Pneumoconioses

- The accumulation of dusts in the lung and reactions, if any, to them
- Radiographically evaluated by B-readers using ILO classification
- CT more sensitive

Which Pneumoconioses Are Fibrogenic?

<table>
<thead>
<tr>
<th>Fibrogenic dusts</th>
<th>Non-fibrogenic dusts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silica (crystalline)</td>
<td>Tin (stannosis)</td>
</tr>
<tr>
<td>Mica</td>
<td>Barium (baritosis)</td>
</tr>
<tr>
<td>Graphite</td>
<td>Iron (siderosis)</td>
</tr>
<tr>
<td>Beryllium</td>
<td></td>
</tr>
<tr>
<td>Coal dust</td>
<td></td>
</tr>
<tr>
<td>Asbestos</td>
<td></td>
</tr>
<tr>
<td>Talc</td>
<td></td>
</tr>
<tr>
<td>Hard metal</td>
<td></td>
</tr>
</tbody>
</table>

Not all patients with pneumoconiosis from the above develop fibrosis
Silicosis

- Silica = SiO$_2$
- From exposure to crystalline silica
- Most common occupational lung disease worldwide
- Characterized by upper lung field nodules
- Can be complicated by:
  - Lung cancer
  - TB

What is this?

Coal workers' Pneumoconiosis
“Black Lung”

- Caused by iron in coal dust

**Types**

Simple coal workers pneumoconiosis
CWP complicated by fibrosis
Silicosis
COPD

- Pathognomonic lesion is the coal dust macule = coal dust filled macrophages
- Smoking not a risk factor
- Not an accepted risk factor for lung ca
- Exposure limits based on amount of silica exposure
What do you see in this slide?

Asbestos

- Natural hydrated magnesium silicate fibers
- OSHA expresses the asbestos PEL as fibers/mm³ in air
- All disease caused only by inhalation exposure
- It is not systemically absorbed by any route but inhaled fibers can migrate

Types of Asbestos Fibers

2 types
1. Serpentine ("white asbestos")
   - chrysotile
   - Fibers tend to be degraded after inhalation
   - Curly fibers
2. Amphiboles ("brown asbestos")
   - 5 sub-types (most disease assoc. with crocidolite)
   - Fibers resist degradation
   - Tendency to migrate
   - Straight fibers
   - This is the form that causes mesothelioma
Asbestos – Related Diseases

• Only clearly established target organ is lung and surrounding tissues
• All have long latencies
1. Asbestosis
2. Malignancies
   A. Bronchogenic carcinoma
   B. Mesothelioma
   C. Larynx
   D. Ovary
3. Non-malignant pleural disease
• Does not cause: COPD

Asbestosis

• A fibrogenic pneumoconiosis
• ↑ Risk c smoking
• Due to persistent inflammation of non-degradable fiber
• CXR may be read by B-reader
• HRCT is better

2 Pulmonary Asbestos-Related Malignancies Established

Bronchogenic Ca
• Risk ↑ > 10 X for smokers
Mesothelioma
• Only non-asbestos cause = eronite (a naturally occurring fiber found in Turkey)
• No ↑ risk with smoking
Asbestos-Related Pleural Disease

- Effusions
- Plaques
  - The most specific sign of asbestos exposure
- Pleural thickening
- Rounded atelectasis

Diagnosis of Asbestos-Related Diseases

- Asbestos bodies are only a marker of exposure, not dose or disease
- Fiber counts
  - Obtained PM, or by bx (not BAL)
  - Correlate with dose, hence risk
- CXR
  - Useful but can be of low sensitivity
- CT (partic high resolution)

ORGANIC TOXIC DUST SYNDROME

- Occurs after inhaling dust containing large amounts of mold spores
- May be due to spores or substances produced by them
- Immunological reaction
Cyanide

• HCN causes the acute toxicity
• pKₐ = 9.5
• So, HCN formed if pH < 10-11
  Ex.
  NaCN + HCl → ↑HCN + NaCl
• This can even happen with H₂O such as when cyanide salts are used in fumigation or rodent burrows

Cyanide detoxification

• Naturally occurs by combination with sulfane sulfur to form thiocyanate
• Rapidly taken up into RBCs
• Has high affinity for Fe³⁺
• Has high affinity for Co²⁺
Cyanide Poisoning

**ACUTE**
- > 10 PPM toxic effects
- > 100 PPM: potentially lethal
- Metabolic acidosis
- Lactic acidosis
- Encephalopathy in brain and myocardium
- Carotid body stimulation → hyperventilation
- Inhibits glutamate decarboxylase → ↓ GABA
- Persistent neuro deficits possible
  - One of the basal ganglia toxins

**Chronic**
- SCN⁻ competes with iodine for uptake into thyroid → goiter & hypothyroidism.
Diagnose CN⁻ poisoning by serum (or plasma) levels

- These best correlate with tissue levels.
- Whole blood levels may be artificially elevated during the analysis.

