OSC|10
Ohio Safety Congress & Expo

Metals toxicology: From the iron age to the computer age

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Thursday, April 1, 2010 10:30 to 11:30 a.m.

Continuing Nursing Education Disclosures

- **Goal:** To educate conference attendees on specific aspects of accident prevention and Ohio's workers' compensation system
- **Learning objectives:**
  - Identify scenarios for exposure to toxic agents in the workplace.
  - Describe the range of health effects that can be produced by exposure to toxic metals.
  - Explain the health concerns posed by most common metals in the workplace.
- **Criteria for Successful Completion:** Attend the entire event and complete a session evaluation.
- **Conflict of Interest:** The planners and faculty have no conflict of interest.
- **Commercial Support:** There is no commercial support for this event.
- **Continuing Education:** Awarded 0.1 IACET general CEUs and 1.0 RN* contact hour.

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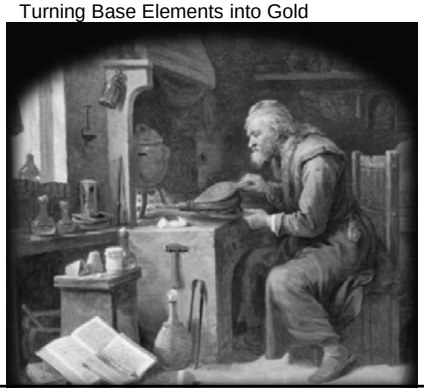
The Alchemist
Turning Base Elements into Gold



Metals are Immutable

- Metals are elements-cannot be created or destroyed
- Chemical element whose atoms readily lose electrons to form positive cations
- Approx. 80 of the 105 elements on the Periodic Chart are metals, approx. 30 are of toxicological importance
- Amongst the oldest of recognized occupational exposures to toxic substances

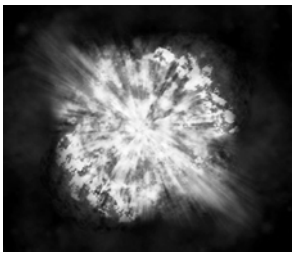
Ancient Metals

- Iron
- Lead
- Copper
- Zinc
- Manganese
- Mercury
- Nickel
- Arsenic

Modern Metals

- Aluminum
- Antimony
- Arsenic*
- Beryllium
- Cadmium
- Chromium
- Cobalt
- Silicon
- Thallium
- Titanium
- Tungsten
- Vanadium
- Radionuclides
- Metal Nanomaterials

*Arsenic compounds such as gallium arsenide, Arsenical compound used in chemotherapy For rare form of leukemia.



Elements (almost all) created during the Big Bang
Humans have just known about some metals longer than others

Metals are Natural and Necessary

- Metals frequently occur in complexes with other inorganic ions, i.e. oxides & sulfides
- Metals are found in all environmental media, plants, and creatures
- Biologically essential metals
  - Enzyme co-factors (Fe, Co, Cr, Cu, Mg, Mn)
  - Fe in hemoglobin
  - Ca, K, Na
- Some metals may exist in more than one valence state
  - can be important determinant of toxicity

Basic Mechanisms of Toxicity

- Non essential metals that can displace essential metals as enzyme co-factors or in other physiological processes are big trouble
  - Especially metals that can replace calcium or iron
- Even essential metals can be big trouble under some circumstances (i.e. Fe toxicity)
- Bind to sulfhydryl groups in proteins and interfere with critical enzyme activities
- Produce reactive oxygen species
- Induce immune response

The Dose Makes the Poison

Depending upon the circumstances of exposure,
A single metal or its compounds may produce a
Variety of health effects.

Many metals are essential to normal physiological
Function and exemplify the concept of **HORMESIS**-
Not enough of the element causes deficiency disease,
Too much results in manifestations of toxicity.

Examples: iron, chromium III, cobalt, copper,
magnesium, manganese, zinc.

