Occupational Lung Disease

Dr. Neil Colman
OEMAC Conference
September 29, 2013

Conflict of Interest

• NONE
Elements of the Occupational History

- Complete
- Determine exposures – direct and indirect
- Anyone else ill?
- Any job – many different exposures
- Any exposure – many different jobs
Pneumoconiosis: Criteria for Diagnosis

• History of exposure, with suitable latency
• Abnormal radiology
• Lack of alternate explanation

Asbestos

• A group of fibrous minerals composed of combinations of silicic acid with Mg, Ca, Na and Fe.
• Two major groups: serpentes (long, curly strands—chrysotile) amphiboles (long, straight rod-like structures—amosite crocidolite, tremolite)
Asbestos - where is it used?

- Brake pads – heat resistant
- Electrical wiring - electrical resistant
- Buildings – insulation and flame resistance
- Ship building
- Railroads
- Refineries
- Up to 9 million workers are exposed in the USA

Exposures

- Mining and milling
- Industrial applications (insulation, cement, textiles, ship-building, cement etc)
- Demolition, construction
- Health risk to occupants of buildings where asbestos is in good repair and undisturbed is not considered significant
Non-occupational Exposures

• May be important in certain settings; e.g. contaminated gravel containing roads, naturally occurring dusts (Southern California)
• Household contacts
Disorders caused by asbestos

• Pleural disease: benign asbestos effusion pleural plaque diffuse pleural thickening mesothelioma
• Parenchymal disease: asbestosis round atelectasis peribronchiolar fibrosis pulmonary carcinoma
Findings in the Normal Elderly

- Groups older than 75, younger than 55
- No known respiratory disease
- Non smokers, no drugs, CVD, occupational exposures etc
- Subpleural reticular opacities found in 24/40 elderly (40%) and none in younger patients

Axial prone thin-section CT image of a 92-year-old woman who had normal pulmonary function shows a subtle bilateral subpleural basal reticular pattern of limited extent (grade 2).

Axial prone thin-section CT image of an asymptomatic 78-year-old woman who was a non-smoker and had been a city dweller for 39 years.

Clinical Manifestations

- History — Latency inversely proportionate to intensity of exposure — usually asymptomatic for 20-30 years after initial exposure
- Physical Exam
Management

- Smoking cessation paramount not only for prevention of malignancy but to diminish risk of progression of asbestosis
- Symptomatic management — oxygen etc.

Pulmonary Function Testing

- The hallmark of asbestosis is said to be restriction with a low diffusing capacity
- However, many patients also have significant airflow obstruction (Kilburn) (smoking, asbestos airways disease, emphysema) with preservation of TLC
- Hypoxemia and worsening gas exchange on exercise
- Impact of pleural disease
Diagnosis

• Blah, blah, but chest radiograph may be normal
• HRCT more sensitive and in questionable cases, should be done in the prone position also

Round atelectasis
Pleural Plaque

• Occurs in about 50% of asbestos-exposed individuals with calcification occurring in 20% (cxr), 50% (CT) and 80% (autopsy) of affected persons
Benign pleural effusion

- Usually small and unilateral but can be larger and bilateral
- Exudative, often hemorrhagic
- Eosinophilia on pleural tap
- Often asymptomatic, may have acute pleuritis
- Need to differentiate from mesothelioma
- Diagnosis of exclusion—may resolve spontaneously
- Visceral pleural thickening a common consequence

Mesothelioma
Lung cancer

- Increased risk of pulmonary carcinoma
- Dependent on exposure intensity and time
- Cigarette smoking is synergistic (59 fold increased risk in exposed smokers vs. non-exposed, non-smokers)
- Risk higher with amphiboles but still significant for chrysotile
- Patients with asbestosis have a 50% chance of developing a pleuropulmonary malignancy

Other Cancers

- Laryngeal cancer is causally related to asbestos exposure with ovarian cancer also carrying a standardized mortality ratio of 1.77 in asbestos-exposed individuals
- Suggestive but not conclusive evidence available for pharynx, stomach, colon and rectum
Lung cancer and asbestos exposure—attrition

- Important legal ramifications
- What is done in Quebec

Definition

- Silica: a mineral composed of regularly arranged molecules of silicon dioxide
- There are three forms:
  - crystalline: quartz, cristobalite
  - microcrystalline: flint, chert
  - amorphous: kieselguhr
Definition

• Silicosis is a spectrum of pulmonary disease caused by inhalation of free crystalline silica (silicon dioxide)

Quartz

• A type of crystalline silica
• Major component of soil and rocks – drilling, cutting, quarrying, breaking, crushing
• Heating crystalline silica or amorphous silica (foundries) produces cristobalite and tridymite
• Emerging sources of exposure include fracking with another outbreak related to sandblasting denim in the textile industry
• Exposures to sandy soil might be a concern (farming)
continued

