance “carcinogenic to humans”.
- Association seen in autopsy series, case-control studies of workers with silicosis, patients with lung cancer, population-based studies of silica-exposed workers. Strongest association with lung cancer occurs in those with silicosis.
- Association seen in miners, foundry, quarry and diatomaceous earth workers; in multiple countries.
Confounders

- Tobacco
- Radon exposure – underground miners (gold miners of South Africa)
- Arsenic
- Asbestos – steel workers
- Effects of scarring (scar carcinoma) in silicosis

Lung cancer and silica exposure

- Steenland et al.* pooled data on 65,890 workers from 10 studies
  - 44,160 miners
  - 21,820 non-miners
  - 1072 lung cancer deaths.
- Quintiles of lifetime exposure
  - Log cumulative exposure was a strong predictor of lung cancer
  - Lifetime risk through age 75 was 1.1-1.7% above background of 3-6%

Liu et. al. studied Chinese tungsten and iron miners and ceramic workers

- Followed 34,018 workers from 1960-2003
- Followed for 34.5 years
- Developed JEM
- 546 Cancer deaths
- Quartiles of lifetime exposure
  - 25 year lagged og cumulative exposure was a strong predictor of lung cancer
  - Smoking and silica were close to multiplicative
  - Lifetime risk through age 65 was 0.51% above background

Conclusions

- Clear relationship between exposure to free silica and development of lung cancer
- Consistent between surrogates for exposure and quantitative exposure estimates
- Relationship to other diseases confirms cumulative exposure calculations
- Cumulative exposure not a surrogate for tenure
- Old OSHA PEL may not be fully protective

Silica exposure, silicosis and mycobacterial disease

- 3-fold increased incidence of Tb in patients with chronic silicosis. [Cowie, AJRCCM 1994]
- Incidence of active TB increases with increasing profusion score. Highest incidence in those with acute and accelerated silicosis. [Ziskind, ARRD 1976]
- In U.S., about 50% of mycobacterial disease in silicotics is due to NTM. NTM in New Orleans sandblasters: M. kansasii (41%), M. intracellulare (14%). [Bailey, ARRD 1974]

Acute silicosis/silicoproteinosis

- Requires intense high exposures – often associated with sandblasters
- Symptoms appear within weeks to 2 years of exposure
- Pathologic findings of alveolar proteinosis

Silica exposure and COPD

- Increased symptoms of chronic bronchitis in silica-exposed with silicosis.
- Emphysema – silica potentiates effects of smoking [Hnizdo Scand J Work Env Health 1998]
- Accelerated rates of FEV1 decline reported in several industries using silica:
  - 87 ml/yr drop in miners with silicosis [Cowie ARRD 1991]
  - Similar excess declines in granite crushers, concrete and pottery workers [Hnizdo OEM 2003]

Silica exposure, silicosis and mycobacterial disease

- 3-fold increased incidence of Tb in patients with chronic silicosis. [Cowie, AJRCCM 1994]
- Incidence of active TB increases with increasing profusion score. Highest incidence in those with acute and accelerated silicosis. [Ziskind, ARRD 1976]
- In U.S., about 50% of mycobacterial disease in silicotics is due to NTM. NTM in New Orleans sandblasters: M. kansasii (41%), M. intracellulare (14%). [Bailey, ARRD 1974]
Lung Function Impairment and Coal Mine and Silica Dust

- Exposure to coal dust related to deficits in ventilatory function: FEV1 and VC.
- Deficits occur regardless of presence or absence of radiologic pneumoconiosis.

Dust Related Diffuse Fibrosis

- Disease often confused with Idiopathic Pulmonary Fibrosis (IPF).
- Cannot be idiopathic when there is significant exposure to mineral dust.
- Irregular opacities on CXR with low diffusion on lung function and restrictive impairment.
- Bridging fibrosis connecting macular, nodular, or PMF lesions.
- Pigmented interlobular septal thickening.

IPF

By international consensus\(^1\) the diagnosis of IPF requires

- Exclusion of other known causes of ILD (e.g., domestic and occupational environmental exposures, connective tissue disease, and drug toxicity).
- There is no basis for this diagnosis in a subject with substantial occupational exposure to dust.

Silica and Autoimmune Diseases

- Rheumatoid arthritis – Caplan’s syndrome
- Systemic lupus erythematosus (SLE)
- Systemic sclerosis – Erasmus Syndrome
- Others

Silica also associated with other autoimmune diseases

- MCTD/SLE - Overlap Syndrome
- Sjögren’s syndrome
- ANCA Associated vasculitis – MPA, GPA
- Polymyositis - Dermatomyositis
- Bullous pemphigoid
- Autoimmune renal disease

Silica associated with SLE

Prevention of Silica Related Disease

New OSHA Standard
Effective June 23, 2016

Old Standard

- PEL = 10 / (\%quartz + 2) mg/m³
  - OSHA regulation for non-mining industrial workplace (TWA)
- 0.05 mg/m³ respirable crystalline free quartz
  - NIOSH

New OSHA Final Rule Enacted

- Reduces the PEL to 0.05 mg effective June 23, 2016.
- Provides medical exam to monitor highly exposed workers
- Construction - June 23, 2017, one year after the effective date.
- General Industry and Maritime - June 23, 2018, two years after the effective date.
- Hydraulic Fracturing - June 23, 2018, two years after the effective date for all provisions except Engineering Controls, which have a compliance date of June 23, 2021.
- Now Under Challenge by Industry
  - Amicus Brief Submitted by ATS
  - Industry called for delay which was not opposed by Trump administration
Prevention of Silicosis – New OSHA Standard
- Current PEL Enacted in 1971
- NIOSH recommended reduction in PEL in 1974
- Current ACGIH 25 µg/m³
- OSHA Proposed the new rule 9/12/13
- New rule effective 6/23/16
- Now facing court challenge
- ATS and ACOEM filed an amicus brief supporting the new OSHA rule 2/10/17

Prevention of Silicosis – New OSHA Standard
- Final PEL of 50 µg/m³ 8 hour TWA.
- Action level of 25 µg/m³ for enhanced exposure assessment.
- Medical Surveillance new component in the rule
  - Required for workers exposed to > 25 µg/m³ for > 30 days out of the year or constructions workers required to use respirators for > 30 days.
  - Includes:
    - History and Physical
    - Pulmonary Function testing – spirometry on hire and every three years

Prevention of Silicosis – New OSHA Standard
- CXR – single PA radiograph on hire and every three years classified by a NIOSH certified B-reader.
- B-reading of > 1/0 requires referral to board certified pulmonologist or occupational medicine specialist
- Other testing as required
  - Creatinine, urinalysis
  - TB testing
  - HRCT scanning for NMRD or lung cancer screening
  - Serologies for collagen vascular disease

Silica exposure has been associated with all of the following except:

A. Renal Disease
B. Tuberculosis
C. Lung Cancer
D. Myocarditis
Silica Related Lung Disease is a broad spectrum of diseases. Which disease has not been shown to result from silica dust exposure?

A. Nodular interstitial lung disease  
B. Emphysema  
C. Asthma  
D. Alveolar proteinosis

Studies of lung cancer in association with silica exposure have been confounded with all of the following except:

A. Diesel exhaust particulate  
B. Tobacco smoke exposure  
C. X-ray exposure  
D. Radon exposure