The impact, assessment, and treatment of heavy metals and radioactive elements on health
Objectives:

1. Understanding the increasing exposure and symptoms of heavy metals and radioactive elements

2. Evaluating for metals and radioactive elements through laboratory, environmental, and clinical testing

3. Basic understanding of treatment through detoxification, diet, targeted nutraceutical and pharmaceutical therapy

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Real Health Medical
Integrated Functional Medicine
Atlanta, GA

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678 990 5401
Toxic Metals are UBIQUITOUS

Exposure is UNAVOIDABLE

Low Level Exposure - ACCUMULATION

METAL TOXICITY - subtle and non-specific

Effects of toxic metals - DEPLETING, INFLAMMATORY, DEGENERATIVE

MINIMIZING body burden = one of HIGHEST PRIORITIES of Preventive/Functional Med

OPTIMIZING nutrient levels is ESSENTIAL to protection / detoxification

Metal Detoxification with Pharmaceutical/Nutraceuticals - SCIENTIFIC, SAFE, EFFECTIVE
Heavy Metals and Radioactive Elements
Heavy Metals vs Toxic Metals vs Minerals vs Radioactive Elements
3/4 of known elements are METALS

- **Metal Properties** - hardness high melting point malleable density conductor of heat / electricity
- **Chromium** - hardest metal - used to strengthen materials
- **Cesium** - softest
- **Gold, Silver, Copper** malleable and ductile
- **Alloy** - mixture of metals
- **Distinguished from non-metals**
- **Capacity to loose electrons = become oxidized** (the receiving atom / molecule = reduced)
- **Oxidized** - increased electrical charge after loosing an electron - form positively charged ions
- **Reduced** - accepting or gaining an electron is reducing the total electrical charge
- **Participating in an oxidation - reduction reaction**
- **Metalloids** - elements on the border between metals and non-metals (Arsenic)
Metals - Estimated to make up for 1/4 of Earth’s mass

Sea water

Volcanoes

Natural weathering

Mining and processing of metals
Use of Metals

1st metals used by humans found in elemental metallic state - copper, gold, silver

Most metals exist in ores - compounds or mixtures of the elements with oxygen or sulfur

Iron and tin - easiest to extract / separate - used earlier in human history

* Mining and processing of ore - leads to build up of “waste or metal materials” - distributed by water

* Released into air environment from burning of coal and fuels and trash incineration
Toxic Metals / Minerals

Metals - toxic elements

1. No known biological function
2. Capable of disrupting normal physiological processes
3. Capable of causing DISEASE
   Ex. mercury, cadmium, lead, aluminum

4. Elements in the wrong form

   Chromium 3+ essential

   Chromium 6+ carcinogenic
Heavy = weight

Toxic = effect “ biological bully “

Cadmium, lead, mercury - heavy and toxic

Molybdenum - heavy and essential ( beneficial )

Beryllium - light but toxic
Modern industrial use of metals

Increased redistribution (from the crust) into environment

More charged/toxic forms

Long lasting complexes within biological systems (fish, animals, humans)

Potential for increasing concentrations at higher levels on the food chain
Toxic Effect of Metals

Displacing an essential metal ion

- Cadmium - for zinc - in function and structure
- Lead - for calcium - in bone

Combing with sulfur based AAs

Metals - consuming / stealing electrons from

- Redox reactions - disrupt biological reactions
- DNA bases
Zinc
- Essential trace element - cannot live without
- **Activator factor in over 100 enzymes**
- Structural ion in RNA transcription
- Functions in all classes of enzymes in humans
- Body contains between 2000-4000 mg
- Brain, muscle, bone, kidney, and liver
- Highest - prostate, semen, and eye
- RNA/DNA metabolism, signal transduction, gene expression, apoptosis
- **10% human proteins bind / interact with zinc**
- Brain - synaptic plasticity - learning - dopamine metabolism
3 Basic Concepts

Think:

- Exposure / accumulation
- Minerals / sulfur status
- Detoxification
Heavy Metals and Radioactive Elements

Summary Points:

Heavy metals / radioactive elements are ubiquitous in environment - man made
Exposure is unavoidable
Metals have a tendency to accumulate in the human body with chronic exposure
Toxic effect of metals is more pronounced in the context of mineral / anti-oxidant deficiencies
Genetic weakness in detoxification

Higher index of suspicion:

- Based on environmental factors - maternal history, vaccines, amalgams, older housing, occupation
- Neurological / kidney related conditions / cancer / chronic resistant infections / auto-immune

Detoxify or Die

- Chelation therapy for heavy metal toxicity is well researched and utilized - throughout the world
- Heavy Metal detoxification - science of Sulfur and Mineral metabolism
Heavy Metal Toxicity

Slowly excreted and easily deposit / accumulate in the body

Slowly and subtly disruption normal processes / homeostasis

Disrupting repair and immune defense

Resulting in degenerative conditions in most tissues

Toxicity is in large part due to their accumulation in biological tissues - prolonged half lives

- Lead - 15 - 27 years in bone tissue
- Cadmium 20-30 years

Severity of adverse health effects is related to the chemical form of heavy metals, duration of exposure, dose

As well as the ability of the body to detoxify and nutrient status (minerals/sulfer)
Mechanism of Toxicity

Displacement of essential minerals
Enzymatic inhibition
Depletion of Sulfur groups
Impaired antioxidant metabolism
Oxidative stress - resulting in DNA damage, lipid peroxidation, and depletion of sulfur based molecules (glutathione)
Slowing / blocking cellular metabolism and function
Loss of normal regulation
Degeneration of cell and tissue function
Immune activation - hyperactive
Recognition of Toxic Substances

Top 10 List

Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances - HHS

The ATSDR 2015 Substance Priority List

<table>
<thead>
<tr>
<th>2015 RANK</th>
<th>SUBSTANCE NAME</th>
<th>TOTAL POINTS</th>
<th>2013 RANK</th>
<th>CAS RN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ARSENIC</td>
<td>1671.6</td>
<td>1</td>
<td>007440-38-2</td>
</tr>
<tr>
<td>2</td>
<td>LEAD</td>
<td>1529.4</td>
<td>2</td>
<td>007439-92-1</td>
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<tr>
<td>3</td>
<td>MERCURY</td>
<td>1458.6</td>
<td>3</td>
<td>007439-97-6</td>
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<tr>
<td>4</td>
<td>VINYL CHLORIDE</td>
<td>1358.9</td>
<td>4</td>
<td>000075-01-4</td>
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<tr>
<td>5</td>
<td>POLYCHLORINATED BIPHENYLS</td>
<td>1345.1</td>
<td>5</td>
<td>001336-36-3</td>
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<tr>
<td>6</td>
<td>BENZENE</td>
<td>1327.6</td>
<td>6</td>
<td>000071-43-2</td>
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<tr>
<td>7</td>
<td>CADMIUM</td>
<td>1318.8</td>
<td>7</td>
<td>007440-43-9</td>
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<tr>
<td>8</td>
<td>BENZO(A)PYRENE</td>
<td>1304.4</td>
<td>8</td>
<td>000050-32-8</td>
</tr>
<tr>
<td>9</td>
<td>POLYCYCLIC AROMATIC HYDROCARBONS</td>
<td>1279.1</td>
<td>9</td>
<td>130498-29-2</td>
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<tr>
<td>10</td>
<td>BENZO(B)FLUORANTHENE</td>
<td>1249.7</td>
<td>10</td>
<td>000205-99-2</td>
</tr>
</tbody>
</table>

Agency for Toxic Substances and Disease Registry (ATSDR)

Federal public health agency within HHS

Focus on minimizing human health risks from exposure to hazardous substances

Works with CDC

Budget $ 80 million

300 full time employees
## Toxic Element Exposure Profile, Hair

<table>
<thead>
<tr>
<th>Element</th>
<th>Result</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic (As)</td>
<td>0.021</td>
<td>&lt; 0.14</td>
<td></td>
</tr>
<tr>
<td>Lead (Pb)</td>
<td>0.38</td>
<td>&lt; 3.0</td>
<td></td>
</tr>
<tr>
<td>Mercury (Hg)</td>
<td>0.21</td>
<td>&lt; 3.0</td>
<td></td>
</tr>
<tr>
<td>Cadmium (Cd)</td>
<td>0.032</td>
<td>&lt; 2.0</td>
<td></td>
</tr>
<tr>
<td>Chromium (Cr)</td>
<td>0.52</td>
<td>&lt; 0.85</td>
<td></td>
</tr>
<tr>
<td>Beryllium (Be)</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Cobalt (Co)</td>
<td>0.018</td>
<td>&lt; 0.15</td>
<td></td>
</tr>
<tr>
<td>Nickel (Ni)</td>
<td>0.54</td>
<td>&lt; 1.0</td>
<td></td>
</tr>
<tr>
<td>Zinc (Zn)</td>
<td>170</td>
<td>&lt; 300</td>
<td></td>
</tr>
<tr>
<td>Copper (Cu)</td>
<td>160</td>
<td>&lt; 70</td>
<td></td>
</tr>
<tr>
<td>Thorium (Th)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Thallium (Tl)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.006</td>
<td></td>
</tr>
<tr>
<td>Barium (Ba)</td>
<td>1.3</td>
<td>&lt; 8.0</td>
<td></td>
</tr>
<tr>
<td>Cadmium (Ca)</td>
<td>&lt; 0.002</td>
<td>&lt; 0.010</td>
<td></td>
</tr>
<tr>
<td>Manganese (Mn)</td>
<td>0.19</td>
<td>&lt; 1.0</td>
<td></td>
</tr>
<tr>
<td>Selenium (Se)</td>
<td>0.70</td>
<td>&lt; 2.1</td>
<td></td>
</tr>
<tr>
<td>Bismuth (Bi)</td>
<td>0.019</td>
<td>&lt; 5.0</td>
<td></td>
</tr>
<tr>
<td>Vanadium (V)</td>
<td>0.049</td>
<td>&lt; 6.20</td>
<td></td>
</tr>
<tr>
<td>Silver (Ag)</td>
<td>0.06</td>
<td>&lt; 1.4</td>
<td></td>
</tr>
<tr>
<td>Arsenic (Sb)</td>
<td>&lt; 0.01</td>
<td>&lt; 0.12</td>
<td></td>
</tr>
<tr>
<td>Palladium (Pd)</td>
<td>0.011</td>
<td>&lt; 0.015</td>
<td></td>
</tr>
<tr>
<td>Aluminum (Al)</td>
<td>24</td>
<td>&lt; 13</td>
<td></td>
</tr>
<tr>
<td>Platinum (Pt)</td>
<td>&lt; 0.003</td>
<td>&lt; 0.010</td>
<td></td>
</tr>
<tr>
<td>Tungsten (W)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.015</td>
<td></td>
</tr>
<tr>
<td>Tin (Sn)</td>
<td>0.30</td>
<td>&lt; 1.0</td>
<td></td>
</tr>
<tr>
<td>Uranium (U)</td>
<td>0.26</td>
<td>&lt; 5.20</td>
<td></td>
</tr>
<tr>
<td>Gold (Au)</td>
<td>0.002</td>
<td>&lt; 0.010</td>
<td></td>
</tr>
<tr>
<td>Tantalum (Ta)</td>
<td>&lt; 0.09</td>
<td>&lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>Gannum (Ge)</td>
<td>0.023</td>
<td>&lt; 0.045</td>
<td></td>
</tr>
<tr>
<td>Titanium (Ti)</td>
<td>0.75</td>
<td>&lt; 2.0</td>
<td></td>
</tr>
<tr>
<td>Gadolinium (Gd)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.006</td>
<td></td>
</tr>
</tbody>
</table>

### Comments:
Insufficient sample to rerun results.

### Details:
- **Sample Type:** Hair
- **Sample Size:** 0.141 g
- **Hair Color:** Brown
- **Treatment:** Shampoo: YES

---

**OCTOBER DATA INC. • ADDRESS:** 576 Illinois Ave., St. Charles, IL 60174 • 
**LAB #:** 010000-0000-0 • **DOCTOR:** Doctor’s Data, Inc.
**CLIENT #:** 12345

**Sample Received:** 11/1/2011
**Data Received:** 12/6/2011
**Date Collected:** 10/24/2011
**Method:** ICP-MS
**Sample:** Hair
**Sample Type:** Hair
**Sample Size:** 0.141 g
**Hair Color:** Brown
**Treatment:** Shampoo: YES
**Comments:** Insufficient sample to rerun results.
# Toxic Elements Exposure Profile

## Elemental Analysis - Whole Blood

<table>
<thead>
<tr>
<th>Element</th>
<th>Result</th>
<th>Units</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>6.78</td>
<td>mg/dL</td>
<td>4.00 - 6.30</td>
</tr>
<tr>
<td>Chlorine</td>
<td>1.5</td>
<td>mg/dL</td>
<td>0.1 - 2.5</td>
</tr>
<tr>
<td>Copper</td>
<td>0.02</td>
<td>µg/mL</td>
<td>0.05 - 1.16</td>
</tr>
<tr>
<td>Iron</td>
<td>0.01</td>
<td>µg/mL</td>
<td>0.01 - 3.0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>2.25</td>
<td>mg/dL</td>
<td>2.64 - 4.25</td>
</tr>
<tr>
<td>Manganese</td>
<td>0.45</td>
<td>µg/mL</td>
<td>0.10 - 2.10</td>
</tr>
<tr>
<td>Selenium</td>
<td>0.05</td>
<td>µg/mL</td>
<td>0.10 - 0.20</td>
</tr>
<tr>
<td>Tl</td>
<td>0.05</td>
<td>µg/mL</td>
<td>0.05 - 0.25</td>
</tr>
<tr>
<td>Arsenic</td>
<td>0.01</td>
<td>µg/mL</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Antimony</td>
<td>0.02</td>
<td>µg/mL</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Beryllium</td>
<td>0.001</td>
<td>µg/mL</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.001</td>
<td>µg/mL</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cobalt</td>
<td>0.001</td>
<td>µg/mL</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Lead</td>
<td>0.08</td>
<td>µg/mL</td>
<td>0.01 - 0.3</td>
</tr>
<tr>
<td>Mercury</td>
<td>0.03</td>
<td>µg/mL</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Nickel</td>
<td>0.01</td>
<td>µg/mL</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Tin</td>
<td>0.06</td>
<td>µg/mL</td>
<td>&lt; 0.1</td>
</tr>
</tbody>
</table>

**Property Rank by QuickSilver**

- Calcium: 30%
- Chlorine: 55%
- Copper: 94%
- Iron: 95%
- Magnesium: 98%
- Manganese: 99%
- Selenium: 99%
- Tl: 99%
- Arsenic: 80%
- Antimony: 90%
- Beryllium: 95%
- Cadmium: 95%
- Cobalt: 95%
- Lead: 95%
- Mercury: 95%
- Nickel: 95%
- Tin: 95%

Please note: results are not diagnostic. They are intended to provide additional guidelines to qualified healthcare professionals with a full knowledge of patient history or must be in close consultation of an appropriate healthcare regimen.

Quicksilver Scientific: 1278 Miner’s Drive, Ste 101, Latham, NY 12028
Director: Christopher W. Sheehy, PhD
www.quicksilverscientific.com
Toxic Metals Profile

<table>
<thead>
<tr>
<th>Element</th>
<th>ppm</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
<th>50% Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>54.0</td>
</tr>
<tr>
<td>Arsenic</td>
<td>40.0</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>15.7</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.30</td>
</tr>
<tr>
<td>Lead</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>20.1</td>
</tr>
<tr>
<td>Mercury</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
<td>13.8</td>
</tr>
</tbody>
</table>

Toxic metals are flagged high when the result is above the 50% Reference Range. Results for whole blood toxic elements that are within normal limits do not rule out metal accumulation in other tissues. This can be evaluated by urinary excretion or 24-hour urine collection challenge tests.
Metals - J Toxicology 2011

Most effected organ - CNS (Arsenic, Lead, Mercury)

1. Neurological disease – Mercury, Lead, Aluminum
2. Most common health effect - Cancer (Arsenic, Lead, Cadmium)
Metals - Most Affected Organs - Most Common Health Effects


Heavy metal

Most affected organs

Chronic health effects
Heavy Metals - Carcinogenic

The International Agency for Research on Cancer (IARC) Classifies

Cadmium - known carcinogen
Inorganic lead - probable carcinogen
Methylmercury - possible carcinogen
Cobalt - possible

International Agency for Research on Cancer (IARC) Agents Classified by the IARC Monographs. 2012;1–106
#3 on ATSDR 2011 Substance Priority List

Once mercury is absorbed / injected into the body:

- **Well distributed** through the body
- **Reacts with SH groups on molecules in all tissues**
- **Potentially interfering with the function of any cellular or sub cellular structure, protein, enzyme**
- **Mercury is primarily a neurological poison**
Table 2

Noncardiovascular health effects of heavy metals.