• Potential exposure in 2 million workers in the USA, with 100,000 of those being at risk for high-risk exposure
• Although control measures are improving, a significant number of workers have exposures in excess of permissible limits
• Silicosis is still the cause of death in 100-200 workers annually in the USA, but a 10 fold decrease since the late 60’s
• situation much worse in “developing” countries

---

continued

• The current ACGIH TLV standard for exposure to respirable crystalline silica is 0.025 mg/m³ but most workers continue to have exposure in excess of this value; 3.6% of workers have exposures in excess of the less restrictive OSHA limits.
• Current Quebec standard is 0.05 to 0.1 mg/m³ (conforms to OSHA but may not be completely protective)
• Diagnosis based on chest x-ray underestimates true prevalence
Radiologic Manifestations

- Small opacities
- Large opacities
- Hilar abnormalities
- Caplan’s syndrome
- Pleural abnormalities
- CT and HRCT
Clinical Manifestations

- Disease occurs after a long exposure to dust and symptoms as well as radiographic abnormalities and may follow withdrawal from exposure
- “accelerated silicosis” = 5-10 years of exposure
- Lymph node “silicosis” alone can occur with lower exposures and may precede parenchymal disease

Pulmonary Function

- May be restrictive or obstructive or both
- Exposure to dust has been associated with both airways disease and with the development of morphologic emphysema, after accounting for the effects of smoking
- Emphysema is more common in workers who have silicosis than in similarly exposed workers who do not
Prognosis and Natural History

• Simple nodular silicosis--life expectancy same as non-exposed population
• complications account for much of the morbidity

Complications of Silicosis

• Lung cancer
• Increased susceptibility to tuberculosis
• Autoimmune disease
• COPD
• Chronic renal disease
Silicosis and Lung Cancer

- Recognized as occupation carcinogen by IARC in 1997
- Risk is higher in the presence of silicosis (about double) than in its absence (RR 1.2) the latter being marginal from the point of view of statistical significance
- Literature compromised by biased or incomplete ascertainment of silicosis, inadequate exposure assessment, and the inherently strong correlation between silicosis and exposure
- Seen in industries without exposure to other carcinogens
- Seen in non-smokers
- Oncogene distribution is unique
- What we do in Quebec

Silicosis, Tuberculosis and other infections

- Silicosis predisposes to tuberculosis, NTM and fungal infection of the lung
- TBC prevalence depends on prevalence of TBC in any given population
- In South Africa, half of the patients are HIV +
- Risk increases with profusion of simple nodular opacities and with the presence of PMF
- May be difficult to identify the organism when there is PMF
A recent review of 790 patients with silicosis revealed RA in 33 (4.2%), scleroderma in 2 (0.3%--Erasmus syndrome) and ANCA vasculitis in 6 (0.8%) providing prevalence ratios of 2-7 for RA, 28.3 for scleroderma, and 25.3 for ANCA-vasculitis.

Smokers who have silicosis are at an especially increased risk.

Silicosis and CVD
Berylliosis

- A granulomatous disease due to exposure to beryllium
- Similar clinically and histopathologically to sarcoidosis

Diagnosis

- History of beryllium exposure
- Positive BeLPT
- Noncaseating granulomas on lung biopsy
- “sensitization” = positive BeLPT in blood or BAL without path (or radiology)
Exposure-Response

• Dose and duration of exposure are associated with risk of sensitization and disease but results are not linear
• Quebec limits are very stringent but sensitization can occur even with very low exposures of short duration, likely related to specific genetic susceptibilities
• Community-acquired cases have been described, sometimes with very long latency after cessation of exposure

Clinical Manifestations

• Similar to sarcoid, non-specific, but including fatigue
• Cutaneous nodules can be seen
Laboratory

• ACE not useful
• Hypercalcemia and hypercalciuria can be seen
• BeLPT necessary
• Diagnosis of sarcoid often made since exposure history not obtained; Beryllium-exposed workers are not immune from sarcoidosis

BeLPT

• Lymphocytes are exposed to three different concentrations of Be at two different times—two or more positive results indicate an abnormal test (one is borderline)
• Sensitivity of a single test is 0.68, high specificity
• Test repeated if negative or borderline
• At CSST, test is sent to two different laboratories
• In the presence of disease, still 30% false negative after two tests; therefore more tests
Diagnosis

- Beryllium lymphocyte proliferation
- BAL
- biopsy

Occupation and COPD

- Population Attributable Risk of 15%; 40% in non-smokers
- At a minimum, work-place exposures are additive to the effects of smoking
- Consistency, strength, and plausibility of the data support a causal relationship between occupational exposures and COPD
Limitations

