Health concerns of the heavy metals and metalloids

Chris Cooksey
- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium
Toxicity - acute and chronic

Acute - $\text{LD}_{50}$

<table>
<thead>
<tr>
<th>Substance</th>
<th>LD50 (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CdS</td>
<td>7080</td>
</tr>
<tr>
<td>NaCl</td>
<td>3000</td>
</tr>
<tr>
<td>As</td>
<td>763</td>
</tr>
<tr>
<td>HgCl</td>
<td>210</td>
</tr>
<tr>
<td>NaF</td>
<td>52</td>
</tr>
<tr>
<td>Tl₂SO₄</td>
<td>16</td>
</tr>
<tr>
<td>NaCN</td>
<td>6.4</td>
</tr>
<tr>
<td>HgCl₂</td>
<td>1</td>
</tr>
</tbody>
</table>
# Hodge and Sterner Scale
(1943)

<table>
<thead>
<tr>
<th>Toxicity Rating</th>
<th>Commonly used term</th>
<th>( \text{LD}_{50} ) (rat, oral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Extremely Toxic</td>
<td>( \leq 1 )</td>
</tr>
<tr>
<td>2</td>
<td>Highly Toxic</td>
<td>1 - 50</td>
</tr>
<tr>
<td>3</td>
<td>Moderately Toxic</td>
<td>50 - 500</td>
</tr>
<tr>
<td>4</td>
<td>Slightly Toxic</td>
<td>500 - 5000</td>
</tr>
<tr>
<td>5</td>
<td>Practically Non-toxic</td>
<td>5000 - 15000</td>
</tr>
<tr>
<td>6</td>
<td>Relatively Harmless</td>
<td>&gt; 15000</td>
</tr>
</tbody>
</table>
# GHS - CLP

<table>
<thead>
<tr>
<th>LD$_{50}$</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=5</td>
<td>1 Danger</td>
</tr>
<tr>
<td>5 - 50</td>
<td>2 Danger</td>
</tr>
<tr>
<td>50 - 300</td>
<td>3 Danger</td>
</tr>
<tr>
<td>300 - 2000</td>
<td>4 Warning</td>
</tr>
</tbody>
</table>

Globally Harmonised System of Classification and Labelling and Packaging of Chemicals
CLP-Regulation (EC) No 1272/2008
Toxicity - acute and chronic

Chronic

The long-term effect of sub-lethal exposure
• Toxicity - acute and chronic
• Arsenic
• Mercury
• Lead
• Cadmium
Arsenic

- Pesticide
  - Inheritance powder
- Taxidermy
- Herbicide
  - Agent Blue
- Pigments
- Therapeutic uses
Inorganic arsenic poisoning kills by allosteric inhibition of essential metabolic enzymes, leading to death from multi-system organ failure.

Arsenicosis - chronic arsenic poisoning.
Arsenic

LD50 rat oral mg/kg

Trimethylarsine
Methanearsonic acid
Dimethyarsinic acid
Arsenic trisulfide
Arsenious oxide
Arsenic acid
Sodium arsenite
Emerald green
Arsine
Arsenic

(A) Chemical structures and oxidation states of arsenic compounds:
- Arsenate ($\text{As}^{5+}$) ($\text{LD}_{50}$ 112-175 mg/kg)
- Arsenite ($\text{As}^{3+}$) ($\text{LD}_{50}$ 15-44 mg/kg)
- Methylarsonic acid (MMA) ($\text{LD}_{50}$ 960 mg/kg)
- Dimethylarsinic acid (DMA) ($\text{LD}_{50}$ 650 mg/kg)

(B) Biochemical forms of arsenic:
- Arsenobetaine ($\text{LD}_{50}$ 10 g/kg)
- Arsenocholine ($\text{LD}_{50}$ 6.5 g/kg)
- Arsenosugar (N/A)

(C) Arsenic minerals and compounds:
- Orpiment ($\text{As}_2\text{S}_3$) (N/A)
- Realgar ($\text{As}_4\text{S}_4$) ($\text{LD}_{50}$ 3.2 g/kg)
- Arsenolite (N/A)
- Arsenic trioxide ($\text{As}_2\text{O}_3$) (32-39 mg/kg)
poisoning by volatile arsenic compounds from mouldy wall paper in damp rooms

- Gmelin (1839) toxic mould gas
- Selmi (1874) AsH₃
- Basedow (1846) cacodyl oxide
- Gosio (1893) alkyl arsine
- Biginelli (1893) Et₂AsH
- Klason (1914) Et₂AsO
- Challenger (1933) Me₃As
- McBride & Wolfe (1971) Me₂AsH
or is it really true?

William R. Cullen, Ronald Bentley
The toxicity of trimethylarsine: an urban myth
*J. Environ. Monit.*, 2004

- Odour threshold 2 ng/kg in water
- \( \text{LD}_{50} \) 7870 mg/kg
Arsenic

The toxicity of arsine and methyl arsines by inhalation arises because of the generation of radicals which cause DNA damage.
Arsenic

Chronic toxicity leading to skin cancers is caused by inorganic arsenic in drinking water


WHO: "the largest mass poisoning in history"; recommends <0.01 mg/L arsenic in drinking water.
• Toxicity - acute and chronic
• Arsenic
• Mercury
• Lead
• Cadmium
Mercury

• Uses
  – Kastner-Kellner cells
  – Measuring instruments
  – Floating lighthouse mirrors
  – Gold extraction
  – Laxative
  – Dental fillings
    • Largest exposure to mercury vapour
Mercury
Mercury