<table>
<thead>
<tr>
<th>Heavy metal</th>
<th>Acute (i)</th>
<th>Chronic (ii)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>(i) Cancer</td>
<td>(ii) Peripheral vascular disease, which is in its severe form called angioneurotic edema</td>
</tr>
<tr>
<td></td>
<td>(a) Digestive</td>
<td>(b) Skin lesions (melanoma, keratin)</td>
</tr>
<tr>
<td></td>
<td>(b) Nervous system</td>
<td>(c) Reproductive toxicity</td>
</tr>
<tr>
<td></td>
<td>(c) Kidneys</td>
<td>(d) Hematologic disorders</td>
</tr>
<tr>
<td></td>
<td>(d)</td>
<td>Neurological disease</td>
</tr>
<tr>
<td></td>
<td>(e)</td>
<td>Developmental abnormalities and neurobehavioral disorders</td>
</tr>
<tr>
<td>Lead</td>
<td>(i) Control</td>
<td>(ii) Cancer</td>
</tr>
<tr>
<td></td>
<td>(a) Nervous system</td>
<td>(b) Kidney damage</td>
</tr>
<tr>
<td></td>
<td>(b)</td>
<td>Neurological disease</td>
</tr>
<tr>
<td></td>
<td>(c)</td>
<td>Hysterotonus</td>
</tr>
<tr>
<td></td>
<td>(d)</td>
<td>Impaired intellectual ability and behavioral problems in children</td>
</tr>
<tr>
<td></td>
<td>(e)</td>
<td>Kidneys</td>
</tr>
<tr>
<td></td>
<td>(f)</td>
<td>Liver</td>
</tr>
<tr>
<td>Cadmium</td>
<td>(i) Kidneys</td>
<td>(ii) Cancer</td>
</tr>
<tr>
<td></td>
<td>(a)</td>
<td>Kidney damage</td>
</tr>
<tr>
<td></td>
<td>(b)</td>
<td>Neurotoxicity, OTC (organochlorine, thioctic)</td>
</tr>
<tr>
<td></td>
<td>(c)</td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td>(d)</td>
<td>Neurological disorder</td>
</tr>
<tr>
<td></td>
<td>(e)</td>
<td>Metabolic damage, fetotoxicity from fumes, the Halide (organochlorine) disease</td>
</tr>
<tr>
<td></td>
<td>(f)</td>
<td>Formation of organisms</td>
</tr>
<tr>
<td></td>
<td>(g)</td>
<td>Neurological system</td>
</tr>
<tr>
<td></td>
<td>(h)</td>
<td>Neurotoxicity</td>
</tr>
<tr>
<td></td>
<td>(i)</td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td>(j)</td>
<td>Impaired intellectual ability and behavioral problems in children</td>
</tr>
<tr>
<td></td>
<td>(k)</td>
<td>Long-term effects</td>
</tr>
<tr>
<td></td>
<td>(l)</td>
<td>Kidney damage</td>
</tr>
<tr>
<td></td>
<td>(m)</td>
<td>Neurological disease</td>
</tr>
<tr>
<td></td>
<td>(n)</td>
<td>Impaired intellectual ability and behavioral problems in children</td>
</tr>
<tr>
<td></td>
<td>(o)</td>
<td>Long-term effects</td>
</tr>
<tr>
<td></td>
<td>(p)</td>
<td>Mental memory loss is an allergen, which may cause contact allergies</td>
</tr>
<tr>
<td></td>
<td>(q)</td>
<td>Toxicity from amalgam fillings may give rise to oral lichen</td>
</tr>
</tbody>
</table>
13th International Conference on Mercury as a Global Pollutant

Providence, Rhode Island, USA

July 16-21, 2017
The International Agency for Research on Cancer (IARC) Classifies

Cadmium - known carcinogen
Inorganic lead - probable carcinogen
methylmercury - **possible carcinogen**

International Agency for Research on Cancer (IARC) *Agents Classified by the IARC Monographs*. 2012;1–106
The International Agency for Research on Cancer (IARC)

Classifies

Cadmium - known carcinogen
Inorganic lead - probable carcinogen
Methylmercury - possible carcinogen

International Agency for Research on Cancer (IARC) Agents Classified by the IARC Monographs. 2012;1–106
Primary target organ is the brain and nervous system

Range of symptoms:

- Cognitive emotional
- Nerve function motor function

Mercury can effect any tissue and system of the body:

- Kidney Allergic
- Fatigue Endocrine
- Chronic infections Gastro-Intestinal

Unique symptoms:

- Burning sensations heaviness in muscles
- Electric shock sensations visual abnormalities
Element of the ancients - power

Hg - Greek "hydrargyrum" - liquid silver

"Quicksilver" - reference to its mobility

Speed and mobility - Roman god, Mercury - messenger to all the other gods

Power - toxic

Mining - 1st mercury related human illness – tremors and cognitive
Public health disasters - Mercury
Minamata Bay, Japan (1956), Niigata, Japan (1960) and Iraq (1971)

Exposure to methyl mercury in Minamata Japan - 1956, 1960
Chemical factory - release of waste water with mercury 1950 - 1968 - accumulated in shellfish and fish
“Epidemic of the central nervous system”
Ataxia, paresthesias, muscle weakness, loss of peripheral vision, decreased hearing and speech
Paralysis, coma
Congenital
Mercury related neurological syndrome - Minamata Syndrome
2265 (2001 figure)
Deaths - 35% early on

Hair Hg
700 ppm - Minamato disease
200 ppm - non symptomatic
4 ppm - living outside of the area of exposure
Iraq - Poison Grain - seeds treated with methymercury fungicide
neurological symptoms
> 650 deaths
> 6000 ill

1970 New Mexico

Family exposed to seed grain contaminated with mercury - fed to their family pigs - who became ill - butchered - fed to family
Children more effected
Youngest 2 children died after prolonged vegetative state
Older children - chronic neurological - visual defects
Mercury
Elemental Pure Liquid
200,000 and 400,000 children in the United States are born each year with

Pre-natal exposure to methylmercury sufficient to put them at risk of neurologic impairment

1994 - United States Public Health Service declared that mercury amalgam exposure was higher than their established minimal risk level standard for the general population

100 million mercury fillings / year in the U.S.

1. Remove mercury in the vaccines administered in the U.S.
2. Recognition of mercury as a toxic agent
Mercury Symptoms / Health Effects

- Chronic fatigue depression anxiety
- Poor memory and cognitive function emotional instability
- Peripheral numbness or tingling
- Decreased senses of touch, hearing or vision
- Slurred speech
- Hypersensitivity and allergies
- Persistent / recurrent infections
- Chronic yeast / fungal overgrowth
- Compromised immune function
- Cardiovascular disease
- Dementia / tremor
- Headaches, joint pain, metallic taste in mouth
Mercury - Environment / Pollution

- Atmospheric exposures - outgassing from rock or through volcanic activity
- Human sources - coal burning and mining (mercury and gold), industrial waste in water
- Atmospheric elemental mercury - settles in water - converted by microorganisms into organic (methyl or ethyl)
- Ingested by smaller creatures which are eventually consumed by larger fish.
- Bio-accumulation - by larger fish - tuna, swordfish, or shark
- **Greatest source of mercury in biosphere** - human origin
- 1/3 emitted naturally
- **Global pollutant** - arctic fish and whales have high mercury
Most human exposure to mercury is caused by

1) Outgassing of mercury from dental amalgam
2) Ingestion of contaminated fish
3) Occupational exposure


Additional significant exposure:

Vaccines  past - childhood vaccines
EPA (1995) - safe daily mercury intake level = 0.1 ug / kg BW

Intake amounts that can be consumed every day over the course of an entire lifetime without significant risk of harm

150 pounds (68 kilograms) - 7 micrograms of daily mercury

5 - 10 ug daily

Low mercury fish - Pacific salmon 1 ug / oz - 4 - 8 oz
Higher mercury - canned Atlantic albacore tuna 13 ug / oz 2 - 4 oz 10x
Mercury - Exposure

EPA (1995) - safe daily mercury intake level = 0.1 ug / kg BW = 5 - 10 ug / day

Vaccines 25 ug (multi-dose flu and meningococcal) 15# / 7 kg = 0.7 ug = 35×

Amalgams 15 ug per amalgam per day / 4 amalgams = 60 ug daily (6 - 12×)
Mercury - Exposure

Occupational:

- Battery manufacturing ink manufacturing chlor-alkali processing
- Fish canning mining electrical component manufacturing
- Fluorescent lighting bronzing photo engraving

Home location - Living near fertilizer, paint, or chlor-alkali manufacturing plants

Medications:

- Nasal sprays and decongestants antibiotic eye solutions
- Skin lightening creams waterproof mascara
- Hemorrhoidal ointments

Home care products: Fungicides, pesticides, drain cleaners
Most human metallic mercury exposure comes from mercury vapor outgassing from amalgam fillings. At a rate of 2 to 28 micrograms per facet surface per day, of which about 80% is absorbed - World Health Organization and Berglund et al.

15 mcg / amalgam per day - mercury vapor / 80% absorbed


Amalgams are NOT stable in the mouth
Release mercury vapor - widely distributed - accumulates - toxic effects

Amalgams

- 300 tons of mercury in U.S.
- Dental office # 2 user

Removal - disposal - environmental contamination – mercury does not biodegrade - water soluble
Intake by animals and fish - converted to methyl mercury - fat soluble - stored / accumulates

FDA advisory: 2010
Amalgams should not be used in vulnerable populations
Amalgam risk should be disclosed to consumers and parents
Mercury Exposure – Lakes

50,000 U.S. lakes - warnings regarding eating fish (20% of U.S. lakes)
(50% of Florida lakes)

3000 lakes are closed due to mercury contamination

Biological toxin

- Primarily a neurotoxin
- Susceptible populations:
  - Children
  - Fetus
  - Kidney disease
Mercury exposure - Reality, history, legal

Dupont chemical company - $50 M settlement with state of Virginia to clean up mercury pollution

Rayon production factory - leaked mercury into the South River - 1929 to 1950

Mercury - tested / discovered in 1970s

High levels of mercury remain 60 years after exposure
3 general recommendations:

- Children, pregnancy - limit fish to 2x weekly
- Restrict total weekly consumption
- Select fish that are lower in mercury
Mercury - Exists in three forms

Elemental / metallic and vaporized mercury – thermometers and vapor out-gasing from amalgams

Inorganic mercury compounds - amalgams

Organic mercury - fish (methyl), vaccines (ethyl - thimerosal)
Mercury - Elemental and Gasous Vapor

Pure - uncombined form - not a natural state - not found significantly in nature

Silver liquid metal (Quicksilver) at room temperature - thermometer
  Poorly absorbed through skin and GI tract

Vapor form - highly absorbed — 80% — through mucous membranes of mouth

Distributed widely in body

Primary target - CNS

Binds tightly to SH groups

Accumulates throughout life

Half-life of mercury in the brain - estimated to be as long as approximately 20 years
Mercury - Inorganic

Inorganic - combining with elements other than Carbon
Mercury ions - found in salts - HgS, HgO, HgCl\textsubscript{2}
Commonly found - white powders / red - HgCl\textsubscript{2} - turns black after exposure to light

More toxic - more reactive - more difficult to eliminate - accumulates

**Used in amalgams** - to capture gold / to harden
**Chewing releases mercury as a vapor**
More water soluble / do not readily cross BBB or BPB
Less absorption - 10%
Tends to effect GI tract

**Greatest concentration** - kidney = major target organ for inorganic
excreted in urine and feces
Mercury - Organic

- Mercury combined with carbon - methylmercury, dimethylmercury, phenyl mercury
- Dietary - methylmercury (fish, seafood)
- Relatively well absorbed - gastrointestinal tract
- Distributed to all tissues
- In the body - methylmercury - mainly bound to the sulfur atom
- In brain, liver, kidney - organic Hg converted to inorganic Hg - stored as divalent mercury cation - reactive
- LOW excretion / Accumulation is significant and life long
- Biliary / fecal elimination - inorganic mercury
- Reviews of Environmental Contamination and Toxicology, 2009
- S. Díez, “Human health effects of methylmercury exposure,”
Massive acute exposure - mercury vapor
Erosive bronchitis and bronchiolitis
Respiratory failure
Tremor
Erethism (mad hatter disease) - severe behavior and personality changes, emotional excitability, loss of memory, insomnia, depression, fatigue, and in severe cases delirium and hallucination
Mercury Vapor - Mad Hatter Disease

Occupational disease among hatmakers - causes by chronic mercury poisoning

Felting exposed to mercury vapors from dyes

Neurotoxic effects - tremor and pathological shyness and irritability

“Danbury shakes” - haymaking industry in Danbury, CT
Elemental and Vaporized Mercury

- Chronic exposure - **Neurological dysfunction**
- Mood swings, nervousness, irritability, and other emotional changes
- Insomnia
- Headache
- Abnormal sensations
- Muscle twitching
- Tremors
- Weakness
- Muscle atrophy
- Decreased cognitive function
- High exposures - kidney malfunction, respiratory failure, and death
Inorganic Mercury Salts Poisoning Symptoms

**ACUTE:**

**Oral mercury salts** - *greater acute health effects*

Mercury salts are more corrosive than elemental mercury

Acute high dose exposure of mercuric salts

- Burning chest pain
- Darkened discoloration of the oral mucous membrane
- Severe gastrointestinal symptoms (corrosive damage)
- Stomatitis
- Impaired kidney function.
- 1 to 4 g of mercuric chloride is fatal in adults

Skin - dermatitis

Metal fume fever - acute phase of mercury vapor exposure

- fever
- headache
- dyspnea
- ejaculatory pain

- chills
- abdominal cramping
- dysuria
- dizziness
Inorganic Mercury Salts Poisoning Symptoms

Chronic:

Inorganic mercury poisoning

Target organ - kidney

Clinical - polyuria, proteinuria, edema, BP

Erethism - excessive sensitivity and reaction

Constellation of irritability, excitability, anxiety, insomnia, and social withdrawal

Chronic inorganic mercury toxicity

Classic Mercury Triad - chronic toxicity - tremors, gingivitis, and erethism

Additional - headache, visual disturbance (eg, tunnel vision), peripheral neuropathy, salivation, insomnia, and ataxia
Inorganic Mercury SALTS Poisoning Symptoms

- Acrodynia - pink disease - mercury toxicity and allergy in children
- Children - teething powders containing mercury compound (i.e., calomel)
  - Sweating
  - Erythematous rash of the palms and soles
  - Painful sensitivity to touch
  - Anorexia
  - Fatigue
  - Irritability
  - Photophobia
- Type of hypersensitivity reaction
- Caused by the deposit of mercuric chloride in the tissues
- Exposure to elemental mercury vapor can produce pink disease in children - paint and lacquer
Mercury Poisoning
Pink Disease
Mercury Poisoning
Pink Disease
Organic Mercury Poisoning Symptoms

- Methylmercury - from ingestion of fish
- Ethyl mercury from vaccines
- Causes neurological dysfunction
- Impaired neurological development - fetal / children

ANY neurological symptom:

- Peripheral vision impairment
- Stinging or needle-like sensations in the extremities and mouth
- Loss of coordination
- Muscle weakness
- Impairments of speech and hearing
- Developmental delay
- Burning and electric shock
Radioactively labeled mercury released from correctly placed amalgam fillings

Appears quickly in the kidneys, brain and wall of the intestines


Mercury - Toxicity

Mercury IM - within 24 hours - mercury is found in the spinal cord and brain

As well as other tissues - kidneys, lungs, connective tissue, and endocrine glands

Mercury does not appear to have a “half-life” in the central nervous system

Mercury - accumulates in nervous system
Pink Ladies: Mercury poisoning in twin girls

20-month-old twin girls presented with weakness, anorexia, papular rash, increasingly swollen, red and painful hands and feet * 1 month's duration.

Irritable and unwell and were diaphoretic

Tachycardia, one had an elevated blood pressure of 130/90 mm Hg

Reduced muscle power and diminished reflexes.

Palms and soles were erythematous and indurated

“Teething powder” from India once or twice a week over the 4 preceding months.

Blood mercury levels were 176 and 209 (normally < 18) μmol/L.

Teething powder still used in other parts of the world (Southeast Asia) Calomel - alternative medicine products
Mercury - Related health conditions

High mercury content in hair was associated with an increased progression of atherosclerosis and risk of CVD


“Mercury accumulation and accelerated progression of carotid atherosclerosis: a population-based prospective 4-year follow-up study in men in eastern Finland,”

Adverse effects on CVD have been observed at methylmercury levels much lower than those associated with neurotoxicity.

In vivo and in vitro studies: Mercury exposure promotes atherosclerosis


Kuopio Ischemic Heart Disease Risk Factor (KIHD) study
Circulation, 1995
“Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in Eastern Finnish men,”
Studies have correlated higher fish intake with lower CHD mortality
Men in Eastern Finland who ate fish had high CHD mortality
Concern was high content of mercury in fish of Eastern Finland
1833 men
No PMHx of CHD, stroke, claudication, and cancer
Dietary intake of fish and mercury
Hair and Urinary mercury
73 AMI
Highest levels of mercury in hair - 2x increase in AMI / 3x increase in cardiovascular death
Correlation - 24-hour urinary mercury excretion and the risk of AMI
Hair and urinary mercury associated significantly with titers of immune complexes containing oxidized LDL.
Increased risk may be due to the promotion of lipid peroxidation by mercury

"Fish oil-derived fatty acids, DHA, DPA, EPA and the risk of acute coronary events

Purpose: investigate the association between the serum om-3 fatty acids DHA, DPA, and EPA and the risk of acute coronary events in middle-aged men.