Health Effects are Related to

- Physical form of the metal
  - Fumes, smoke, dusts
  - Size of particles
  - Liquid solutions (pH, K_{ow})
- Chemical composition
  - Trace metal elements in alloys, i.e. different steels
  - Chemical complexes
- Route of exposure (inhalation, skin, ingestion)
- Intensity and duration of exposure

General Categories of Health Effects

- Respiratory
  - Pneumoconiosis, pneumonitis
  - Metal fume fever
  - COPD
  - Respiratory tract cancers
- Neurological
- Immune system (sensitization)
- Cancers (other than respiratory)
- Other organ system effects

Workplace Exposures to Metals

- Inhalation
  - Fine particles & aerosols
  - Fumes & vapors
- Skin contact
- Ingestion
  - Incidental to inhalation (mouth breathing)
  - Or incidental to skin contact

Some Activities that Can Lead to Exposure

- Mining
- Ore refining & smelting
- Production of steel alloys
- Welding
- Soldering
- Grinding
- Finishing, plating & anodizing
- Production of metal nanomaterials (i.e. TiO_2)

Ancient Metals Still a Concern

Lead Plumbing
From Roman Bath-above left
Supply line
Solder

Lead (Plumbum-plumbing)

- Natural in food, soil & dust
- Occupational
  - Refining & smelting of Pb, Cu, Zn ores
  - Metal foundries
  - Automotive parts manufacture (i.e. Pb-containing bearings)
  - Glassmaking (Pb can be leached by acidic liquids)
  - Lead solders
  - Pb-containing plastics (e.g. electrical insulation)
  - Firing weapons (i.e. police and military) especially indoors

Lead: Toxicity

- Toxic manifestations related to concentrations in blood (good dose-response info)
- Effects start to become apparent (children) 10-15 ug Pb/deciliter of blood
- Blood-Pb levels in the US population have been declining over the past 20 years as a result of removing sources of Pb (leaded gasoline)
- Young children most at risk
- Some occupations are still potentially high risk

Occupational monitoring: based on blood lead concentrations

Lead: Biological Actions

- Interferes with the incorporation of the iron atom into the hemoglobin molecule
- Interferes with the formation of critical neural connections in the developing brain
- Can cause neurotoxicity even in adults at high enough levels of exposure

Mercury
Ancient Metal with a Bad Reputation

- Historically an occupational risk
- Current concerns primarily environmental
- Valence state is critical to toxicity
  - elemental mercury vapor: neurotoxic
  - inorganic salts: kidney toxicity
  - organo-mercury: neurotoxic, teratogenic
- Hg primarily binds to SH groups, also interfere with function of neurons

The Mad Hatter's Tea Party

Mad as a Hatter

- Mercury (and other toxic metals) used in tanning and felt-making
- Nervous system toxicity
  - CNS from Hg vapors
    - "asthenic-vegetative syndrome"
    - "micromercurialism"
- "Recent" poisonings have involved methyl mercury (environmental) and inorganic mercury vapors
- Indoor environmental issue: Hg light ballasts; Hg-containing resilient floors

Steel: Ancient, modern and essential.

Steel Alloys

- Metals in addition to iron (and carbon) that give steel desirable properties
  - Cadmium
  - Chromium
  - Cobalt
  - Manganese
  - Molybdenum
  - Nickel
  - Zinc
- High potential for occupational exposure!

Cadmium

- Inhalation
  - Acute high concentration of fumes
    - Chemical pneumonitis, pulmonary edema
    - Symptoms may be delayed onset after acute exposure
    - Flu-like illness (metal fume fever) can be fatal
  - Chronic exposures
    - Chronic bronchitis, progressive fibrosis of lower airways, emphysema
    - Respiratory tract cancers in occupationally exposed cohorts
    - Supporting evidence from laboratory animals

Cadmium: Toxicity

- Inhalation and ingestion
  - Nephrotoxicity
    - Damage to renal tubules from release of free Cd
    - Progressive kidney failure
    - Body burden of cadmium stored in kidneys
  - Cardiovascular system
    - Cd may be involved in hypertension
    - ECG changes in rats

