Occupational Hematology

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Assistant Professor of School of Medicine
Occupational Exposure

- Blood Cell Survival (Denaturated Hb & Hemolysis)
- Metabolism (Porphyria)
- Blood cell Formation (Aplasia)
- Hematopoietic Neopelasms (Preleukemia & leukemia)
- Coagulation (Thrombocytopenia)
- Decreased Oxygen Saturation (CO)
Disorders Associated With Shortened Red Blood Cell Survival

• Methemoglobinemia and Hemolysis Produced By Oxidant Chemical
• Hemolysis Associated With Exposure To Heavy Metals
• The Porphyrias
Methemoglobinemia and Hemolysis

Produced By Oxidant Chemical

• Methemoglobin is formed by oxidation of ferrous Hb (Fe2+) to ferric Hb (Fe 3+)
• Ferric Hg : incapable of delivering oxygen to the tissues
• An NADH-dependent enzyme, methaemoglobin reductase, reduces ferric iron back to ferrous Hb
**Heinz body anemia**

- Oxidation of Hb was toxic to RBC and could be followed by and acute hemolysis known as **Heinz body anemia**

- Heinz body are RBC inclusions that represent precipitated Hb are classically seen in individuals with a deficiency G6PD after exposure to an oxidant stress
Pathophysiology of Oxidant Hemolysis

• Oxidation Hb → Denaturation Hb → Precipitated Hb within RBC → Alter the surface membrane of RBC and increased rigidity and leakage → Extravascular hemolysis → Bite cell or blister cell
### Chemicals associated with methemoglobinemia or oxidative hemolysis

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aniline</td>
<td>Rubber, dye stuffs, production of MBI (Methylene Bisphenol Isocyanat)</td>
</tr>
<tr>
<td>Nitroaniline</td>
<td>Dyes</td>
</tr>
<tr>
<td>Toluidine</td>
<td>Dyes, organic chemicals</td>
</tr>
<tr>
<td>P-Chloraniline</td>
<td>Dyes, pharmaceuticals, pesticides</td>
</tr>
<tr>
<td>O-Toluidine</td>
<td>Laboratory analytic reagent, production of trypan blue stain, chlorine test kits, test tapes</td>
</tr>
<tr>
<td>Naphthalene</td>
<td>Fumigants used in clothing industry</td>
</tr>
<tr>
<td>Paradichlorobenzene</td>
<td>Fumigants used in clothing industry</td>
</tr>
<tr>
<td>Nitrates</td>
<td>Soil fertilizers</td>
</tr>
<tr>
<td>Trinitrotoluene</td>
<td>Explosives</td>
</tr>
</tbody>
</table>
## Clinical presentation

<table>
<thead>
<tr>
<th>Met-Hb %</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-30</td>
<td>Cyanosis, Mild fatigue, Tachycardia</td>
</tr>
<tr>
<td>30-50</td>
<td>Weakness, Breathlessness, Headache, Excise intolerance</td>
</tr>
<tr>
<td>50-70</td>
<td>Altered consciousness</td>
</tr>
<tr>
<td>&gt;70-80</td>
<td>Coma, Death</td>
</tr>
</tbody>
</table>
Clinical presentation

- Patient appear deeply cyanotic (Blue worker)
- Normoxia or mild hypoxia at pulse oximetry
- Normal oxygen tension in ABG
- CO-oximetry
- Reticulocytosis in PBS
- Bite or blistered red cell in PBS
- Polycythemia in chronic methemoglobinemia
- Heinz body anemia +/- methemoglobin formation
Prevention

• Minimize atmospheric and cutaneous exposure to oxidizing chemicals such as coal tar

• Biologic monitoring in the workplace by measuring methemoglobin levels and reticulocyte counts

• Screening for G6PD deficiency before a hemolytic episode or 1-2 month after the hemolysis
Treatment

- Removal of the offending agents
- Decontamination
- Mild intoxication (<\%20) → observation
- Moderate to severe (>\%30) → oxygen\%100, methylene blue solution %1 at a dose of 1-2 mg/kg over 10 minutes
- Exchange transfusion
Aniline

- **Use in:** synthesis of aniline dyes, accelerator and antioxidant in rubber industry, production of pesticides, plastics, paints and varnishes

- Fat-soluble and readily penetrate the skin, even through clothing

- Vapor form may entry to the body through the lung
Hemolysis Associated With Exposure To *Heavy Metals*

- Arsine
- Lead
- Mercury
- Copper
- Antimony

- Mechanism of hemolysis is unknown, but it is thought to be related to the affinity of this directly cytolytic metals to thiol groups such as are found on the surfaces of RBC
Arsine

- Volatile, colorless, non-irritating gas, Garlicky odor
- Produced by the action of acid on a metal contaminated with arsenic
  \[6 \text{ H}_2 + \text{As}_2\text{O}_3 \rightarrow 2 \text{AsH}_3 + 3 \text{H}_2\text{O}\]
- Most occupational exposure:
  1) Preparation of crystals and conducting devices in the semiconductor industry
  2) Smelting & refinery +/- stibine
  3) Chemical industries.
- Respiratory tract is the most important portal of entry
Clinical Presentation

• Acute arsine poisoning: acute and massive IV hemolysis +/-delayed 2-24 h after exposure
• Nausea, vomiting, abdominal cramping, headache, malaise and dyspnea
• Tea-colored urine
• P/E: Peculiar garlicky odor of arsine, fever, tachycardia, tachypnea and hypotension
• Jaundice, generalized nonspecific abdominal tenderness
Lab. Findings

• Hemoglobinuria
• Decreased plasma haptoglobin & increased free HB levels
• The plasma may be brownish-red from the presence of methemalbumine
• Poikilocytosis, basophilic stippling and polychromasia at PBS
• Decreased HCT, increased indirect bilirubin and DIC (low fibrinogen level & prolonged PT)
• Altered renal function → increased serum Cr
Treatment