1871 men

Highest om-3 levels 44% less risk of AMI compared to lowest om-3 levels

Highest om-3 level and low hair Hg 67% less risk of AMI compared to lowest om-3 / high hair Hg

DHA+DPA were the protective oils

Conclusions: fish oil–derived fatty acids reduce the risk of acute coronary events

High mercury could reduce this protective effect
Mercury - Related Health Conditions

European Multicenter Case-Control Study on Antioxidants, Myocardial Infarction, and Cancer of the Breast (EURAMIC) study


“Mercury, fish oils, and the risk of myocardial infarction,”

High mercury content may diminish the beneficial effects of fish consumption on cardiovascular health

Health Professionals Follow-up Study (HPFS)

Increased cardiovascular risk following mercury exposure among dentists
Mercury – Toxicity - Mechanism of Action

- Methyl mercury reacts with **sulfhydryl groups** throughout the body
- **Potentially interfering with the function of any cellular or subcellular structure**
  - Interfere with DNA transcription and protein synthesis
  - Destruction of endoplasmic reticulum and disappearance of ribosomes
- Cell membrane integrity
- Reduction in Natural Killer cell activity
- Imbalance in Th2:Th1 ratios favoring autoimmunity
- Disruption of DNA repair
Mercury - Toxicity - Mechanism of Action

Induces oxidative stress
Depletes sulfhydryl - effects detoxification and antioxidant systems
Alters mitochondrial function
Induces apoptosis
Excessive immune activation
Imbalance in redox:
Increased reactive oxygen species generation
Reduced antioxidants defense capacity

“The pharmacology of mercury compounds,”

“Stimulation of lipid peroxidation by methyl mercury in rats,”

Toxicology, vol. 124, no. 3, pp. 211–224, 1997
“Mercuric compounds inhibit human monocyte function by inducing apoptosis: evidence for formation of reactive oxygen species, development of mitochondrial membrane permeability transition and loss of reductive reserve,”

Biochemical Pharmacology, vol. 45, 1993
“Studies on Hg(II)-induced H2O2 formation and oxidative stress in vivo and in vitro in rat kidney mitochondria,”
Mercury - Toxicity - Mechanism of Action

**Inhibit anti-oxidant systems**

- Strong binding for GSH - lowering and depleting levels
- Inhibits the activities of two key enzymes involved in GSH metabolism: GSH synthetase and GSH reductase.14


- Inhibits enzymes catalase, superoxide dismutase, and GSH peroxidase.

**Altered mitochondrial function**

- Mercury alters the structural integrity of the mitochondrial inner membrane / loss of normal cation selectivity

“Studies on Hg(II)-induced H2O2 formation and oxidative stress in vivo and in vitro in rat kidney mitochondria,”
Mercury - Toxicity - Mechanism of Action

- Inhibiting the activation of NF-κB (through SH binding)
  - Promote lipid peroxidation
  - Suppress NO production - inactivating the expression of iNOS gene

- Methyl mercury reacts with sulfhydryl groups throughout the body potentially interfering with the function of any cellular or subcellular structure.
Binding to Selenium - depletion
Mercury - high affinity for selenium - forms insoluble mercury selenide complexes
Reduce the bioavailability of selenium
Impair the activity of glutathione peroxidase
Promoting lipid peroxidation - atherosclerosis

“Mercury: selenium interactions and health implications,” Seychelles Medical and Dental Journal, vol. 7, 2004

** selenium - potential protector against methylmercury toxicity in populations consuming seafood

Selenium: relation to decreased toxicity of methylmercury added to diets containing tuna,” Science, vol. 175, 1972
Mercury - Toxicity - Mechanism of Action

Displaces Minerals:

Hg and Cd displace Zn and Cu from metallothione

- can cause functional deficiency of these minerals
Auto-immune
Hypothyroidism
Hypoglycemia
Fibromyalgia
Immune suppression - chronic infections
Induces antibiotic resistance in bacteria,

Mercury
1. Distributed throughout the body
2. Reacts with sulfhydryl groups throughout the body,

Potentially interfering with the function of any cellular or subcellular structure
TOXICOLOGICAL PROFILE FOR MERCURY
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service
Agency for Toxic Substances and Disease Registry
March 1999

Human Health Effects of Methylmercury Exposure
Reviews of Environmental Contamination and Toxicology - 2009
# 2 on ATSDR 2015 Substance Priority List

EPA “probable human carcinogen”
### Priority List of Hazardous Substances

<table>
<thead>
<tr>
<th>2015 RANK</th>
<th>SUBSTANCE NAME</th>
<th>TOTAL POINTS</th>
<th>2013 RANK</th>
<th>CAS RN</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>ARSENIC</td>
<td>1671.6</td>
<td>1</td>
<td>007440-38-2</td>
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<tr>
<td>2</td>
<td>LEAD</td>
<td>1529.4</td>
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<td>007439-92-1</td>
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<td>3</td>
<td>MERCURY</td>
<td>1458.6</td>
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<td>4</td>
<td>VINYL CHLORIDE</td>
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<td>000075-01-4</td>
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<td>5</td>
<td>POLYCHLORINATED BIPHENYLS</td>
<td>1345.1</td>
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<td>001336-36-3</td>
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<td>6</td>
<td>BENZENE</td>
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<td>CADMIUM</td>
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<td>007440-43-9</td>
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<tr>
<td>8</td>
<td>BENZO(A)PYRENE</td>
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<tr>
<td>9</td>
<td>POLYCYCLIC AROMATIC HYDROCARBONS</td>
<td>1279.1</td>
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<td>130498-29-2</td>
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<tr>
<td>10</td>
<td>BENZO(B)FLUORANTHENE</td>
<td>1249.7</td>
<td>10</td>
<td>000205-99-2</td>
</tr>
</tbody>
</table>
LEAD

NOT essential or needed for normal human metabolism

- Serves NO useful purpose in the human
- Can affect every organ system
- Mechanisms for toxicity
  - Inhibit or mimic the actions of calcium
  - Interact / disrupt with proteins (sulfhydryl, amine, phosphate and carboxyl groups)

Nervous system - most sensitive target

No lower threshold for some of the adverse neurological effects of lead in children

Neurological effects in children - documented at exposure levels once thought to cause no harmful effects (<10 µg/dL)

No safe level

Increased susceptibility based mineral / nutrient levels, genetics, environmental exposure(Chemical, Vaccine)
Primary Organ Sites for Noticeable Toxic Effects

Neurological / Kidney / Bone

Wide range of neurological effects - some irreversible

#1 Storage Tissue Site for Lead

Bone
2 forms - organic and inorganic

Inorganic lead - old paint, soil - more common exposure

Organic Lead - lead based gasoline / occupational / industrial uses

- more toxic - more readily absorbed
Most lead exposure is inorganic - lead in old paint / soil / pipes

Public health concern - children - more sensitive and greater long term impact on health

Landrigan (2002) estimate - U.S. incurs $43.4 billion annually in the costs of all pediatric environmental disease
  - Childhood lead poisoning accounting for the vast majority
  - Medical costs, disability, education and parental lost work time.

The most widespread source of lead for U.S. children - lead paint that remains in older building and homes

Children - increased significant risk of lead poisoning
  - Due to their hand to mouth activity - house dust and soil
  - Due to higher oral absorption and neurological distribution due to incomplete BBB
  - Due to physiology and greater impact on developing neurological tissue
Banned from consumer use paint and as an gasoline additive in the U.S. - 1970s

Released into the home environment by peeling, chipping, chalking, friction, or impact, home renovation

85% of all homes built before 1978 in the U.S. have lead-based paint in them (CDC 1997a)

Lead may be tracked into homes in significant quantities from exterior soil - contaminated by historical use of lead in paint, gasoline, or industries.

Concentrations in soil, air, and water can be especially high near historic or ongoing mining operations or smelters

Soil concentrations can be high on farms lands with past use of leaded gasoline and in yards of older homes

Occurs in drinking water through leaching from lead-containing pipes, faucets
Industrial and commercial products
- Bright red and yellow paints on bread bags and candy may contain lead (ATSDR 2005; Mushak et al. 1989 as cited in AAP 1993).
- Imported cans may still contain lead
Food or beverages may be stored in lead-containing vessels
- “Safe” pottery and ceramic-ware can become harmful if the protective glaze wears off and exposes people to lead-containing pigments.
- Lead-glazed pottery - imported
Lead - Exposure

- Major exposure - industrial: inhalation and ingestion of lead-bearing dust and fumes
- Smelting, refining, and manufacturing industries experience the highest and most prolonged occupational exposures
- Increased risk for occupational lead:
  - Battery manufacturing plants, construction workers - renovation/rehabilitation
  - Rubber products and plastics industries, soldering
  - Steel welding/cutting operations, bridge maintenance and repair workers
  - Municipal waste incinerator workers
  - Radiator repair mechanics, pottery/ceramics industry employees
Exposure - Common - Ubiquitous

Lead exposure is a **global issue** - Lead mining and lead smelting in many countries - children and adults

Inhalation, ingestion > dermal contact.

- Inhalation - workers in lead-related occupations - >90 absorption
- Ingestion - Lead exposure in the general population (including children) - > 50% absorption
Lead paint is the major source of lead exposure for children.

Lead paint deteriorates or pulverizes due to friction (e.g., in windowsills, steps and doors).

House dust and surrounding soil may become contaminated.

Enters the body through normal hand-to-mouth activity. (Sayre et al. 1974 as cited in AAP 1993)

Children are still at significant risk of lead poisoning:
- Due to their hand to mouth activity
- Due to higher oral absorption and greater neurological distribution (incomplete BBB)
- Due to greater sensitivity of developing neurological tissue

Children who live in older housing are more likely to have elevated BLLs.
Most adult exposures are occupational

Between 0.5 and 1.5 million workers are exposed to lead in the workplace (ATSDR, 1999)

Lead dust can be transferred to homes
Lead - Exposure

Additional exposure:

Home renovation

Lead related hobbies and activities:

- Car repair
- Electronics soldering
- Glass or metal soldering
- Glazed pottery making
- Stained-glass making
- Target shooting
- Molding of bullets, slugs, or fishing sinkers
- Cosmetics - Imported

Supplements - Herbal (China, India)

Artificial turf

Toys and toy jewelry

Tattoos, hair dyes
Toxic effects of lead - Neurological have been observed at low lead levels

NO SAFE level

2012 - CDC 5 μg/dL  upper reference range value for BLLs in children
Advisory level for environmental and educational intervention

2015 - NIOSH <5 μg/dL  the reference blood lead level for adults

National Institute for Occupational Safety and Health (NIOSH) –
Conducts research and making recommendations to HHS
For prevention of work-related injury and illness
Under HHS / CDC
Sister agency for enforcement is OSHA
Main sources of lead contamination of food:

- Soil
- Industrial pollution
- Agricultural technology
- Food processing

Sources - account for most cases of lead exposure:

- Gasoline additives
- Food-can soldering
- Lead-based paints
- Ceramic glazes
- Lead pipe water systems
- Folk remedies

Decreasing Blood Lead Levels (BLL) in U.S.

Average BLL - adults 18-74 years of age - (CDC 1997b)
1976-70 14.2 μg/dL from
1988-1991 3.0 μg/dL

Overall prevalence of elevated BLLs (> 10 μg/dL) - U.S. population - 0.7%. = 3 million (CDC 2005)

WHO-OSHA safe BLL in workers < 40 μg/dL

No safe level of lead exposure has yet been defined - by studies
Lead exposure can lead to kidney dysfunction / conditions
   Fanconi-like syndromes - impaired absorption at proximal renal tubule
      - bicarbonate - renal acidosis
      - phosphorous - bone disorders - osteomalacia, Ricket’s

Chronic nephropathy

Gout

Most lead-associated renal effects or disease are a result of

- Ongoing chronic exposure
- Latent effect of chronic past lead exposure
95% Body Burden - Bones and teeth - adults (children 75%)

Accumulates in the most metabolically active bone

Trabecular bone (inward, spongy) and growth plates during childhood

Cortical (outer hardened) and trabecular bone in adulthood

Two physiological STORAGE compartments exist for lead

- Relatively inactive bone can store lead for decades
- More active bone component readily exchanges bone lead with the blood

Bone-to-blood lead mobilization:

- Pregnancy lactation menopause physiologic stress
- Chronic disease hyperthyroidism kidney disease broken bones advanced age
- Vit D / Calcium deficiency
The nervous system = Most sensitive target of lead exposure

Neurological effects of lead in children have been documented at exposure levels once thought to cause no harmful effects (<10 µg/dL).

Otherwise asymptomatic individuals may experience neurological effects from lead exposure.

Contribute significantly to socio-behavioral problems such as juvenile delinquency and violent crime (Needleman 2002, Nevino).

Correlation between of higher BLL

The lower IQ
Higher hyperactivity / attention
Hearing impairment
Adults generally require higher exposure to be effected

**Neuro-Cognitive - Psychiatric symptoms - lead-exposed workers - BLLs ranging from 40 to 120 µg/dL**

<table>
<thead>
<tr>
<th>Symptom</th>
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<tbody>
<tr>
<td>Decreased libido</td>
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<tr>
<td>Diminished cognitive performance</td>
</tr>
<tr>
<td>Diminished reaction time</td>
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<tr>
<td>Dizziness</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Impaired concentration</td>
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<tr>
<td>Increased nervousness</td>
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<tr>
<td>Lethargy</td>
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<tr>
<td>Paresthesia</td>
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<tr>
<td>Weakness</td>
</tr>
<tr>
<td>Peripheral nerve dysfunction</td>
</tr>
<tr>
<td>Depression/mood changes, headache</td>
</tr>
<tr>
<td>Diminished hand dexterity</td>
</tr>
<tr>
<td>Diminished visual motor performance</td>
</tr>
<tr>
<td>Dullness</td>
</tr>
<tr>
<td>Forgetfulness</td>
</tr>
<tr>
<td>Impotence</td>
</tr>
<tr>
<td>Irritability</td>
</tr>
<tr>
<td>Malaise</td>
</tr>
<tr>
<td>Reduced IQ scores</td>
</tr>
<tr>
<td>Postural balance</td>
</tr>
</tbody>
</table>

*Slowed nerve conduction and forearm extensor weakness (wrist drop)*
Lead - Toxicity

Bone Marrow

Inhibition of hemoglobin production

>50 µg/dL for occupationally exposed adults

>25 µg/dL for children

2 types of anemia - Basophilic stippling of the RBC
Acute high-level lead exposure - Hemolytic anemia
Chronic lead exposure - Frank anemia

Hypochromic
Normo- or microcytic
Reticulocytosis

Basophilic stippling of RBC - 1899 - Classic laboratory sign
Aggregations of ribosomes - Only found in RBCs
Lead Toxicity - Anemia

Basophilic strippling os RBC

1899

Classic Laboratory sign

Aggregations of ribosomes – only found in RBC’s

Lead and Arsenic Metal Toxicity
Lead Toxicity - Anemia

- Basophilic stippling of RBC
- 1899: Classic laboratory sign
- Aggregations of ribosomes - only found in RBCs
- Lead and Arsenic metal toxicity
BLLs > 30

Hypertension
Hypertensive Heart Disease
Cerebrovascular Disease


Continued decline in blood lead levels among adults in the United States: the National Health and Nutrition Examination Surveys

2 Nationally representative cross-sectional surveys

Third National Health and Nutrition Examination Survey

1988-1994 (n = 16,609)

1999-2002 (n = 9961)

1. Declining BLLs

2. Higher blood lead levels - associated - hypertension among non-Hispanic blacks and Mexican Americans.

3. Greater risk - chronic kidney and peripheral arterial diseases among the overall population
Lead – Male Reproductive Effects

Current occupational exposures / BLL > 40 ug / dL

- Decrease sperm count totals and motility
- Increase abnormal sperm frequencies

At higher occupational / environmental exposure levels - adverse pregnancy outcomes

Increased frequency of spontaneous abortions (Nordstrom et al. 1979)

Miscarriages and stillbirths (Baghurst et al. 1987; McMichael et al. 1986)

Women with BLL 5-9 µg/dL 2-3x more likely to have a spontaneous abortion than were women with BLL lesser than 5 µg/dL. (Borja-Aburto et al. 1999).
Prenatal exposure to low lead levels (BLLs of 14 µg/dL) may increase the risk of reduced birth weight and premature birth.

Increased risk for minor congenital abnormalities (minor skin abnormalities and undescended testicles).

Lead - bone development / growth

Lead can result in delayed growth in children.

Increased likelihood of osteoporosis (weakened bones later in life) in animals exposed to lead.