Methemoglobin as a cyanide antidote

- Effective because:
  - Affinity of CN⁻ for Fe⁺³
  - Concentration of CN⁻ in RBCs
- Sodium nitrite:
  - Dose: 300 mg (adult) = 10 cc of 3%
  - Generates MetHg fraction in the teens
  - MetHb fraction ↑ with anemia or children so ↓ dose
  - Pediatric dose (of HCT) 10 mg/kg = 0.33 cc of 3%/kg
  - May also work as a vasodilator
- 4-Dimethylaminophenol
  - Also a MetHb former
  - Used primarily in Germany

\[
\text{MetHb} \rightleftharpoons \text{CN}^- \rightleftharpoons \text{Cytochrome aa}_3
\]
Sodium Thiosulfate

- Source of sulfane sulfur
- Synergistic with nitrites (or hydroxocobalamin)
- Adult dose 12.5 grams (50 cc of 25%)
- Pediatric dose:
  - 410 mg/kg (1.65 cc of 25%/kg)

The antidotal treatment of cyanide poisoning has completely changed

- The old – cyanide treatment kit
  1. Amyl nitrite pearls – good for getting high, doesn’t do much for cyanide toxicity
  2. Sodium nitrite
    1. MetHb former
    2. Vasodilator
  3. Sodium thiosulfate – complexes with CN–
- The new – hydroxocobalamin

Hydroxocobalamin

What it is
- "Vit B12" (cobalamins) = a group of compounds that can be interconverted
- Hydroxocobalamin (HC) is one
- The most common is cyanocobalamin
- The active form is methylcobalamin.
- HC + CN– → cyanocobalamin (irreversible)

Methylcobalamin Urine

Geraci 2011
Doses of hydroxocobalamin to know

- Adults:
  - 5 g IV over ≥15 min
- Peds:
  - 70 mg/kg over ≥ 15 min
- Adverse effects:
  - Flushing
  - Turns skin red
  - Interferes with colorimetric tests
  - ↑BP

NITROGEN OXIDES

- NO\textsubscript{x} =
  - Nitric oxide (NO)
  - Nitrogen dioxide (NO\textsubscript{2})
  - Nitrogen tetroxide (N\textsubscript{2}O\textsubscript{4})
- NO\textsubscript{2} has low water solubility
  - Penetrates deep into resp tract
  - Causes oxidative injury
  - Excreted after oxidation as nitrate
  - Chronic low level exposure can cause ↑ airway reactivity and respiratory illnesses.
- NO has low water solubility
  - Penetrates deep and is absorbed as NO
  - Very high affinity for Hb → metHB
  - Excreted as urinary nitrate.

Sources of NO\textsubscript{x} to know

- Major environmental source is the burning of fossil fuels
- Contact of nitrogen acids with organic material
- Ice skating rinks (from Zambonis)
- Welding
- Gas stoves
- Silos (Silo Filler’s disease)
Acute inhalation of NO\textsubscript{x} may have a multiphasic course

1. Acute pulmonary sx at time of exposure
   - CXR may be normal at this time
   - Initial sx can be mild
   - Can see bronchospasm
   - Use minimal oxygen supplementation
2. May have asymptomatic period of hours (up to 12)
3. May then develop ALI (can see methemoglobinemia in this stage)
4. Apparent recovery
5. May develop BO up to a month after exposure
   - Initially prevents as acute febrile illness
   - May occur even in absence of stage 3
6. Some patients may develop chronic bronchitis with obstructive or restrictive patterns on PFTs

Sulfur Oxides

SO\textsubscript{2} is the principal one
- Highly irritating
- Water soluble → affects upper resp tract and mucus membranes and bronchoconstriction
- Massive exposures can cause deep pulmonary injury
- Pungent odor

What causes the effects of SO\textsubscript{2} exposure?

Effects may be due to:

1. SO\textsubscript{2}
2. H\textsubscript{2}SO\textsubscript{4}
3. Bisulfite (strong bronchoconstrictor in asthmatics)
   - Asthmatics and atopics have ↑ susceptibility
4. Hydrogen bisulfite
H₂S

- Irritant
- Rotten egg odor
- Combines with Fe³⁺
- Sources:
  - Decomposition of organic matter
  - Oil wells/petroleum refineries
  - Kraft Paper mills
  - Smelters
  - Tanning processes
  - Natural springs
  - Waste water treatment
- Can be released when sulfur containing molecules are acidified

H₂S Poisoning

- "Gas eye": Keratoconjunctivitis
- Mucus membrane and pulmonary irritant
  - Impairs ciliary action → pneumonia
- Pulmonary edema/ARDS
- Respiratory depression at approx. 1,000 PPM
- CNS depression
- AA3 poison
- Non-specific enzyme inhibitor
- Forms sulfHb, but levels not clinically predictive
- Darkens coins
- Does not bioaccumulate

Treatment of H₂S Poisoning

- Supportive care/O₂
- Rescuers beware:
  - Knock down potential at approx. 1,000 PPM
  - Olfactory fatigue at approx. 100 PPM
  - Rescuers have been poisoned by mouth-to-mouth resuscitation
- ? methHb induction with sodium nitrite
  - No role for thiosulfate
- HBO - anecdotal
Extrinsic Allergic Pneumonitis

• AKA: hypersensitivity pneumonitis
• Ex: Farmer’s lung, Bird-Feeders Lung
• Alveolar inflammation d/t hypersensitivity rxn to inhaled organic dusts (most often fungal spores from mold)
• 2 Forms:
  = Acute:
    • Sxs start w/ hours and resolve w/ days of exposure.
    • Dyspnea, constitutional sxs, hyposxia
    • Abnormal CXR, CT(high-res is best), DLCO
  = Chronic:
    • Slow and progressive onset and partial resolution
    • Fibrotic pulmonary changes
    • May require lung bx for DX
• RX: avoid re-exposure, corticosteroids

PATHOGENESIS
OF EAA

That’s it.
Good Luck on the boards!!