- ATS conclusions (2003) based on 20 different publications (only)
- “breathlessness” and “chronic bronchitis” are poor surrogates for established COPD
- BUT, correction was made for smoking and data is highly consistent

Later Studies (2007)

- Compared to non-smoking, non-exposed to vapors, gases, dusts or fumes in the workplace during longest-held job:

- Odds Ratios for COPD or emphysema (excludes chronic bronchitis):
  - 2.4 for occupational exposure alone
  - 7.0 for smoking alone
  - 18.4 for both
Even Later Studies

• Have confirmed earlier analyses and are in keeping with an additive effect of smoking and occupational exposures.
• In areas where occupational exposures are more prevalent and/or in regions where smoking prevalence is declining, then occupational causes become relatively even more important

Work-related Asthma—Current Terminology

• **Work-exacerbated asthma**: pre-existing or concurrent asthma that is worsened by workplace conditions (ATS)
• **Occupational Asthma**: asthma attributable to a particular sensitizing exposure in the workplace and not due to stimuli found outside the workplace
• Even this classification is subject to discussion...
How common?

• Estimates are that 5%-10% of adult patients who have new onset asthma have OA
• Therefore any asthmatic—begin with that first important question
• 2%-8% of workers exposed to HMW compounds (lab animals, latex, flour dust) will develop OA with sensitization being more common within the first few years of exposure
• 5%-10% of workers exposed to LMW compounds (isocyanates, methacrylates, amines) will develop OA

Agents Responsible for OA

• Over 350 agents have been described and can occur in thousands of different settings:
Health-care workers and OA

- Latex
- Glutaraldehyde
- Antibiotics
- Psyllium
- Aerosolized medications
- Methacrylates
- Isocyanates
- Metals in dental alloys
- Formaldehyde
- Quaternary ammonium compounds
Risk Factors for OA

• Exposure intensity—initial high-dose exposure may sensitize, then reactions can occur with very low dose exposure
• The nature of the exposure; e.g., animals >> latex
• Atopy—for HMW exposures (30% risk)
• Cigarette smoking with some agents
• Genetics explains at least part of the risk

Diagnosis

• Sensitizing agents can be recognized in most patients who have OA
• What is a fiche
• Onset follows a latency period varying from weeks to years; symptoms occur at work but may also follow the work day
• Following sensitization, even low exposures can provoke asthma
• Improvement seen with withdrawal from exposure
• Diagnosis should be proven
• Distinguish from asthma worsened in the workplace—history alone is not sufficient for diagnosis—sensitivity is good but specificity is poor
• Eliminate alternate diagnoses: hyperventilation, VCD, rhinitis, cardiac disease etc

Objective Testing
• Pft and methacholine in a symptomatic patient should confirm a diagnosis of asthma
• A major tool is specific provocational testing in the lab and/or in the workplace
• Responses are commonly “dual” and associated with an increase in airway hyperresponsiveness and sputum eosinophilia
Why Important

• Outcome improves with early removal from the workplace but the majority has residual disease
• Other workers may require protection and identification
• Many medico-legal issues

Work-exacerbated asthma

• Up to 20% of asthmatics will have worsening in the workplace; WEA is pre-existing or concurrent asthma worsened in the workplace
• Irritant chemicals, dust, second-hand smoke, allergens (not unique to workplace such as molds), physical exertion, cold, stress...
• Effects are comparable to those of OA
• Improvement in asthma with withdrawal from exposure (but perhaps less than with OA)
Criteria for Diagnosis

• Pre-existing or concurrent asthma (onset while employed but asthma not due to exposures at work—but are some of those really “low-dose” irritant-induced asthma?)
• Asthma-work temporal relationship (self-report, medication use, objective data)
• Conditions at work can exacerbate asthma
• OA unlikely

Occupational Rhinitis

• Can be irritant (with immediate response)
• When allergic, there is a period of latency while allergic responses develop
• Rhinitis frequently antecedes onset of occupational asthma-the typical history
• Irritant exposures may prime the airway for increased allergic response and pre-existing inflammation may augment intensity of allergic response
Work-related Irritable Larynx Syndrome

• Hyperkinetic laryngeal symptoms triggered by odours or irritants in the work place
• Includes VCD, dysphonia, globus, or chronic cough
• These conditions can imitate or exist with work-related asthma

Irritant-induced asthma

• What is RADS
• Is there anything else
How do things work in Quebec

• CMPP

What to do

• Fill out the forms
Whom to refer

• All patients suspected of having occupational lung disease
• Plaque alone or silicotic nodes alone do not constitute a pneumoconiosis

Whom to remove from work

• All patients with pneumoconiosis
• All patients with occupational asthma
• Patients with work-exacerbated asthma...tricky business but consider workplace conditions, severity of illness