Suspected factor in human osteoporosis.
Lead - Carcinogenicity / Cancer

EPA - classified lead and inorganic lead as Group 2B: **probable human carcinogens**. (ATSDR 1999)

National Toxicology Program classifies lead and lead compounds as “reasonably anticipated to be a carcinogen” (NTP 2004)
Lead - clinical presentation / symptoms
Most patients who suffer from lead poisoning are asymptomatic

THUS - importance of exposure assessment and screening

1st Signs in children:
- Subtle neurobehavioral problems
- Changes in classroom behavior and social interaction
- Developmental, speech, and hearing impairments

Most people with lead toxicity are not overtly symptomatic

Some of the health effects of lead exposure on the various organ systems (see “Physiological Effects” section) are permanent or latent and may appear after exposure has ceased.
Lead Exposure - Continuum of signs / symptoms

Lowest Exposure Dose Signs and Symptoms:

- Impaired Abilities / often appears asymptomatic
- Decreased learning and memory
- Lowered IQ
- Decreased verbal ability
- Impaired speech and hearing functions
- Early signs of hyperactivity or ADHD
Low Exposure Dose Signs and Symptoms:

Myalgia or paresthesia
Mild fatigue
Irritability
Lethargy
Occasional abdominal discomfort
Moderate Exposure Dose

Signs and Symptoms

- Arthralgia
- General fatigue
- Difficulty concentrating/Muscular exhaustibility
- Tremor
- Headache
- Diffuse abdominal pain
- Vomiting
- Weight loss
- Constipation
High Exposure Dose Signs and Symptoms

Paresis or paralysis
Encephalopathy—may abruptly lead to seizures, changes in consciousness, coma, and death
Lead line (blue-black) on gingival tissue
Colic (intermittent, severe abdominal cramps)
Lead poisoning

Lead buildup in the body causes serious health problems

**Symptoms**
- Headaches
- Irritability
- Reduced sensations
- Aggressive behavior
- Difficulty sleeping
- Abdominal pain
- Poor appetite
- Constipation
- Anemia

**Additional complications for children:**
Lead is more harmful to children as it can affect developing nerves and brains
- Loss of developmental skills
- Behavior, attention problems
- Hearing loss
- Kidney damage
- Reduced IQ
- Slowed body growth

Source: MedlinePlus/Mayo Clinic
Lead - Screening

Every child with:

- Behavioral disorder
- Speech impairment
- Who may have been exposed to lead
- Siblings, housemates, and playmates of children with suspected lead toxicity

Any person living:

- Older houses
- Certain occupations and farming conditions
- Degenerative neurological, kidney, and bone diseases
Lead Testing

Usual 1st test in suspected on-going exposure - blood lead level

Capillary blood draws (fingersticks) - not reliable for diagnosis - used for screening

Urine chelation challenge - for estimating body burden

Hair - screening test - of recent exposure

Greater risk of contamination using the finger-stick method, an elevated BLL obtained through finger-sticking should always be confirmed through venipuncture. (AAP 1993 and CDC, 1997a)

Most blood is stored in bone - BLL often under-represent the total body burden

Longbone radiographs - "lead lines" - increased density on growth plates of the bone - finding of chronic exposure.
Lead Lines

Longbone Radiograph of knees - "lead lines"

3 yo girl - blood lead level of 10.6 µg/dL
Lead - Detoxification/Treatment

Chelation - EDTA, DMPS, DMSA - effective / safe

Essential elements - calcium, zinc, iron, selenium, and antioxidant vitamins - counteract the toxic effects of lead

“Interaction of lead with some essential trace metals in the blood of anemic children from Lucknow, India,”

Cadmium - Toxicity

Chronic cadmium exposure is associated with hypertension and diabetes.

Studies - cadmium may exert effects on the cardiovascular system at extremely low exposure levels.

In-vitro studies data - initiation of pathophysiological changes in the vessel wall.

Potentiates some diabetic complications related to renal tubular and glomerular function.

National Health and Nutrition Examination Surveys (NHANES)

Significant association between high urinary Cd levels and elevated fasting blood glucose levels.

- Arterial dysfunction
- Promoting atherosclerosis

Blood cadmium level was independently associated with myocardial infarction.


May contribute to the pathogenesis of CVD

- Increased oxidative stress - in vivo
- Depletion of glutathione and alteration of sulfhydryl homeostasis
- Indirectly increasing oxidative stress and lipid peroxidation

Vascular lining - allow for increased transport of cadmium across the endothelium

Retaining high amounts of cadmium in smooth muscle cells disrupts endothelial integrity
Interferes with the homeostasis and function of other minerals

Disruption of transport mechanisms - zinc (Zn2+), iron (Fe2+), manganese (Mn2+), calcium (Ca2+)

Replacement of other metals in cellular proteins (metallothionein)

**Higher zinc levels protective against Cd toxicity** - probably through metallothionein induction
Cadmium – Toxicity
Cadmium - Toxic Effects

Itai-itai disease - severe anemia - suppression of erythropoietin production

Increased rates of autoimmunity
Increased production of nonspecific antibodies
Decreased production of antigen-specific antibodies
Suppressed Lymphocyte proliferation and natural killer cell activity

“Effects of physiological concentrations of heavy metals both individually and in mixtures on the viability and function of peripheral blood human leukocytes in vitro,” Journal of Toxicology and Environmental Health A, vol. 71, no. 19, pp. 1327–1337, 2008
Disruption endocrine capacity - dis regulating pituitary hormones

2007-8 NHANES survey

Increased blood Cd levels were associated with **suppressed TSH production**


Cadmium - Metalloestrogen

In vitro and in vivo animal studies

Binding of Cd to breast cancer estrogen receptors


Rat Studies

**Male infertility** - damage to the blood-testis barrier, decreasing germ cell adhesion leading to germ cell loss, reduced sperm count and subfertility or infertility

Increased prostaglandin F2alpha

Male - cavernosal vasoconstriction - *suppressed testosterone synthesis* and secretion

Female - *destruction of corpus luteum* and fetus in the female.

Human epidemiological studies have not associated Cd as a cause of male infertility or erectile dysfunction

Cadmium - Toxicity

Insulin resistance / Diabetes


Metabolic syndrome.

Nerve cells

- Oxidative stress and membrane disturbances in the central nervous system
- Reduction in acetylcholinesterase activity
- Increase in oxidative stress markers
- Depletion of glutathione, superoxide dismutase 2, and other antioxidants
- Depletion of catalase, glutathione peroxidase, and glutathione-S-transferase
- Apoptosis of cortical cells in the central nervous system
- Decreased attention level and memory decreased learning ability.
- Decreased low-frequency hearing


Zinc 25 - 100 mg

MIT - Metallothionein Induction Therapy

Minerals - selenium, manganese

Vit C - 5000 mg

Dietary - meat, seeds

Chelation DMPS, EDTA, DMSA

SH - GSH, Methionine

Sauna - odor or taste sensation, fatigue, moody, pain in kidneys and bones, facial and skin burning rash

Cadmium Detoxification - Chelation

EDTA > DMSA, DMPS

**EDTA - mobilizes intracellular / tissue cadmium**

Enhanced excretion - GSH, Methionine, Zinc

Dose: EDTA 1 gram / hour - not sooner than 5 days apart

I one gram per hour nor in dosage greater than three grams per session.

Replacement of essential minerals between sessions.
Chelation Protocols - by national physician associations


American College for Advancement in Medicine, Chelation Module, American College for Advancement in Medicine, Irvine, Calif, USA, 2010.

Advanced Medical Education and Services Physician Association, Introduction To Clinical Metal Toxicology, Advanced Medical Education and Services Physician Association, San Antonio, Tex, USA, 2007.

Autism Research Institute, Clinician Seminar Level 1, Autism Research Institute, San Diego, Calif, USA, 2010.
Significantly increased during sauna

Cadmium - Basic considerations

Average absorption - 5%

Younger population - higher cadmium absorption rates - 20–40% - reuptake via enterohepatic circulation

Zinc, Calcium, and Iron deficiency: INCREASE Cd absorption

Prevention of Cadmium Toxicity - #1 Zinc / #2 Minerals

Cd - generally higher in women - lower iron levels

Smokers - 2x cadmium body burden vs. Nonsmokers

Binds tightly to metallothionein - not efficiently excreted from body

Poor excretion = accumulation

Irreversibly accumulates in the human body - kidneys and liver and testes (metallothionein production)

Kidney - most affected organ - accumulation and toxicity
Aluminum
Aluminum

#3 abundant element (8 percent) in the Earth’s crust (oxygen - 47% and silicon - 28 percent)

Not essential / vital to human metabolism and health

**Tendency to accumulate** - with continued exposure

Less toxic than mercury, arsenic, lead or cadmium / **more persistent / more insidious**

Aluminum = neurotoxin / excitotoxin

Brain - most sensitive organ to Al - even more true for a developing nervous system

**Impossible to avoid** - but awareness / prevention - proactive - remediation - limiting
Aluminum - Toxicity

MSDS (Material Safety Data Sheet)

Aluminum is a poison that accumulates in the brain and tissues of the body

TOXICOLOGICAL PROFILE FOR ALUMINUM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Agency for Toxic Substances and Disease Registry

400 page
September 2008
Aluminum – Toxicity Clinical

- Personality changes, altered mood, depression
- Fatigue, lethargy
- Diminished alertness, brain fog
- Microcytic anemia, weakness, fatigue
- Visual and auditory hallucinations
- Epileptic seizures
- Memory loss
- Dementia
- Bone Disease / Osteomalacia / Osteodystrophy
- Speech and language impairment
- Motor disturbances (tremors, myoclonic jerks, ataxia, convulsions, asterixis, motor apraxia, muscle fatigue)
Aluminum Toxicity

- Memory Loss
- Mental Confusion
- Allergies
- Irritability
- High Blood Pressure and Heart Problems
- Weight Gain
Aluminum - Toxicity

Notable symptoms of aluminum toxicity:

Diminishing *intellectual* function

**Forgetfulness**

Inability to *concentrate*

In high doses:

**Dementia** and large enough doses - *cardiac arrest*
Steady increase of aluminum in our environment and diet

U.S. production of aluminum

1986 1.4 million tons.

2006 2.37 million tons

Total amount of Al in adult: 50 to 150 mg

Estimated amount ingested through food and water: 10 - 100 mg DAILY

2007 JECFA (Joint Expert Committee on Food Additives)
provisional tolerable weekly intake (PTWI) for aluminium from all sources
1 mg/kg of body weight (FAO/WHO, 2007)
70 mg/week
10 mg/day
Half of the water utilities use aluminum sulphate to clarify drinking water.

Most of the utilities in Europe and the United States exceed the maximum safe amount of aluminum (100 mcg. per liter).

Some of these by as much as 60 times the amount considered "safe."
Aluminum in OTC:

Maalox® extra strength 306 mg. of aluminum hydroxide for each dose

Mylanta® contains 500 mg
Cooking utensils—aluminum pots, teflon pans and foil-wrapped foods
Beverages in aluminum cans—phosphoric acid leaches
Anti-caking agent to salt and sugar
Baking powder
Bleaching agent in white flour
Emulsifier in processed cheeses
Cake mixes, self-rising flour and frozen dough
Commercial teas
Antiperspirants
Toothpaste
Sunscreen lotions
Cosmetics
Cigarette filters
**Infant formulas—soy formulas 10x**
Vaccines
OTC medications: anti-acids, buffered aspirin, vaginal douches, anti-diarrheal
Occupational—welding and smelting
Primary - brain and bones

Less toxic, more insidious, more persistent
A deficiency in essential mineral - accumulation / deposition aluminum - bones, lungs and brain

50 % skeleton,
25 % lung tissue
25 % brain

Ascorbates, sulfur and magnesium contribute to body’s ability to excrete aluminum efficiently
Effects of aluminum on the central nervous system

(1) Nucleus and gene expression

Binding to DNA
Binds to histone-DNA complex and induces conformational changes of chromatin.
Induces topological changes of DNA.

Altered gene expression
Induces decreased expression of neurofilament and tubulin.
Induces altered expression of genes of neurofilament, APP, and neuron specific enolase.
Induces decreased expression of transferrin receptor.
Induces altered expression of RNA polymerase I.
Induces downregulation of mitochondrial cytochrome c oxidase.
Induces altered expression of calbindin-D28k.
Induces decrease in the expression of nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF).
Induces expression of pro-inflammatory genes and pro-apoptotic genes.
Induces elevated expression of APP.
Induces altered expression of oxidative stress marker genes (SOD1, glutathione reductase, etc.).
Induces decreased expression of neprilysin.
Induces altered expression of β-APP secretase (BACE1 and BACE2).
Table 1: Effects of aluminum on the central nervous system.

(2a) Cellular functions

- Energy metabolism
  - Inhibits Krebs cycle enzymes
  - Inhibits the activity of hexokinase
  - Inhibits the activity of phosphofructokinase
  - Inhibits the activity of glucose-6-phosphate dehydrogenase
  - Causes mitochondrial dysfunction and depletion of ATP
  - Decreases in activity and expression of TCA-cycle related enzymes (succinate dehydrogenase (SDH), alpha-ketoglutarate dehydrogenase (KGDH), isocitrate dehydrogenase-NAD+ (IDH), fumarase (FUM), aconitase (ACN), and cytochrome c oxidase (Cyt C Ox)).

- Phosphorylation and dephosphorylation
  - Inhibits the activity of protein phosphatase.
  - Increases the activity of protein kinase C and cytoskeleton proteins.
  - Accelerates phosphorylation and accumulation of neurofilament.
  - Enhances Ca2+/Calmodulin dependent protein kinase activity.
  - Accelerates phosphorylation of MAP 2 and neurofilament.
  - Inhibits dephosphorylation of tau.
  - Induces nonenzymatic phosphorylation of tau.
Table 1: Effects of aluminum on the central nervous system.

(2b) Cellular functions

Abnormal accumulation of proteins
- Causes the conformational change and the accumulation of neurofilament and MAP1A, MAP1B
- Accelerates the phosphorylation of tau and its accumulation
- Causes the accumulation of tau protein in neuroblastoma cells or in primary cultured neurons
- Causes the accumulation of tau protein in experimental animals
- Causes neurofibrillary degeneration in vivo
- Causes the accumulation of AβP in cultured neurons or in neuroblastoma cells
- Causes the accumulation of AβP in vivo

Neurotransmitter release / receptor inhibition
- Inhibits glutamate release
- Impairs synaptic transmission
- Inactivates glutamate dehydrogenase
- Inhibits NMDA-type glutamate receptor
- Inhibits choline acetyl transferase and tyrosine hydroxylase, glutamate decarboxylase.
Aluminum - Toxicity

**TOXIC** to cells and central nervous system

Exposure - **ubiquitous / unavoidable**
Accumulation - **gradual**
**Subtle and non-specific changes**
Difficult to detect
**Greater risk** - with nutrient / anti-oxidant deficiencies and oxidative stress / inflammation

**Activates immune system** to the Th2, or antibody driven immune system - allergic responses and auto-immune
Purpose: vaccine adjuvant - when mixed with the antigen of virus / bacteria - greater immune response

Higher Abs

Helps overcome the anti inflammatory effect of breast milk

Safety: studies to support claims of safety - LACKING
Which vaccines typically contain aluminum?

Live vaccines do not contain aluminum.

Killed/inactivated viruses / "toxoid" vaccines DO contain aluminum.

17 aluminum based vaccines in U.S.

ex. DTaP and hepatitis B vaccines
How Much Aluminum?
Vaccine Exposure

1970s 4 vaccines - 1200 mcg
2010 17 vaccines

In 18 months = 4,925 micrograms (mcg) of aluminum

100% absorbed —— transported - distributed

2016 6150 mcg
Aluminum Exposure - Vaccines

- 5000 mcg  4,925 micrograms (mcg) of aluminum within the first 18 months of life (plus formula, water)

- 200 - 600 additional 170 to 625 mcg by the age of 6

- 6000 mcg once completed all vaccines

- 6 mg

- 100% absorbed vs. orally ingestion - 1%
Inactivated Vaccines (Aluminum containing) - higher risk of reactions / toxicity

African study - 2014

Mortality during 12 months of follow-up after vaccination with live versus inactivated vaccines.

Some children received multiple injections of live vaccines
Others received both live and inactivated vaccines

Death rate - over the following six months:

8x - live and inactivated vaccines

64 percent higher mortality rate
Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau.

Studies from low-income countries indicate co-administration of inactivated DTP and live attenuated MV = increased mortality compared with receiving MV only.

Pentavalent (DTP-H. Influenza type B-Hepatitis B) vaccine is replacing DTP in many low-income countries.

2007-2011 randomised placebo-controlled trial

2331 children

Placebo - live vaccines only (MV or MV+YF)

Combination - live and inactivated vaccines (MV+DTP or MV+YF+pentavalent)

6 month follow up - mortality rate ratio

3.2 live and inactivated vaccines vs live only

7.3 MV+YF+pentavalent - live and inactivated vs live only

CONCLUSION:

In line with previous studies of DTP, the present results indicate that pentavalent vaccine co-administered with MV and YF is associated with increased mortality

2X INCREASED MORTALITY WHEN PENTAVALENT VACCINE + LIVE VIRUS VACCINES
Aluminum Toxicity – Vaccine Auto-Immune Reaction

Autoimmune - Inflammatory Syndrome Induced by Adjuvants (ASIA)

Shoenfeld's syndrome - autoimmune - proposed by Israeli immunologist Yehuda Shoenfeld in 2011

J Autoimmun. 2011

'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants.

In recent years, four conditions LINKED to adjuvants:

- Siliconosis
- Gulf war syndrome (GWS)
- Macrophagic myofasciitis syndrome (MMF)
- Post-vaccination phenomena
Translocation of bio-persistent particles (aluminum) from muscle to brain

252 patient reports of alum-associated ASIA

Mouse experiments - assess bio-distribution of vaccine-derived aluminum and of alum-particle fluorescent surrogates injected in muscle

Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection

Particles linearly accumulated in the brain up to the six-month endpoint

Occurs at a very low rate in normal conditions explaining good overall tolerance of alum despite its strong neurotoxic potential.

However, continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe, especially in the case of over immunization or immature/alter blood brain barrier.
Bio-persistence and brain translocation of aluminum adjuvants of vaccines.

Concerns - causative role in the so-called macrophagic myo-fasciitis (MMF) lesion - patients with myalgic encephalomyelitis/chronic fatigue/syndrome.

MMF revealed - long-lasting bio-persistence of alum within immune cells

Promptly phagocytosed in muscle and the draining lymph nodes - disseminate within phagocytic cells throughout the body and slowly accumulate in brain

Strongly suggests that long-term bio-persistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity

ADMISSION: The understanding of basic mechanisms of particle bio-persistence and brain translocation represents a major health challenge...

** Unknown

** The toxicity of aluminum in vaccines—may even exceed the toxicity of mercury in the human body
Aluminum Exposure - Breast milk vs Formula

Breast milk - 21 mcg of aluminum / day

Conventional formula - 114 mcg / day

5x fold increase exposure
Rabbit studies: **80 to 94 percent** - retained 28 days after IM

Autopsy examinations: accumulated - kidneys, spleen, liver, heart, lymph nodes, and brain.

Long-term - bones
Aluminum Exposure - accumulation

- Studies on human infants - **aluminum is not excreted**
- Blood and urine levels of aluminum over 12 hours
- No increase in blood levels of aluminum following vaccination
- No significant increase in urinary excretion
- “stays at the site of injection” “not a risk to nervous system”
- Excretion of aluminum is not as efficient in infants and young children
- Non excretion = accumulation
Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report.

Aluminium - neurotoxin and occupational exposure to aluminium has been implicated in neurological disease including Alzheimer's disease.

The first comprehensive and unequivocal data demonstrating significantly elevated brain aluminium content in an individual occupationally exposed to aluminium.

CASE PRESENTATION: 66-year-old Caucasian man who died with Alzheimer's disease.

Significantly elevated brain aluminium content, 2.98 (2.73) μg/g dry weight

Following occupational exposure to aluminium over a period of 8 years.
Aluminum - “normal levels and safety“

2013 Children's Hospital of Philadelphia's (CHOP) vaccine education center website:

"Aluminum is considered to be an essential metal with quantities fluctuating naturally during normal cellular activity.

It is found in all tissues and is also believed to play an important role in the development of a healthy fetus."
Aluminum - widely recognized neurotoxin

Inhibits more than 200 biologically important functions

Causes various adverse effects in plants, animals, and humans

Aluminum may play crucial roles as a cross-linker in β-amyloid oligomerization
Heavy Metals - Tattoos

Known toxins and carcinogens:

Heavy metals - mercury, cadmium, aluminum, arsenic, nickel, cobalt, chromium, titanium

Benzopyrene

Phthalate
Allergic reactions to metals and metal salts used in pigments for tattoos are surprisingly frequent.

Mass spectrometry analysis of tattoo dyes:

**Highest elements**
Chromium, Nickel, Cadmium

**Lower elements**
Cobalt, Mercury, Beryllium

**Color - Metal Relationships:**

- **Red**
  - Hg, Cd

- **Blue**
  - Co, Al

- **Yellow**
  - CD

- **White**
  - Ni, Cd

- **Green**
  - Chr
American Environmental Safety Institute (AESI)

index card (3 by 5 inch) sized tattoo - average of 1.23 ug lead

>2x amount permitted per day (0.5 ug) - California’s Proposition 65
Tattoo Takeover

Visible tattoos on their child's primary school teacher or pediatrician is unlikely to raise eyebrows across a variety of professions.

3 in 10 U.S. adults have at least 1 tattoo up from 2 in 10 in 2012.

Do no harm.
Prevalence of Tattoos - Exposure to Heavy Metal

Pew Research Center - 2013 - **45 million Americans**

Harris Poll - 2015 - `2,225
U.S. adults - online survey

30% tattoos vs. 20% (2010) - 70% have more 2 or more

47% of Millennials

$ 1.6 Billion annually in U.S.
2007 lawsuit - American Environmental Safety Institute (AESI)

Two tattoo ink manufacturers must now place warning labels on their product containers, catalogs and websites

“Inks contain many heavy metals, including lead, arsenic and others” and that the ingredients have been linked to cancer and birth defects.

FDA does not regulate or approve tattoo pigments does have the authority and ability to investigate should health concerns warrant
Common reactions to tattoo ink and tattooing process:

- Allergic rashes
- Infection
- Inflammation from sun exposure
- Chronic skin reactions

Cutaneous tuberculosis and non-tuberculous mycobacterial infections - (contaminated ink or diluting water)

Red ink is associated more frequently with long-term reactions
- Granulomatous and pseudo lymphomatous phenomena
- Morphea-like lesions
- Vasculitis - Hg, Cd

J Cutan Aesthet Surg. 2015 Jan-Mar;8(1):30-6
Complications of Tattoos and Tattoo Removal: Stop and Think Before you ink.
Chemical research on red pigments after adverse reactions to tattoo

20% of tattooed patients - adverse reactions
Allergic contact dermatitis psoriasis with Koebner's phenomena and granulomatous reactions (red)

A medical-toxicological view of tattooing.

little is known about the toxicological risks of the ingredients used
Tattoos, inks, and cancer.

A large amount of metallic salts and organic dyes remain in the skin for lifetime. Potential local and systemic carcinogenic effects of tattoos and tattoo inks.

Reviewed the literature and found 50 cases of skin cancer on tattoos:

- 23 cases of squamous-cell carcinoma and keratoacanthoma
- 16 cases of melanoma
- 11 cases of basal-cell carcinoma

The number of skin cancers arising in tattoos is low - considered as coincidental.
Cadmium - Toxic Metal

Periodic table of chemistry: cadmium below zinc

“Zinc blocking metal” - 200 enzymes effected

Toxic heavy metal - one of the more toxic - #7 on ATSDR 2015 Substance Priority List

Disrupts biological systems at much lower level than most toxic metals

Cigarette smoking - most significant source of human cadmium exposure

Primary organ of toxic impact in the human - kidney

Other organ: cardiovascular, bone, skin

Human studies - estimated 7% of the general population have renal tubule dysfunction from Cd exposure

Health effects of cadmium exposure, a review of the literature and a risk estimate
Scand. J. Work Environ. Health 24(Suppl.):1–51
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Periodic table -
Renal insufficiency cough
Prostate cancer carcinogenic
Bone diseases - demineralization
Ovarian dysfunction - progesterone / testosterone

Cadmium may be a risk factor for osteoporosis

The toxicity of cadmium and resulting hazards for human health

Cadmium may be a risk factor for osteoporosis

The Scientific World Journal - Volume 2013
Review Article
Cadmium Toxicity and Treatment
Cadmium Toxicity
Effects / Symptoms:

Zinc deficiency - antagonizes zinc (more than 300 enzymes)
Infertility in men - low sperm count
DNA / RNA processing - Defective gene expression
Copper accumulation / dominance
Mental / Behavioral - ADHD, violence, anti-social, hardened personality
Degenerative - premature aging and hardening of tissue - arteries and kidneys
renal insufficiency
High blood pressure
Chronic cough, lung cancer
Birth Defects

Inhalation of vapor / particles during industrial exposure (welding or soldering) - chemical pneumonitis
Arsenic

Induced Skin Cancer
Arsenic

Mees Lines
White Discoloration
ArSENiC
Keratosis
Arsenic
Skin
Arsenic
PTW Wood
Laboratory indicators / changes in Heavy Metal Toxicity
Laboratory indicators/changes in Heavy Metal Toxicity
Indications of Mitochondrial Dysfunction
Uncoupling of oxidative phosphorylation
Elevated fatty acid metabolites
Elevated lactate
Elevated hydroxymethylglutarate
Multiple partial blocks in Krebs cycle
Elevated 3-methyl histidine
Elevated sarcosine
Elevated pyroglutamate
Elevated vanilmandellate
Elevated homovanillate
Fractionated urine porphyrins
Elevated coproporphyrin
Elevated precoproporphyrin
Porphyriins Profile
Immune System Tests

- High IgE
- Low IgG
- Low IgG subclasses
- Low CD8
- Low NK
- High CD3/CD26
Tests for Oxidative Stress

Low SOD
Low reduced GSH
Low GSH peroxidase
High lipid peroxides
Tests for Neurotransmitters

High blood / platelet serotonin

High epinephrine / norepinephrine

Urine wasting of sulfur / sulfate

Low plasma sulfate with normal urine sulfate / creatinine
Heavy Metal Testing
Heavy Metal Testing

Options

- Blood
- Urine
- Hair
- Stool
- BioEnergetic

Additional considerations

- Minerals
- GSH
- Sulfur - cysteine
Testing for Mercury / Metal Toxicity

Which metal and which method

Current vs Past Exposure

**Blood, hair, unprovoked urine** - NOT a good method for testing for past exposures

**Mercury and other metals** - short half-life (weeks) in the blood

Hair and unprovoked urine

- Measure of recent exposure - days (urine) / weeks (hair)
- Reflect ability to excrete toxic metals
- Affected by heavy metal body burden
- Body's glutathione level (controls excretion)

Blood and Unprovoked Urine - measure of recent exposure

Provocation Test: - IV / oral / rectal / topical chelators before and during collection of urine or stool sample

1) metal was present in the body
2) increased body burden
3) demonstrates that the detoxification agent can promote its excretion
4) not equivalent to body burden (CNS/brain)
Testing for Mercury / Metal Toxicity

Blood - antibodies - very specific / auto-immune

Urine Porphyrins - more accepted test for chronic metal toxicity in the traditional medical community

Bio-energetic - clinical AK / computer biofeedback - least accepted TMC / growing prevalence in CAM
Blood, hair, and unprovoked urine mercury

- reflect recent exposure
- does not correlate with total body burden

Hair - Maternal scalp hair may be the best indicator of fetal brain levels

Blood and unprovoked urine levels correlate fairly well to each other

Kazantzis, “it has not been possible to set a level for mercury in blood or urine below which mercury related symptoms will not occur”

Mercury symptoms can occur at any blood or urine level, blood and urine levels often usually under reflect tissue levels and even more so CNS levels
<table>
<thead>
<tr>
<th>Porphyrin Pathway Intermediates</th>
<th>Results</th>
<th>Quintile Ranking</th>
<th>95% Reference Range</th>
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<td>16.6</td>
<td>&lt;= 27.2</td>
</tr>
<tr>
<td>2. Heptacarboxyporphyrin</td>
<td>2.6</td>
<td>5.9</td>
<td>&lt;= 11.2</td>
</tr>
<tr>
<td>3. Hexacarboxy porphyrin</td>
<td>&lt;DL</td>
<td>2.1</td>
<td>&lt;= 3.3</td>
</tr>
<tr>
<td>4. Pentacarboxy porphyrin</td>
<td>&lt;DL</td>
<td>7.5</td>
<td>&lt;= 5.4</td>
</tr>
<tr>
<td>5. Precoproporphyrin*</td>
<td>7.2</td>
<td>33</td>
<td>&lt;= 14.8</td>
</tr>
<tr>
<td>6. Coproporphyrin I</td>
<td>16</td>
<td>89</td>
<td>&lt;= 56</td>
</tr>
<tr>
<td>7. Coproporphyrin III</td>
<td>35</td>
<td></td>
<td>&lt;= 159</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calculated Values</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Total Porphyrins</td>
<td>61</td>
<td>143</td>
<td>&lt;= 233</td>
</tr>
<tr>
<td>9. Precopro/Uro I &amp; III</td>
<td>1.01</td>
<td>0.64</td>
<td>&lt;= 1.11</td>
</tr>
<tr>
<td>10. Copro I/Copro III</td>
<td>0.46</td>
<td>0.53</td>
<td>&lt;= 0.87</td>
</tr>
</tbody>
</table>

Creatinine = 175 mg/dL
## Elemental Analysis - Whole Blood

### Inductively Coupled Plasma/Mass Spectrometry

#### Annie Tucker

<table>
<thead>
<tr>
<th>Ciliator</th>
<th>Rhett Bergeron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Of Birth</td>
<td>03-25-1961</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Element</th>
<th>Present (mg/dL)</th>
<th>Analyzed (mg/dL)</th>
<th>Percentile by Quintile</th>
<th>Percentile by Quintile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfur</td>
<td>5.18</td>
<td>NA</td>
<td>4.20-6.25</td>
<td>41%</td>
</tr>
<tr>
<td>Ferrum</td>
<td>92</td>
<td>NA</td>
<td>58-112</td>
<td>66%</td>
</tr>
<tr>
<td>Iodine</td>
<td>0.33</td>
<td>NA</td>
<td>&lt;0.1-0.67</td>
<td>37%</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3.20</td>
<td>NA</td>
<td>2.72-4.65</td>
<td>37%</td>
</tr>
<tr>
<td>Cadmium</td>
<td>6.6</td>
<td>NA</td>
<td>3.7-13.0</td>
<td>54%</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.5</td>
<td>NA</td>
<td>&lt;0.2-1.3</td>
<td>75%</td>
</tr>
<tr>
<td>Copper</td>
<td>142</td>
<td>NA</td>
<td>88-339</td>
<td>19%</td>
</tr>
<tr>
<td>Zinc</td>
<td>564</td>
<td>NA</td>
<td>376-725</td>
<td>55%</td>
</tr>
</tbody>
</table>

### Metallic Toxic Elements

<table>
<thead>
<tr>
<th>Element</th>
<th>Present (ug/mL)</th>
<th>Percentile by Quintile</th>
<th>Percentile by Quintile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni</td>
<td>0.38</td>
<td>54%</td>
<td>48%</td>
</tr>
<tr>
<td>Pb</td>
<td>0.38</td>
<td>48%</td>
<td>45%</td>
</tr>
<tr>
<td>Cu</td>
<td>2.86</td>
<td>99%</td>
<td>73%</td>
</tr>
<tr>
<td>Sr</td>
<td>4.17</td>
<td>99%</td>
<td>73%</td>
</tr>
<tr>
<td>Cr</td>
<td>0.38</td>
<td>58%</td>
<td>47%</td>
</tr>
<tr>
<td>Sb</td>
<td>24</td>
<td>58%</td>
<td>47%</td>
</tr>
</tbody>
</table>

Notes: Test results are not intended for the diagnosis of disease. They are intended for interpretation by qualified healthcare professionals with a full knowledge of patient history to assist in their administration of appropriate healthcare measures.

Quick Silver Lab

1576 Miller's Dr. Ste. 101
Lafayette, CO 80026
(303)-531-0661

Lab Director: Christopher W. Shade, Ph.D.
www.quicksilverscientific.com

E-MAILED: Received Date

[Signature]
Testing for Mercury / Metal Toxicity

Provoked urine challenges - DMSA / DMPS / EDTA

Extensive history, literature, controversy, and ignorance

Limited danger - but real - dosing and compatibility is important
Heavy Metal Testing

- Heavy Metal Testing - provoked urine
- Example - nurse with memory concerns
- ex. oral DMSA (Chelex) urine lead - 60
- ex. IV DMPS urine lead - 120
- lead levels were 2x the levels after DMPS
Testing for Mercury / Metal Toxicity - basic considerations of urine provoked testing

DMSA - methylmercury or organic mercury
DMPS - inorganic mercury

DMSA - does not effect or pull from amalgams
DMPS - pulls from amalgams

Consider using both compatibly
Testing for Mercury / Metal Toxicity - basic considerations of urine provoked testing

- Decreased glutathione level can mask a high body burden of metals
- Repeated detoxification and supporting therapy (minerals, sulfur) - before significant excretion occurs
- Lower doses of chelator agents may fail to increase excretion significantly
- Higher doses may be needed for provocation testing vs. lower doses for long-term treatment
- Detoxification / chelating agent may preferentially bind to one metal first - hide the presence of other metals
- Mercury can be tightly bound to body tissue - may not be removed until significant amounts of other toxic metals have been removed
Warning - Na₂EDTA - provoking and treatment

**Na₂EDTA - EDTA (slow) vs. CaNaEDTA (fast)**

Acute fatal hypocalcemia have been reported following the improper administrations


**Deaths resulting from hypocalcemia after administration of edetate disodium: 2003-2005**

From 2003 to 2005, deaths of 3 individuals as a result of cardiac arrest caused by hypocalcemia during chelation therapy were reported to the Centers for Disease Control and Prevention. Two were children.


Pediatric fatality secondary to EDTA chelation.

**CASE REPORT:**

A five-year-old autistic male - while receiving his third treatment he went into cardiac arrest - had been given edetate disodium rather than edetate calcium disodium - profound hypocalcemia / cardiac arrest - that led to his death.
American College of Medical Toxicology

Heavy metals are ubiquitous in the environment
Exposure is constantly occurring

Chelating agents

- Bind metallic and metalloid elements
- Have been shown to increase their elimination from the body.
- Mobilize metals in healthy individuals who have a body burden considered normal for a standard reference population
- Mobilize metals in those who are determined to have a high body burden

Chelating agents may

- Increase the elimination of certain essential elements (zinc, copper, iron)
- Promote target organ redistribution of metallic elements of concern such as mercury

Position of the American College of Medical Toxicology - post-challenge urinary metal testing has not been scientifically validated

- Has no demonstrated benefit
- May be harmful when applied in the assessment and treatment of patients in whom there is concern for metal poisoning
Testing for Antibodies - Metals and Their Binding Proteins

Metals can bind to different amino acids and become antigenic.