Chromium

Chromium: Toxicity

- Primarily hexavalent compounds in industrial settings
  - Caustic, produce burns on contact
  - Inhalation of Cr VI fumes – perforation of nasal septum
  - Carcinogenic by inhalation (rodent studies)
  - Positive & negative epidemiologic evidence for people
- Trivalent Cr most common in environment
  - Enzyme co-factor involved in glucose metabolism

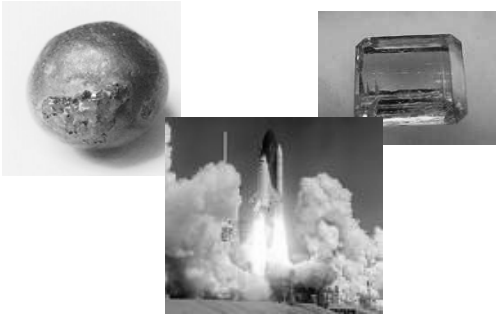
Other Metals in Steel Alloys

- Cobalt
  - Essential trace element
  - Pneumonitis & fibrosis
  - Sensitizing agent-dermatitis
  - Cardiomyopathy (i.e. “beer-drinkers cardiomyopathy-requires really high level of exposure!)
- Manganese
  - Unusual neurotoxicity
  - “Mask of manganism”

Other Metals in Steel Alloys

- Molybdenum
  - Joint & muscle pain & weakness
  - Possible liver toxicity
- Nickel
  - Sensitizing agent, dermatitis
  - Nickel subsulfide & nickel carbonyl considered occupational respiratory carcinogens
- Zinc
  - Essential trace element
  - Pneumonitis & metal fume fever at high levels of dust & vapor

Beryllium
A Space Age Metal



Beryllium

- Lightweight, corrosion-resistant
- Non-magnetic, good thermal conductance
- Major uses
- Aerospace components
- Non-sparking tools (Be-Cu alloys)
- Electronics, fluorescent lamps, space telescope mirrors

Beryllium: Toxicity

- Dermal contact
  - Contact dermatitis & skin granulomas
- Inhalation
  - Acute Be pneumonitis (very rare)
  - Chronic berylliosis
  - OSHA standard for Be in workplace air 0.002 mg/m^3

Beryllium: Biological Action

- Be-protein complex acts as antigen
- Cell mediated immune response
- May also destroy the membranes of lung cells
- Low prevalence of Be disease in exposed people-may be genetic susceptibility component

Nanomaterials

Tiny Particles New Products

New Concerns for Exposure

Metal Nanomaterials

- Avg. size of particles <100 nm
- Large surface area/mass ratio
- Metals act differently in nano-scale
  - Usefulness of nanomaterials related to chemical & physical properties
  - Not same as metal alloys or pure metals we are familiar with
- Inhalation primary route of exposure

Metal Nanomaterials

- Corrosion resistant coatings
- Anti-microbial coatings & fabrics (silver)
- Cosmetics & sunscreens
- Sensors
- Imaging
- Catalysts, pigments
- Personalized medicine & drug delivery scaffolds

Common Metal Oxides in Nanomaterials

- Titanium TiO_2
- Iron
- Silver
- Gold
- Zinc
- Copper
- Cobalt

May be in engineered with carbon structures

Health Concerns

- Nanoparticles inhaled into alveoli
- May accumulate in lungs
  - Asbestos-like response
  - Granulomas
- Inflammatory response & reactive oxygen species
  - Impairment of macrophage response
- May enter blood stream and translocate
  - Implicated in adverse cardio-pulmonary toxicity

Regulatory Initiatives

- Current OSHA PEL for TiO_2 is 15 mg/m3
  - Particle size not specified
  - Considered possible carcinogen based on rodent studies
- NIOSH draft guideline for TiO_2 ultrafine particulate
  - PM0.1
  - Proposed 1.5 mg/m3 for fine & 0.1 mg/m3 for ultrafine TiO_2

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