• Sources
  – 65% coal fired power plants
  – 11% gold extraction
  – Cremation
    • 1300-2200 t in fillings (EU + EFTA, 2003)
  – volcanos
Mercury in the Fremont glacier

- Mt St Helens 1980
- Krakatau 1883
- Gold rush
- Tambora 1815

Year

mercury ng/L
Mercury

LD50 (rat oral)

<table>
<thead>
<tr>
<th>Compound</th>
<th>mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>mercuric sulfide</td>
<td>0.01</td>
</tr>
<tr>
<td>mercurous chloride</td>
<td>0.1</td>
</tr>
<tr>
<td>phenyl mercuric nitrate</td>
<td>1</td>
</tr>
<tr>
<td>ethyl mercuric nitrate</td>
<td>10</td>
</tr>
<tr>
<td>mercuric chloride</td>
<td>100</td>
</tr>
<tr>
<td>mercuric cyanide</td>
<td>1000</td>
</tr>
<tr>
<td>methyl mercuric chloride</td>
<td>10000</td>
</tr>
<tr>
<td>phenyl mercuric acetate</td>
<td>100000</td>
</tr>
<tr>
<td>mercuric oxide</td>
<td>1000</td>
</tr>
<tr>
<td>dimethyl mercury</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Methyl mercury

- Japan Nitrogenous Fertilizer Company
  - Nihon Chisso Hiryō - Kabushiki Kaisha (1908)
  - Calcium carbide - cyanamide - calcium nitrate
  - Acetylene - acetaldehyde (Hg catalysed) (1932 - 1968)
    - Waste containing methyl mercury $\text{CH}_3\text{Hg}^+$ was discharged into the sea
  - Minamata
Dimethyl mercury

- readily crosses the blood-brain barrier
- causes ataxia, sensory disturbance and changes in mental state, birth defects
- inhibits several stages of neurotransmission in the brain
- very slowly excreted from the body
Dimethyl mercury

- First published record of fatal occupational MeHg poisoning, Edwards 1865
- Report on organic mercury poisoning in acetaldehyde production workers, Koelsch 1937
- Official acknowledgment of MeHg as cause of Minamata disease 1968
Methylmercury

- Introduced as a fungicide for seeds in 1914
  - Pakistan in 1961
  - Guatemala in 1965
  - Iraq in 1970–1971
Mercury

- Directive 2007/51/EC
  - mercury-in-glass thermometers banned

- Recommendation 2003/4 on Controlling the Dispersal of Mercury from Crematoria.
  - 50% reduction in emissions by 2012
• Toxicity - acute and chronic
• Arsenic
• Mercury
• Lead
• Cadmium
Lead

While it is being melted, all the apertures in the vessel should be closed, otherwise a noxious vapour is discharged from the furnace, of a deadly nature, to dogs in particular.

Pliny XXXIV, 50
AN ESSAY,
Concerning the CAUSE of the ENDEMIAL COLIC of DEVONSHIRE,
Which was read in the Theatre of the College of Physicians, in London, on the Twenty-ninth Day of June, 1767,
BY GEORGE BAKER,
Fellow of the College of Physicians, and of the Royal Society, and Physician to her Majesty’s Household.

LONDON:
Printed by J. Huens, near Lincoln’s-Inn-Fields.
M.DCC.LXVII.

'i: Anni M.DCC.LXIX.
Lead

A Case of Lead Poisoning by Beer
E. Rice Morgan, BMJ, 1900, 1373
Tetraethyllead

- Carl Jacob Löwig (1803 - 1890)
- Thomas Midgley (1889 - 1944)
- Clair Cameron Patterson (1922 - 1995)
Relative amount of anti-knock compound required for a given effect
Ethyl Gasoline Corporation

- 1 February 1923
Clair Patterson

• Measured U/Pb ratios in old rocks
• Concluded (1953) that the age of the Earth was 4550 my
The amount of lead used for gasoline additives

- **X-axis (Year):** 1960 to 1995
- **Y-axis (Thousands of metric tons/year):** 0 to 300

The graph shows a decline in the amount of lead used for gasoline additives over the years, from a peak in the mid-1970s to near zero by the late 1980s.
- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium
Cadmium

Cadmium is a recent discovery (1817)

Karl Samuel Leberecht Hermann (1765 – 1846)
Friedrich Stromeyer (1776 – 1835)
Cadmium

Sovet [poisoning caused by powder used in cleaning of silver ...]

*Presse Med Belge* 1858, 10, 69-70

CdCO$_3$ dust inhalation
Cadmium

By the 1950s the hazards of working with cadmium were well established, causing

– Emphysema and proteinuria from inhalation
Cadmium

The first chronic poisoning was reported in 1940


rhinitis and pharyngitis in plating workers
Cadmium

Jinzu River valley in Japan
Mitsui Mining & Smelting (1910)
First poisoning reported 1912
1939-1954 200 people affected by *itai-itai*, 100 died
- renal osteomalacia
- bone disease with fractures and severe pain
Cadmium

Dr Noboru Hagino (1957)
Suggests the cause is waste water from factories

(1961) Especially cadmium discharged during mining in Kamioka by Mitsui Mining Company

May 1968 the Ministry of Health and Welfare announced the disease was caused by cadmium poisoning
Jinzu River
River water containing 1 mg/kg Cd was used to irrigate rice fields
Cadmium

A drinking-water guideline value of 0.005 mg/litre has been set for cadmium (WHO, 1984)
• Toxicity - acute and chronic
• Arsenic
• Mercury
• Lead
• Cadmium