Activate T-cells - production antibody (IgG, IgM, IgA) - auto-immune

Ex. nuclear proteins - fibrillarin and chromatin (30-50% of children with autism + Abs)
Cyrex - Neurological Autoimmune Reactivity Screen

- IgG and IgA
- Myelin basic protein
- Asialoganglioside
- Alph and Beta Tubulin
- Cerebellar
- Synapsin
<table>
<thead>
<tr>
<th>ARRAY S</th>
<th>Normal</th>
<th>Ab</th>
<th>Cut-off</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid Cell + A1ATase</td>
<td>X</td>
<td>0.1-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Intestinal Factor</td>
<td>X</td>
<td>0.2-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>ANCA + ANA</td>
<td>X</td>
<td>0.1-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>X</td>
<td>0.3-3.3</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>X</td>
<td>0.3-3.3</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Thyroid Peroxidase</td>
<td>X</td>
<td>0.3-3.3</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Perinuclear Cytoplasmic</td>
<td>X</td>
<td>0.3-3.3</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Cytoplasmic</td>
<td>X</td>
<td>0.3-3.3</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Cytoplasmic/PAS</td>
<td>**</td>
<td>**</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Serum &amp; Intra-Cell</td>
<td>X</td>
<td>0.4-7</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Glomerular Basement Membrane</td>
<td>X</td>
<td>0.1-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Cardiolipin</td>
<td>X</td>
<td>0.1-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Alpha-fetoprotein</td>
<td>X</td>
<td>0.2-7.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>C-Reactive Protein</td>
<td>X</td>
<td>0.1-1.4</td>
<td>**</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Serum 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**All analytes are tested for IgG and IgM combined.**

**Ovary and Testes are tested together to avoid any confusion arising out of potential cross-reactivity.**

*Reference ranges are calculated based on the mean ± 2 (2 standard deviations). Results < 0.5 and > 10.0 above the mean are considered to be abnormal. An approach to avoid the cross-reactivity is to use separate analytes and suppress test-positive results. Results > 2 SD are considered out of range, invalid, or abnormal.*
Mercury Exposure and Antinuclear Antibodies among Females of Reproductive Age in the United States: NHANES

1,352 females from the National Health and Nutrition Examination Survey (NHANES) 1999–2004

Examined associations between mercury biomarkers and antinuclear antibody (ANA) positivity and titer strength.

Hair, blood, urine

16% ANA positive - speckled staining pattern

The higher the ANA, the stronger the correlation with mercury levels

Methylmercury, at low levels generally considered safe, was associated with subclinical autoimmunity among reproductive-age females

Autoantibodies may predate clinical disease by years
Heavy Metal Testing - Porphyrrins

Porphyrin pathway - eight enzymes - 4 steps in mitochondrial / 4 steps in cytosol

Important in heme and cytochromes synthesis

Effects energy and detoxification

Urinary porphyrin testing - 1940s
Porphyrin Pathways

**Synthetic Pathway**

1. Succinyl CoA + glycine
2. δ-Aminolevulinic acid
3. Porphobilinogen
4. Hydroxymethylbilane
   - UP-1: Uroporphyrinogen III
   - CP-1: Coproporphyrinogen III
5. Protoporphyrinogen
6. Protoporphyrin
7. Heme

**Enzyme**

- Aminolevulinate synthase
- Aminolevulinate dehydratase
- Porphobilinogen deaminase
- Uroporphyrinogen synthase
- Uroporphyrinogen decarboxylase
- Coproporphyrinogen oxidase
- Protoporphyrinogen oxidase
- Ferrochelatase

**Type of Porphyria**

- ALADD
- AIP
- CEP
- LCP/HEP
- HCP
- VP
- EPP
Urine porphyrins - biomarkers of toxins

1. Pathway is highly active - large accumulations of intermediates
2. Enzymes of the porphyrin pathway are widely distributed in body
3. Highly sensitive to the presence of various toxins
# Conditions That Can Cause Porphyria

## Genetic Disorders
- 
- Hereditary hyperbilirubinemias
  - Dubin–Johnson syndrome
  - Rotor’s syndrome
- Bronze baby syndrome
- Erythrohepatic protoporphyria
- Hereditary tyrosinemia

## Metabolic Disturbances
- Diabetes mellitus
- Myocardial infarction
- Hematologic diseases
  - Hemolytic, siderochrestic, sideroblastic, aplastic anemias
  - Ineffective erythropoiesis (inframedullary hemolysis)
  - Pernicious anemia
  - Thalassemia
  - Leukemia
  - Erythroblastosis
- Disturbance of iron metabolism
  - Hemosiderosis
  - Idiopathic and secondary hemochromatosis
  - Iron deficiency anemia

## Diseases
- Infectious diseases
  - Mononucleosis
  - Acute polymyositis
- Liver diseases
  - Cirrhosis
  - Active chronic hepatitis
  - Toxic and infectious hepatitis
  - Fatty liver
  - Alcoholic liver syndromes
  - Drug injury
  - Cholestasis
  - Cholangitis
  - Biliary cirrhosis
- Malignancies
  - Hepatocellular tumors
  - Hepatic metastases
  - Pancreatic carcinoma
  - Lymphomatosis

## Other Conditions
- Pregnancy
- Carbohydrate fasting

---

### Conditions That Can Cause Porphyria

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Hereditary hyperbilirubinemias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dubin–Johnson syndrome – Rotor’s syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Bronze baby syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Erythrohepatic protoporphyria</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Hereditary tyrosinemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Myocardial infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hematologic diseases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Disturbance of iron metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diseases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Infectious diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver diseases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Malignancies</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Other Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th>Carbohydrate fasting</th>
</tr>
</thead>
</table>
Inherited porphyrin enzyme deficiencies - 90% are healthy throughout adulthood until their porphyria is triggered

1. Toxic chemicals or drugs
2. An acute illness or worsening chronic condition
3. Major dietary change
Altered porphyrin metabolism as a biomarker of mercury exposure and toxicity

<table>
<thead>
<tr>
<th>Environmental Toxin-induced Porphyrinurias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Environmental toxin</strong></td>
</tr>
<tr>
<td>Urinary porphyrin elevation (or as noted)</td>
</tr>
<tr>
<td><strong>Arsenic</strong></td>
</tr>
<tr>
<td>Uroporphyrins Coproporphyrin I High Copro I/III ratio</td>
</tr>
<tr>
<td><strong>Mercury</strong></td>
</tr>
<tr>
<td>Precoproporphyrin Pentacarboxyporphyrin Coproporphyrin (total)</td>
</tr>
<tr>
<td><strong>Lead</strong></td>
</tr>
<tr>
<td>Aminolevulinic acid (ALA) Coproporphyrin III Coproporphyrin I (sometimes) Zinc protoporphyrin</td>
</tr>
<tr>
<td><strong>Hexachlorobenzene</strong></td>
</tr>
<tr>
<td>Uroporphyrins</td>
</tr>
<tr>
<td><strong>Methyl chloride</strong></td>
</tr>
<tr>
<td>Coproporphyrins</td>
</tr>
<tr>
<td><strong>Dioxin</strong></td>
</tr>
<tr>
<td>Uroporphyrins</td>
</tr>
<tr>
<td><strong>Polyvinylchloride</strong></td>
</tr>
<tr>
<td>Coproporphyrins</td>
</tr>
<tr>
<td><strong>Polybrominated biphenyl</strong></td>
</tr>
<tr>
<td>Coproporphyrins (Uroporphyrins)</td>
</tr>
</tbody>
</table>
Heavy Metal - evaluation / testing - additional considerations:

Mineral

Anti-oxidant markers / detoxification - Sulfur status
Detoxification pathways - genetics and functional
<table>
<thead>
<tr>
<th>Test</th>
<th>Reference Range</th>
<th>Sample Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>1.00 - 2.50 mg/dl</td>
<td>1.20 mg/dl</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.8 - 2.6 mg/dl</td>
<td>2.00 mg/dl</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>2.5 - 4.5 mg/dl</td>
<td>3.0 mg/dl</td>
</tr>
<tr>
<td>Sodium</td>
<td>135 - 145 mEq/l</td>
<td>140 mEq/l</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5 - 5.0 mEq/l</td>
<td>4.0 mEq/l</td>
</tr>
<tr>
<td>Chloride</td>
<td>98 - 106 mEq/l</td>
<td>102 mEq/l</td>
</tr>
</tbody>
</table>

Credible Concentration
URINE OVALES (or urine) Leucocytes: 1,200

Protein Content: 24.2 g/dl

Specimen: Fresh urine; freezing or refrigeration was not used.
sample - genova mineral metal sample report
### Quick Silver

#### Sample Report

#### Minerals

#### Metals –

---

**Element Analysis - Whole Blood**

<table>
<thead>
<tr>
<th>Element</th>
<th>Result</th>
<th>Units</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>4.59 g/dL</td>
<td>&lt;4.00 - 5.20</td>
<td></td>
</tr>
<tr>
<td>Chlorine</td>
<td>8 µg/dL</td>
<td>&lt;3.1 - 11.1</td>
<td></td>
</tr>
<tr>
<td>Copper</td>
<td>90 µg/dL</td>
<td>40 - 116</td>
<td></td>
</tr>
<tr>
<td>Iodine</td>
<td>&lt;1 µg/dL</td>
<td>&lt;1 - 10</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>4.25 mg/dL</td>
<td>2.84 - 3.32</td>
<td></td>
</tr>
<tr>
<td>Molybdenum</td>
<td>0.44 µg/dL</td>
<td>&lt;0.4 - 1.9</td>
<td></td>
</tr>
<tr>
<td>Selenium</td>
<td>486 µg/dL</td>
<td>158 - 305</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>65 µg/dL</td>
<td>46 - 112</td>
<td></td>
</tr>
</tbody>
</table>

---

**Potential Trace Elements**

<table>
<thead>
<tr>
<th>Element</th>
<th>Result</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimony</td>
<td>5.5 µg/dL</td>
<td>&lt;11</td>
</tr>
<tr>
<td>Arsenic</td>
<td>1.7 µg</td>
<td>&lt;5.1</td>
</tr>
<tr>
<td>Barium</td>
<td>3.6 µg/dL</td>
<td>&lt;4.1</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.8 µg/dL</td>
<td>&lt;0.8</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.9 µg/dL</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Lead</td>
<td>1.04 µg/dL</td>
<td>&lt;2.51</td>
</tr>
<tr>
<td>Mercury</td>
<td>0.1 µg/dL</td>
<td>&lt;0.4</td>
</tr>
<tr>
<td>Silver</td>
<td>&lt;0.3 µg/dL</td>
<td>&lt;0.3</td>
</tr>
<tr>
<td>Selenium</td>
<td>5 µg/dL</td>
<td>&lt;43</td>
</tr>
<tr>
<td>Silicon</td>
<td>6.8 µg/dL</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>

---

**Percentile Rank by Quartile**

- 10th: 40th: 90th: 100th

---

*Please note: results are not for the diagnosis of disease. They are intended to provide additional information to qualified healthcare professionals with a full knowledge of patient history to assist in the implementation of an appropriate healthcare regimen.*

Quick Silver Scientific

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Lafayette, CO 80026

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Lab Director: Christopher W. Shade, Ph.D.

www.quicksilverscientific.com
Quick Silver
Sample Report
Minerals
Metals-
Page 2
Genomic Profile
Genomic Profile

**Phase II Detoxification: Conjugation of Toxins and Elimination**

In Phase II detoxification, large water-soluble molecules are added to toxins, usually at the molecular site formed by Phase I reactions. After Phase II modifications, the body is able to eliminate the transformed toxins in the urine or bile (through the liver).

**Methylation**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Location</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMT</td>
<td>V159M</td>
<td>?</td>
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</table>

**Acetylation (N-acetyltransferase)**

**Slow Metabolizer Polymorphism**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Location</th>
<th>Effect</th>
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</thead>
<tbody>
<tr>
<td>NAT1</td>
<td>PM4N</td>
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<tr>
<td>NAT1</td>
<td>P189TQ</td>
<td>Liver/Dist</td>
</tr>
<tr>
<td>NAT2</td>
<td>1147TQ</td>
<td>Liver/Dist</td>
</tr>
<tr>
<td>NAT2</td>
<td>3807TQ</td>
<td>Liver/Dist</td>
</tr>
<tr>
<td>NAT2</td>
<td>2282NE</td>
<td>Liver/Dist</td>
</tr>
<tr>
<td>NAT2</td>
<td>PM4G</td>
<td>Liver/Dist</td>
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**Fast Metabolizer Polymorphism**

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<th>Gene</th>
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</tr>
</thead>
<tbody>
<tr>
<td>NAT2</td>
<td>K289R</td>
<td>Liver/Dist</td>
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</table>

**Glutathione Conjugation (GSHtransferase)**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Location</th>
<th>Effect</th>
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<tbody>
<tr>
<td>GSTM1</td>
<td>1913C</td>
<td>Liver/Kidney</td>
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<tr>
<td>GSTP1</td>
<td>1105V</td>
<td>Brain/Skin</td>
</tr>
<tr>
<td>GSTP1</td>
<td>5114V</td>
<td>Brain/Kidney</td>
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**Oxidative Protection**

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<tr>
<td>SOD1</td>
<td>C203A</td>
<td>Cytosol</td>
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<tr>
<td>SOD1</td>
<td>A14V</td>
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</tr>
<tr>
<td>SOD2</td>
<td>A94V</td>
<td>Mitochondrion</td>
</tr>
</tbody>
</table>

**Key**

- Neither chromosome carries the genetic variation.
- One chromosome (of two) carries the genetic variation.
- Both chromosomes carry the genetic variation.

*(You inherit one chromosome from each parent)*
Cadmium - Toxicity – “Cd - female personality”

- Tough cowgirl or “tom” girl
- Older physical appearance memory impairment
- Unhappy or anger demeanor crudeness
- Increased libido critical or negative regarding males
- Aggressiveness / violence lack of compassion
- Energy vampires
Cadmium Exposure

Cigarette smoking Marijuana
Tap water Coffee
Hydrogenated vegetable oils Cigarette paper
Shellfish Large ocean fish - tuna, cod, haddock
Maternal transfer Water contamination
Braking systems

Manufacturing / Industrial:

Plating, galvanizing, semiconductor, links, pigments in dyes and paints
Television screens, lasers, batteries, paint pigments
Cosmetics
Barrier in nuclear fission
Used with zinc to weld seals in lead water pipes < 1960s
Detection / Assessment for Cadmium:

Tissue Hair Analysis - can be under reflected

Accumulates more in bones, kidneys, and brain

Urinary (unprovoked) cadmium - not reflective of body burden

Blood cadmium - indicator of recent exposure - 3 month

Provoked urine challenge - deposited stores in kidneys and rough estimate of body burden

Reasonable to screen high risk individuals (smokers, persons with industrial exposure)
Cadmium Toxicity Effects / Symptoms:

- Zinc deficiency - antagonizes zinc (more than 300 enzymes)
  - Infertility in men - low sperm count
  - DNA / RNA processing - Defective gene expression
- Copper accumulation / dominance
- Mental / Behavioral - ADHD, violence, anti-social, hardened personality
- Degenerative - premature aging and hardening of tissue - arteries and kidneys
- Renal insufficiency
- High blood pressure
- Chronic cough, lung cancer
- Birth Defects
- Inhalation of vapor / particles during industrial exposure (welding or soldering) - chemical pneumonitis
Cadmium - Toxicity - “Cd - Female Personality”

- Tough cowgirl or “tom” girl
- Older physical appearance
- Unhappy or anger demeanor
- Increased libido
- Aggressiveness / violence
- Energy vampires
- Memory impairment
- Crudeness
- Critical or negative regarding males
- Lack of compassion
Cadmium - Exposure

Cigarette smoking, Tap water, Hydrogenated vegetable oils, Shellfish, Maternal transfer, Braking systems

Manufacturing / Industrial:

Plating, galvanizing, semiconductor, links, pigments in dyes and paints, television screens, lasers, batteries, paint pigments, Cosmetics, Barrier in nuclear fission, Used with zinc to weld seals in lead water pipes < 1960s

Marijuana, Coffee, Cigarette paper, Large ocean fish - tuna, cod, haddock, Water contamination
Detection / Assessment for Cadmium

- Tissue Hair Analysis - can be underestimated

- Accumulates more in bones, kidneys, and brain

- Urinary (unprovoked) cadmium - not reflective of body burden

- Blood cadmium - indicator of recent exposure - 3 month

- Provoked urine challenge - deposited stores in kidneys and rough estimate of body burden

- Reasonable to screen high risk individuals (smokers, persons with industrial exposure)
OligoScan – Spectro-Photometry
• Using light to measure absorbance level or optical density of specific molecule

• Every molecule reflects light in a unique way - measurable

• Based on Beer-Lambert law - absorbance or light interaction - directly proportional to concentration of molecules

• Surface of the hand - epidermis analysis

• Tissue / intracellular levels
OligoScan – Sample report
• J Occup Med Toxicol. 2006
• The toxicity of cadmium and resulting hazards for human health
• Renal insufficiency cough
• Prostate cancer carcinogenic
• Bone diseases - demineralization
• Ovarian dysfunction - progesterone / testosterone
• Cadmium may be a risk factor for osteoporosis
• The Scientific World Journal - Volume 2013
• Review Article
• Cadmium Toxicity and Treatment
Heavy Metal Poisoning and Cardiovascular Disease