- Vigorous hydration
- Exchange transfusion if plasma Hb levels $>400-500\, \text{mg/dl}$
- Hemodialysis if ARF developed
- All survivors of acute arsine poisoning must be evaluated for at least 1 years for RF
- Reduction of exposure or removal from exposure in chronic arsine poisoning
Lead

- Suppression erythropoiesis and heme synthesis
- Hemolytic anemia

- Pathogenesis of lead induced hemolysis is related to inhibition of *pyrimidin 5-nucleotidase*
The Porphyrias

- Genetic disorder OR Acquired
- Abnormalities in *heme* biosynthetic pathway
- Accumulation of heme precursors (*δ* Aminolevulinic acid)
Clinical Syndromes

- **Neurotoxicity**: abdominal colic, constipation, autonomic dysfunction, sensorimotor neuropathy and psychiatric problem (direct toxic effect of the urine-soluble heme precursor)

- **Cutaneous photosensitivity**: repetitive vesiculation, scaring and deformity with hypertrichosis of sun-exposed areas of the skin (result of urine insoluble heme precursor)
Toxic substances associated with *acquired porphyria* in human

<table>
<thead>
<tr>
<th>Toxin</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexachlorobenzene</td>
<td>Fungicide</td>
</tr>
<tr>
<td>2,4 Dichlorophenol</td>
<td>Herbicide</td>
</tr>
<tr>
<td>2,4,5 Trichlorophenol</td>
<td>Herbicide</td>
</tr>
<tr>
<td>2,3,7,8Tetrachlorodibenzo-p-dioxin</td>
<td>Herbicide contaminant</td>
</tr>
<tr>
<td>O-Benzyl-p-chlorophenol</td>
<td>Cleanser and disinfectant</td>
</tr>
<tr>
<td>2-Benzyl-p-dichlorophenol</td>
<td>Commercial disinfectant</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>Plastics</td>
</tr>
<tr>
<td>Lead</td>
<td>Paint compounds</td>
</tr>
<tr>
<td>Aluminum</td>
<td>Phosphorus binder</td>
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</tbody>
</table>
Disorders Affecting Blood Cell Formation & Morphology

• Aplastic anemia
• Myelodysplastic Syndromes
• Multiple Myeloma
• Toxic Thrombocytopenia

✔ Cytogenetic study
Aplastic Anemia

• Idiopathic (50%)
• Secondary:
  1) Drugs: chloramphenicol, acetazolamide, phenylbutazone, phenytoin, sulfonamide, cytotoxic drugs such as antimetabolites and alkylating agents
  2) Chemicals: Benzene
  3) Ionizing Radiation
  4) Infection
  5) Immunologic
  6) Hereditary disease
Benzene

• **Occupational exposure:** *Rubber manufacturing, shoemaking, petroleum and chemical production, printing, steel working*

• **OSHA (PEL):** 1 PPM

• **BM:** Hypocellularity with fatty replacement

• **Prognosis:** Up to 40% patient may recover completely after removal of exposure

• **Treatment:**
  1) Supportive: transfusion, GFE, GCSF, GMCSF, Androgens
  2) Allogenic BM trasplantation
### Chemical causes AA in an occupational setting

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<th>Chemical</th>
<th>Use</th>
</tr>
</thead>
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<tr>
<td>Benzene</td>
<td>Intermediate in the synthesis of fabrics, pesticides, rubber, solvent for glues, varnishes, paints, octane booster for gasoline</td>
</tr>
<tr>
<td>Trinitrotoluene</td>
<td>Production of explosive</td>
</tr>
<tr>
<td>Hexachlorocyclohexane</td>
<td>Pesticides</td>
</tr>
<tr>
<td>Pentachlorophenol, DDT</td>
<td></td>
</tr>
<tr>
<td>Arsenic</td>
<td>Manufacture of glass, paint enamels, weed killers, tanning agent, pesticide</td>
</tr>
<tr>
<td>Ethylene glycol monomethyl or monobutyl ether</td>
<td>Production of paints, lacquers, dyes, inks, cleaning agents</td>
</tr>
</tbody>
</table>
Mylodysplastic syndromes

• **Exposure:** Benzene & Ionizing radiation

• Several case reposts: exposure to pesticides, solvents, farming, textile work, health professions.

• Lab data: cytopnea and ↑ MCV.

• Dx: bone marrow transplantation.
Multiple Myeloma

- There is no definitive link between occupational exposure & risk of M.M

- **Exposure**: petroleum products, organic solvents, heavy metals, pesticides & asbestosis. (all are hypothetical)

- **Worker at risk**: agricultural workers, chemical workers, miners, smelters, stokers, furniture workers

- High dose radiation has confirmed relation
<table>
<thead>
<tr>
<th>Toxic agent</th>
<th>Use</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toluene diisocyanate</td>
<td>Polymerizing agent</td>
<td>immune</td>
</tr>
<tr>
<td>2,2-dichlorovinyl-dimethylphosphate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dieldrin</td>
<td></td>
<td></td>
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<tr>
<td>Pyrethrin</td>
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<tr>
<td>Hexachlorocyclohexa-ne (lindane)</td>
<td></td>
<td></td>
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<tr>
<td>Chlorophenothane (DDT)</td>
<td></td>
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<tr>
<td>Turpentine</td>
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<tr>
<td>Vinyl chloride</td>
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<tr>
<td></td>
<td>Organic solvent</td>
<td>immune</td>
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<tr>
<td></td>
<td>plastics</td>
<td>Liver insufficiency with hypersplenism</td>
</tr>
</tbody>
</table>
Thanks For Your Attention

Any Question?