Cardiovascular disease (CVD) is an increasing health problem and traditional risk factors fail to account for all deaths from CVD

Environmental, dietary and lifestyle behavioral factors that are the control keys in the progress of this disease

Evidence for the link between heavy metals with CVD and the proposed mechanisms of toxicity
Metal Detox Treatment
Heavy Metal Detoxification - Chelation Therapy:
Heavy Metals - Basic Facts

- Exposure - unavoidable / low grade / continuous
- Levels - accumulation
- Toxicity - non-specific and subtle changes - unrecognized
- Every person needs heavy metal assessment - at some time
- Response - Responsibility - Detoxify or Die
- Metal Detoxification - safe and effective
Heavy Metal - BASIC TREATMENT STRATEGY

Identify / remediate exposure

Comprehensive strategy - more successful / better tolerated

Chelation
Minerals
Anti-oxidants
Supporting elimination
Energetic - biocompatibility testing

The earlier in life, the better the outcomes

The slower, the better

Repeat / on-going maintenance protocols
Heavy Metal - BASIC TREATMENT STRATEGY

• Identify exposure and discontinue / eliminate – fish, amalgams, vaccines, lead pain and pipes, treated wood

• Optimize minerals - ZINC, selenium

• Support Anti-oxidant pathways

• Support sulfur based biochemistry

• Support optimal elimination / excretion in liver-bile, colon, kidneys, skin

• Target - Detoxify loosely bound / systemic metals - 1st

• Detoxify CNS - last

• Oral chelation can be effective ALONE and enhances IV chelation
Metal Detox Treatment - Components

- Elimination / Drainage Support - lymph, kidney, liver, skin
- Herbal, Homeopathic, Laser-assisted, Sauna
- Minerals - zinc, magnesium, selenium
- Sulfur - MSM, garlic, methionine, NAC
- Rx chelators - DMPS, DMSA, EDTA
- Nutraceutical / Metabolic chelators - GSH, ALA, PC
- Plant / Herbal based - chlorella, cilantro, garlic
- BioEnergetic - Homeopathic, Laser assisted
- IV Therapy - Vit C, PC, GSH, NAC, ALA, DMPS, EDTA, Minerals
1. Diet - reduce inflammatory / processed foods / increase fiber
   Optimize minerals and sulfur - baseline mineral assessment
   Deficiencies of minerals and sulfur - risk factor in metal accumulation / poor response to treatment
   MSM 1/8 - 1 tsp. 1 - 2x daily
   Fresh garlic 1-2 cloves per day

2. Mineral Replacement
   Multi mineral - without copper
   Zinc 25 - 100 mg daily
   Liquid/ Ionic minerals

3. Enhance mineral / nutrient uptake
   HCL / Digestive enzyme
   Repair leaky gut

4. Support intestinal elimination
   HCL / Fiber / Vit C / Magnesium
   Whole flaxseed - 1 - 2 tbsp. - freshly ground - add to yogurt / smoothie / oatmeal
Types of Chelators

- Pharmaceutical Rx
- Dietary
- Plant / Herbal
- Plant Nutraceutical
- Nutritional / Metabolic Chelators
- Homeopathic
Metal Detoxification

Pharmaceutical Chelation Therapy

- Well studied - through world
  - Effective
  - Safe

- Metal mobilization does not always equal metal excretion

- Risk of redistribution

- Can increase the excretion of minerals / induce or worsen mineral deficiencies

- Possibility of side effects - kidney damage, death, allergic reactions,

- Worsening of neurological symptoms from redistribution
• Chelation was developed to combat arsenic based gas; then was gradually applied to other heavy metals
• Cant Lewis PhD - U.S. researcher - developed Lewisite - arsenic based chemical weapon, but then the Germans obtained it and threatened to use it
• British developed British anti-lewisite (BAL) - dimercaprol - sulfur / thiol based molecule
• BAL increased urinary excretion of Ar and significantly decreased the time of dermatitis (60 to 20 days)
• Arsenic based antibiotics in treatment of syphilis - dermatitis and hepatotoxicity
• Charity Hospital, New Orleans - Ar expose children
• **Side effects** of BAL / Dimercaprol: Nausea and vomiting (most common), hypertension, excessive sweating and tears, pain at intramuscular injection sites
Metals - History of heavy metal detoxification / chelation therapy

Early studies on di-thiols: 1940s
Dithiol compounds as antidotes for arsenic

British anti-lewisite (BAL)

Nature. 1945; 156:616–619
Diagnosis and treatment of lesions due to vesicants.

The effect of BAL on the excretion of arsenic in arsenical intoxication.

Metals - History of heavy metal detoxification / chelation therapy

The Role of Chelation in the Treatment of Arsenic and Mercury Poisoning

DMPS, DMSA, Dimercaprol - mainstay of chelation treatment of arsenic and mercury intoxication for more than half a century

Animal experiments and some human data: dithiol chelators enhance arsenic and mercury excretion

Controlled animal experiments support a therapeutic role for these chelators in the prompt treatment of acute poisoning by arsenic and inorganic mercury salts.
1st studies –
Mice injected with arsenic - DMPS or DMSA or saline injected intraperitoneal
Rabbits - single injection of BAL
Injection given 5 min after arsenic exposure:
100 % survival
Delayed treatment > 6 h: 0% survival

Established principle -
Efficacy of chelation is greatest when administered promptly (minutes to hours) after arsenic exposure delayed chelation is diminished chelation
History of metal detoxification - chelation

Chelation and Mercury
1949 Longcope and Luetscher, John Hopkins
Oral mercuric chloride (commonly used for suicide 1920-40s)

Before availability of chelation BAL / only supportive treat - 30%
mortality with BAL within 4 hour - 0% mortality

Ann Intern Med. 1949; 31:545–553
The use of BAL (British Anti-Lewisite) in the treatment of the
injurious effects of arsenic, mercury, and other metallic poisons
Chelation Protocols - by National Physician Associations


2) American College for Advancement in Medicine, Chelation Module, American College for Advancement in Medicine, Irvine, Calif, USA, 2010.

3) Advanced Medical Education and Services Physician Association, Introduction To Clinical Metal Toxicology, Advanced Medical Education and Services Physician Association, San Antonio, Tex, USA, 2007.

Autism Research Institute, Clinician Seminar Level 1, Autism Research Institute, San Diego, Calif, USA, 2010.
1990 rat studies - Mercuric Chloride

Immediate high dose chelation with inj. BAL or oral DMPS or oral DMSA vs control
90% mortality in controls
High survival in treated groups
100% survival in DMPS
Chelation is effective if started promptly
Delayed treatment - loose the benefit
Hum Exp Toxicol. 1991; 10:423–430

Effect of four thiol-containing chelators on disposition of orally administered mercuric chloride.
Lower dose chelation in rats - examining acute nephrotoxicity of mercuric chloride with DMPS iv:

Immediate treatment with DMPS (54 mg/kg iv) - 100% protecting against oliguric renal failure delayed treatment (>24 hr.), 0% protective effect


The effect of immediate and delayed treatment with DMPS on the distribution and toxicity of inorganic mercury in mice and in fetal and adult rats
DMPS – Mercury Detox Test - Standardized procedure for urine metal testing

Evaluation of the mercury exposure of dental amalgam patients by the Mercury Triple Test.

Hg levels in scalp hair, urine (pre-and post-challenge DMPS 200-400 mg oral), Hg release from amalgams after chew test

#2223
1.3 µg Hg/g creatinine in basal urine
32 µg Hg/g creatinine after DMPS = 32x

Conclusions:
A standardized procedure for evaluation of the magnitude and origin of the Hg burden of individuals has been developed, which, by comparison with the database presented here for the first time, can serve as a diagnostic tool.
Metal Detoxification - Rx chelators

- DMSA
- DMPS
- EDTA
Mercury Compartmentalization

Metals are stored in different body compartments

- Intracellular
- Intravascular
- Intestinal wall
- Extracellular (connective tissue)
- Kidneys / liver
- Central nervous system

Each compartment requires different detoxification approaches

Priority of compartments

1. Intestinal / kidneys / liver
   - Chlorella / Garlic
2. Extracellular / connective tissue
   - Chlorella / DMPS
3. Central nervous system
   - DMSA / cilantro / ALA
DMPS

2 free sulfhydryl groups

Water-soluble complexing / chelation agent

Developed in the 1950s in the Soviet Union

Chelates - heavy metals / minerals - zinc, copper, arsenic, mercury, cadmium, lead, silver, and tin

Used effectively treat metal intoxication since the 1960s

Extensive international research / excellent safety record

Registered / approved in Germany - treatment of mercury poisoning

Not FDA approved in U.S.

Patients should be informed of the unapproved / experimental status full disclosure/informed consent document in the medical chart
“Treatment mercury toxicity is well established and accepted”

“Clearly demonstrated elimination effects on the connective tissue”


DMPS is primarily excreted in the urine

Oral

40% absorption - better than DMSA
Lower dosages / better absorption
Less GI side effects
Clinical Patient Monitoring - during DMPS

- CBC
- CMP
- RBC Minerals
- Serum copper / Plasma zinc
- Serum iron
74. Promotes maximal excretion of heavy metals within 2-3 hours after infusion
   - Combining with Chlorella may increase the amount of mercury / metals mobilized and excreted
   - U.S. - Compounded Rx - injectable, oral, topical, suppository
   - Oral 100 - 400 mg daily
   - IV 3-5 mg/kg - injected slowly intravenously over 5 - 15 minutes
   - Repeat every 1 - 4 weeks - depending on tolerability....
   - After IVC 25 grams
   - ** Should not be used for on-going treatment in patients that still have amalgam fillings **
   - Can mobilize mercury from amalgams
   - May cause seizures, cardiac arrhythmias, fatigue
   - Not mutagenic, teratogenic or carcinogenic
DMPS Safety:

Hurlbut - volunteers were given large dose of DMPS (3 mg/kg intravenously over 5 minutes) ex. 150 mg
Transient 20 mmHg drop in systolic blood pressure during infusion

DMPS Side Effects:

Use with great caution - biocompatibility
Hypotensive effects, allergic reactions and skin rashes
High affinity for copper and zinc - replenishment


“The Mt. Diwata study—Treatment of mercury intoxicated inhabitants of a gold mining area with DMPS

Workers in gold mine - chronic exposure to elemental mercury
Fish eaters - methyl mercury
Controls without significant known mercury exposure
Lab - blood, urine and hair mercury levels
Symptoms (tremor, sleeplessness, memory loss, etc.)

106 # - oral DMPS 400 mg per day - 14-day trial - only complication was an allergic rash in one patient

Blood mercury did not decrease during the trial, despite increases in urine mercury up to 85-fold

Significant improvements - objective measures of neurological function / symptoms
Most reported subjective improvement in memory, sleeplessness, metallic taste, fatigue, anxiety, and paresthesias

Treatment efficacy - similar in both groups
DMPS Decreases the Body Burden of Mercury in Humans Exposed to Mercurous Chloride (topical)

Journal of Pharmacology and Experimental Therapeutics October 1998, 287 (1) 8-12

Workers involved in the production of calomel skin-bleaching lotion
In direct contact with mercurous chloride
Elevated baseline urine levels of mercury

#8 workers

All the subjects responded to the challenge dose of DMPS by increased urinary excretion of mercury.

Before 333 ug/l (50-1000)

After 4282ug/l (2000-8000)

10x fold increase in urinary elimination
DMSA Succimer: the first approved oral lead chelator.

DMSA - Succimer effective oral lead chelating agent

Approved for outpatient treatment of children with elevated blood lead levels higher

Side effects: gastrointestinal symptoms, rash and transient elevations of serum aminotransferase levels, are uncommon and mild

Isolated cases of neutropenia have been reported.

Weekly monitoring - CBC, LFT - recommended during treatment

Blood lead levels should be checked weekly to identify rebound from bone and soft tissue mobilization
Controlled study of DMSA for the management of childhood lead intoxication.

#19 children with BPb concentrations of 50 to 69 micrograms/dl

- 5-day inpatient oral course of DMSA (1050 mg/m2 per day)
  - BPb concentration decreased by 61%

#4 children

- 5-day course of IV Na2CaEDTA
  - BPb concentration decreased by 45%

Treatment with DMSA was more effective CaNa2EDTA in reducing blood lead and in restoring metabolic activity to the heme pathway.

Well tolerated
A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning


DMSA - more effective in reducing the kidney lead concentration

Sodium calcium EDTA - more effective in reducing bone lead concentrations

No consistently observed effect of chelation therapy on brain lead concentrations

DMSA and sodium calcium edetate - comparable impact on lowering blood lead concentrations
A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning


ADVERSE EFFECTS:

EDTA can cause dose-related nephrotoxicity

Both agents deplete zinc and copper (zinc / sodium calcium edetate)

Transient increase in LFT - more common with DMSA

No significant hepatic toxicity

Skin lesions during treatment with EDTA are unusual - attributed to zinc deficiency.

DMSA has occasionally been associated with a severe mucocutaneous reaction necessitating discontinuation of therapy
A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning

CONCLUSIONS:

Oral DMSA and IV sodium calcium edetate are both effective chelators of lead.

Both antidotes resolve the symptoms of moderate and severe lead toxicity rapidly.

Description of 3,180 courses of chelation with DMSA in children ≤ 5 y with severe lead poisoning

PLoS Med. 2014 Oct 7;11(10)

Extensive lead poisoning impacting several thousand children in rural northern Nigeria

400 fatalities had occurred over 3 mo.

(CDC) confirmed widespread contamination from lead-rich ore being processed for gold

1,156 children ≤ 5 y of age who underwent between one and 15 courses of chelation treatment.

Overall improvement - 74.5%

Oral DMSA effective chelating agent for the treatment of severe childhood lead poisoning in a resource-limited setting.
Abstract

Efficacy and safety of meso-2,3-dimercaptosuccinic acid (DMSA) in children with markedly elevated blood lead (BPb) concentrations.

# 19 children with BPb concentrations of 50 to 69 micrograms/dl

5-day inpatient oral course of DMSA (1050 mg/m2 per day)
BPb concentration decreased by 61%

# 4 children

5 day course of IV Na2CaEDTA
BPb concentration decreased by 45%

Treatment with DMSA was more effective CaNa2EDTA in restoring metabolic activity to the heme pathway

Well tolerated
Metal Detoxification - Chelation therapy - EDTA

CaNaEDTA and Na₂EDTA

Na₂EDTA - slow, continuous intravenous infusion

CaNaEDTA - slow IVP or 15 min infusion

Indications: lead, aluminum, cadmium

Side effects - malaise, headache, fatigue, chills or fever, myalgia, anorexia, nasal congestion, watery eyes, anemia, transient hypotension, clotting abnormalities, and kidney failure (Jang 2011)

Chelate essential trace metals, such as zinc, copper, and manganese (Flora 2010)

Sodium EDTA (without calcium) can cause life-threatening hypocalcemia (Brown 2006), death

Lab - monitor kidney function

Informed consent
Metal Detoxification - Chelation therapy - EDTA

Dosing:

**IV -** 50 mg / kg body weight

- 70 Kgm person - 3.5 Gm dose

- 2 - 3 grams are usual - detoxification therapy

- 1.5 - 2 grams for maintenance

Caution - start with lower dose - 1 gram in elderly or low body weight - gradually increase dose

**Oral -** 500 mg to 6000 mg daily

Oral EDTA enhances elimination of metals during IV therapy
EDTA - Chelation Therapy - TACT trial

TACT - Trial to Assess Chelation Therapy

Large scale, multi-center study - 20x larger than any previous study
safety and efficacy of EDTA chelation for CHD
placebo-controlled, double blind

1708 #

Results

- Modestly reduced the risk of some cardiac events in adults who had
  previously had a heart attack
- Treatment effect lasted over the 5-year follow-up period
- 18% reduced risk of subsequent cardiac events such as heart attack,
  stroke, hospitalization for angina, or coronary revascularization
- Greater benefit - diabetes and CHF
- Side effects - Events occurred in 25% of the patients with diabetes
  who received EDTA chelation and in 38% of those who received
  placebo.
- Death from any cause was 43% lower in those patients with diabetes
  who received chelation
38 people (16%) receiving chelation and 41 people (15%) receiving placebo cited an adverse event as the cause of discontinuing study infusions.

4 unexpected severe adverse events that were possibly or definitely attributed to study therapy
- 2 in the chelation group (1 death)
- 2 in the placebo group (1 death)

Heart failure was reported in 57 (7%) chelation patients, and 71 (8%) placebo patients.

55,222 infusions
- 330 (0.6%) were administered at least 30 minutes too rapidly


Cutler Metal Detox Protocol

Low dose / higher frequency

DMSA or DMPS alone, followed by adding ALA

DMSA / DMPS - extracellular metals

ALA - brain / intracellular metals

- Added later, after lowering systemic levels

- Avoiding redistribution to brain
Cutler Metal Detox Protocol

DMSA 4 hours
DMPS 8 hours
ALA 3 hours
Combination 3 hours

Cycle 3 days on / 11 days off
Variation - 3 days on / 4 days off
Longest 14 days on

DMSA 1/16 - 1/2 mg / # BW / dose
DMPS 1/4 - 1 mg / # BW / dose
ALA 1/16 - 1/2 mg / # BW / dose
Cutler Metal Detox Protocol

Monitor Copper (ALA) - it may tend to increase

When combing with ALA, decrease DMPS 50% (taking every 3 hours)

Basic supplements
Zinc B complex
Magnesium Molybdenum

Epsom Salt baths (sulphate/magnesium)
Sauna
Start with DMSA or DMPS, later add ALA

1/8 mg / # BW - increase slowly to 1/2 mg / # BW

Increase every 5 cycles - 3 days on / 11 days’ off

DMSA 4 hours
DMPS 8 hours
ALA 3 hours

6 months to 2 years
Metal Detoxification - Therapeutics - Pharmaceutical Chelators

Low Dose / Frequent Dosing Protocol - Cutler Protocol

Supportive:

Vit C  500 - 2000 mg daily  3x daily

Magnesium  100 - 200 mg  3x daily

Zinc  25 - 50 mg  1-2x daily

Mineral  1  2x daily

Not advised:

- IV chelation
- Cilantro and chlorella
Algae

Cell wall absorbs toxic metals - bind cadmium (in animal models) and zinc, copper, and lead (in vitro)

Detoxify wastewater of metal contaminants (Almaguer Cantu 2008; Shim 2008; Uchikawa 2010).

Accelerated the excretion of methylmercury (Uchikawa 2010)

Accelerated the excretion of cadmium (Shim 2009)

Reduced lead-induced bone marrow toxicity (Queiroz 2011)

Enhances mobilization of mercury in connective tissues (muscles, ligaments, connective tissue, and bone)

Enhances biliary - intestinal excretion (particularly important - mercury - 90%)
Metal Detoxification - Therapeutics - Natural Chelators

Dose: 1 - 3 grams' daily
Dose: 500 mg tablet 1/4 tsp. 1x daily - check tolerability
Gradually increase dose 3x daily - 1 tsp. or 6 tablets
Pulse large doses 1 tbsp. or 16 tablets 500 mg

Radioactive metals or exposure
Amalgam tattoos - topical application


Cilantro

Chinese parsley

Mercury and Tin

CNS and the brain

Use later in process - after other body stores are minimized / cleared

Fresh cilantro
daily on food

pesto - blend: fresh organic cilantro, small amount of water, sea salt and olive oil

1 tsp. - tbsp.  1-3 times / day with meals
Garlic sulfur rich compounds

Metal-chelating properties

Anti-oxidants

Protect from metal-catalyzed oxidative damage

Garlic (sulfur) and Metal Detoxification

Comparative study on the efficacy of Allium sativum (garlic) in reducing some heavy metal accumulation in liver of wistar rats.

Rats fed garlic as 7% of their diet for 1 week - before, after, or during exposure to heavy metal toxins

Significantly reduced lead, cadmium, or mercury accumulation in their livers for 6 weeks

Comparison of therapeutic effects of garlic and d-Penicillamine in patients with chronic occupational lead poisoning.

Previous studies on animals - garlic (Allium sativum) is effective in reducing blood and tissue lead concentrations.

Investigate therapeutic effects of garlic and compare it with d-penicillamine in patients with chronic lead poisoning.

117 workers at a car battery plant

3x daily * 4 weeks
- Garlic 1200 μg allicin
- d-penicillamine 250 mg

Clinical improvement was significant in both groups

Lead levels decreased:
- Garlic 426 to 347 μg/L
- d-penicillamine 417 to 315 μg/L

Garlic - safer clinically and as effective as d-penicillamine
Metal Detoxification - Therapeutics - Natural Chelators

Porphorazyme

Chlorophyll (Biotics Labs)
Group of different porphyrins
Facilitates metal excretion
1 - 3 tablets 1 - 3x / day for extended periods of time
Three studies - mobilization / excretion of metals from body stores -
Arsenic, Mercury, Cadmium, and Lead
5 - 20 grams / day

1. 15 g of MCP daily for 5 days and 20 g of MCP on day 6

   Significant urinary excretion of arsenic, mercury, cadmium, and lead
   150% increase in cadmium excretion
   560% increase in lead excretion on day 6 (Eliaz 2006).
   Essential minerals such as calcium, zinc, and magnesium did not increase in the
   urinary analysis.

2. Series of case reports, 5 patients with different illnesses took MCP alone or in combination
   with alginate for up to 8 months. The patients showed a 74% average decrease in toxic heavy
   metals after treatment (Eliaz 2007).

3. 7 children with blood lead levels >20 µg/dL received 15 g/day of MCP for 2 to 4 weeks. Blood
   lead levels dropped an average of 161%, and urinary lead excretion increased by an average of
   132% (Zhao 2008).
Metal Detoxification - Therapeutics - Natural Chelators

Silica / silicon - Orthosilicic acid and Zeolite

Studies:

- Decreased aluminum absorption from GI tract
- Decreased accumulation in brain
- Increased aluminum excretion in urine
- Decreased lead levels in tissues

In human subjects, soluble silicon (orthosilicic acid) decreases aluminum absorption from the digestive tract and decreases its accumulation in the brain (Jurkic 2013).

Alzheimer’s patients drank up to 1 L of mineral water daily (containing up to 35 mg of silicon/L) for 12 weeks. Over the study period, urinary excretion of aluminum increased without affecting urinary excretion of the essential metals iron and copper. In addition, there was a clinically relevant improvement in cognitive performance in at least 3 out of 15 individuals (Davenward 2013).

Inclusion of zeolite (clinoptilolite) in high-lead diets of laboratory mice reduced tissue lead concentration by 77-91%, increased the percentage of healthy red blood cells, and reduced chromosomal damage (Topashka-Ancheva 2012; Beltcheva 2012).


Metal Detoxification - Supporting Therapy / Natural chelators

Sulfur - Biochemical Neutraceuticals

<table>
<thead>
<tr>
<th>Methionine</th>
<th>Cysteine</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAC</td>
<td>SAM</td>
</tr>
<tr>
<td>ALA</td>
<td>GSH</td>
</tr>
<tr>
<td>Redoxal</td>
<td></td>
</tr>
</tbody>
</table>

Alpha-Lipoic Acid / Glutathione

Sulfur- compounds complex with heavy metals chelate a number of metals in cell culture

Cadmium, lead, zinc, cobalt, nickel, iron, and copper - (Patrick 2002)

In a rat model, ALA and glutathione reduced some of the adverse changes in blood parameters, including drops in red blood cell number and size as well as reductions in hemoglobin concentration brought about by intoxication with lead, cadmium, or copper (Nikolic 2013).

ALA and glutathione in a rat model both reduced cadmium-associated oxidative stress and improved the activity of the antioxidant enzyme catalase in kidney tissue (Veljkovic 2012)
N-Acetyl Cysteine

N-acetyl cysteine (NAC) provides a source of sulfur for glutathione production.

Effective at reducing oxidative stress due to heavy metal toxicity (Patrick 2006).

Capable of binding and sequestering divalent copper (II), trivalent iron (III), lead, mercury, and cadmium ions (Samuni 2013).

Chronic exposure to toxic metals can decrease cysteine levels (Quig 1998).

In animal models and cell culture experiments
Enhanced renal excretion of lead (Pb IV)
Lowered concentrations of mercury
Protected against cadmium-induced liver cell damage (Samuni 2013)

600 - 2400 mg daily
Selenium

Animal models - selenium blocks the effects of lead when administered before exposure and reduces mercury toxicity (Patrick 2006)

Human studies - selenium increases mercury excretion in humans (Li 2012; Zwolak 2012)

100-200 mcg/day reduced blood and hair levels of arsenic in Chinese farmers with arsenic poisoning (Zwolak 2012)

Mitigate the toxicity of heavy metals - cadmium, thallium, inorganic mercury, and methylmercury (Whanger 1992)

100 mcg of selenium (selenomethionine) daily for 4 months: 34% reduction in hair levels of mercury (Seppanen 2000).
Metal Detoxification - supporting therapy - Folate

Cofactor in sulfur-containing amino acid metabolism

Cysteine / methionine - precursors to internal detoxifiers / anti-oxidants - alpha-lipoic acid and glutathione


Relation between serum folate status and blood mercury concentrations in pregnant women

1105 pregnant women

Higher blood folate levels were associated with lower blood mercury levels during pregnancy
Cadmium, lead and mercury exposure in nonsmoking pregnant women.

173 pregnant non-smokers

Not supplementing folic acid or iron supplements during pregnancy was associated with higher blood cadmium levels (Hinwood 2013)

Folate supplementation: 1 - 5 mg
Trapping and metabolizing xenobiotics or heavy metals

Lactobacillus rhamnosus (LC-705 and GG), Lactobacillus plantarum (CCFM8661 and CCFM8610), and Bifidobacterium breve Bbi 99/E8 bind both cadmium and lead in laboratory studies (Ibrahim, Halttunen 2006; Halttunen 2008).

In mouse models, two different Lactobacillus plantarum strains reduced tissue accumulation of cadmium and lead and protected against oxidative stress (Zhai 2013; Tian 2012).
Metal Detoxification - Therapeutics - Supporting Remedies

Homeopathic / Herbal Drainage and Organ Support –

Liver, Lymph, Kidney

Solidago
Burbur
Glutathione
Mobilizes metals - promotes excretion
Anti-oxidant - cell and enzyme protection
Recycle antioxidants - C, E

Oral - capsules, liposomal liquid
IM
IV
Topical
Nebulizer

Dose - 200 - 5000 mg

129,000 PubMed articles

- Anti-oxidant and anti-atherogenic properties of liposomal glutathione: studies in vitro, and in the atherosclerotic apolipoprotein E-deficient mice. Atherosclerosis. 2007;195(2):e61–e68
- Recent advances in the treatment of neurodegenerative diseases based on GSH delivery systems. Oxidative Medicine and Cellular Longevity. 2012;2012:12 pages. 240146
William Walsh, Ph.D. / Pfeiffer Treatment Center

1,200 published articles describing MT synthesis, activation, and redox mechanisms

Cysteine rich protein on Golgi apparatus - 1/3 AA = cysteine

Each molecule of MT requires 7 atoms of zinc (Zn) for proper functioning

Zn-MT = "magnet" for toxic metals

Autism risk - congenital / acquired deficiency (toxicity, deficiencies)
Metallothionein - Function:

- Binding of metals
- Storage site for zinc / copper
- Ccavenger of reactive oxygen species / free radicals
- Controls oxidative stress
- Protect cells from apoptosis induced by oxidative stress and metals

- Regulates zinc and copper concentration in the blood.
- Development and functioning of our immune system.
- Development of nerve cells (neurons) in the brain together with Omega-3 fatty acids.
- Protects against excessive yeast growth in the intestines.
- Prevents intestinal infections.
- Involved in gastric acid production.
- Influences taste and texture sensation of food in the mouth.
- Regulating influence on hippocampal behaviour.
- Emotional development and socialization (amygdala).
Metallothionein Induction Therapy

Phase 1

Zinc preloading 4-8 weeks; start low, gradual increase
Goal Zn > 100 (reference range 60 - 100 umol/L)
Daily dosage = mg / lb + 20 mg

Also - P6P, Mn gluconate, C, E
Add - taurine - if seizure tendency

Phase 2

Add Glutathione, Selenium, SH-AA
Heavy Metal Toxicity – Interaction - Potentiation of Toxicity

“Interaction Profiles” - US Agency for Toxic Substances and Disease Registry report

1. Renal toxicities are greater - mixtures of lead plus mercury

2. Neurological toxicities of mixtures of lead plus arsenic, lead plus methylmercury, and lead plus cadmium are supra-additive

Recommendation: mercury assessment in all patients presenting with hypertension or any vascular disease

No person is without some level of toxic metals in their bodies - circulating and accumulating.

Children and the fetus are most at risk of harm - lower IQ and dysfunctional behavior.

Older populations - low grade metal exposure / life time accumulation - at risk:
- Early cognitive decline
- Kidney and cardiovascular disease
- Diabetes
- Osteoporosis

Metal Detoxification - Sauna Therapy

Blood flow to the skin increasing from baseline of 5–10% to 60–70% of the cardiac output

5 - 10 x increase in blood flow

Maximal sweating can occur within 15 minutes

Primarily decreases metals - blood / extracellular space - ? intracellular

Fluid loss may be as high as 2 L/h ("acclimatized" person who regularly sweats)

Adult sweat: 1 quart sweat (2 #) = 100 mg DMSA every 4 hours that day

Reviewed Medical Literature

Significantly increased excretion of lead, cadmium, mercury, arsenic

Sweat - 10x increase in lead (lead-exposed workers)
Sauna Detoxification - added benefit

Increases excretion of toxic chemicals

Observed in New York rescue workers
Persistent flame retardants
Bisphenol-A

“Methamphetamine expo- sure and chronic illness in police officers: significant improvement with sauna-based detoxification therapy,” Toxicology and Industrial Health


Sauna Detoxification – Added benefit - Combination therapies

Overall detoxification of metals and chemicals can be enhanced

GSH, NAC, Vit C, Minerals, Garlic, Chlorella, Rx Chelating agents
Sauna Detoxification – Support / Enhancement

Autonomic nervous system / heat regulatory mechanism - decreased sweating ability

- Hydration
- Brushing the skin
- Niacin - vasodilation
- Exercise prior to sauna use
- Persistence and ample hydration patients do eventually start to sweat.
Metal Detoxification - Sauna

With acclimatization and regular use - generally well tolerated by all ages

Medical supervision - considered / recommended - initial sessions for children and elderly

Contraindications (R) - unstable angina pectoris, recent myocardial infarction, severe aortic stenosis, and pregnancy


Spanish Era and its colonies - significant mercury exposure

Ill workers sent to warmer climes

- Away from the exposure
- Drink weak beer

Alcohol inhibited hydrogen peroxide / catalase oxidation of elemental mercury to ionic mercury

- Increasing mercury in exhaled breath
- Work in the heat to sweat out toxins

Effective strategy - tremors, salivation, and mouth ulcers resolved within a few weeks


RadioActive Elements / Metals
RadioActive element - atom with unstable nucleus
Naturally emits energy to become more stable
High energy rays / high speed particles = ionizing radiation
Alpha / beta particles / gamma rays

Effects - alters / damage DNA and cellular molecules and processes
1. Directly ionizing DNA molecules
2. Indirectly by ionizing water in body cells - free radicals formed - damage DNA

Ionizing radiation - harmful / toxic to human tissue

In food radiation - change food structure - destroys or reduces nutrients creates radiolytic products - formaldehyde, benzene, formic acid, and quinone sex. Gamma Radiation - cobalt 60 / cesium 137
Radioactive Elements – Health Concerns

- Ionizing radiation - radiation damage
- Long half life in environment
- Increasing exposure - "no place to hide"
- Anti-oxidant and nutritional deficiencies - increase risk of toxic effects of low dose exposure
- One of primary concerns - increased risk of cancer
  
  ex. radon in lung cancer in non-smokers
  ex. radon in lung cancer - increasing risk in smokers

- Degenerative conditions - premature aging
<table>
<thead>
<tr>
<th>RadioActive Elements – Common uses</th>
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</thead>
<tbody>
<tr>
<td>Iodine-131</td>
</tr>
<tr>
<td>Bismuth-212</td>
</tr>
<tr>
<td>Technetium-99</td>
</tr>
<tr>
<td>Uranium -235</td>
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<tr>
<td>Americium-241</td>
</tr>
<tr>
<td>Cobalt-60</td>
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<tr>
<td>Cesium-137</td>
</tr>
<tr>
<td>Radon</td>
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<tr>
<td>Radium 88</td>
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<tr>
<td>Strontium 90</td>
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<tr>
<td>Element</td>
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<tr>
<td>Iodine-131</td>
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<tr>
<td>Radium 88</td>
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<tr>
<td>Tritium H3</td>
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<tr>
<td>Strontium 90</td>
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</tbody>
</table>
### RadioActive Elements – Treatment - Standard / Conventional

<table>
<thead>
<tr>
<th>Element</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesium 137</td>
<td>Prussian blue 1-3 grams 3x daily * 30-60 days - insoluble ferric hexacyanoferrate</td>
</tr>
<tr>
<td>Cobalt 60</td>
<td>DMSA, EDTA, NAC</td>
</tr>
<tr>
<td>Iodine 131</td>
<td>Potassium iodide / propylthiouracil</td>
</tr>
<tr>
<td>Radium 226</td>
<td>Aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate</td>
</tr>
<tr>
<td>Strontium 90</td>
<td>Aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate</td>
</tr>
<tr>
<td></td>
<td>IV Calcium gluconate</td>
</tr>
<tr>
<td>Uranium 235</td>
<td>IV Sodium bicarb - facilitates renal excretion - urine pH 8-9 - 3 days</td>
</tr>
<tr>
<td>Tritium H-3</td>
<td>H2O water diuresis - 3 to 4 liters daily * 3 weeks</td>
</tr>
</tbody>
</table>
Discovered Marie and Pierre Curie in 1898

Radioactivity of isotope Ra226 - basis for historical unit for radioactivity - curie

Isotopes of radium are highly radioactive

The most stable isotope - Ra 226 - half life of 1600 yrs - decays into radon gas (Radon 222)

Radium isotopes - exist in environment - decay products from uranium and thorium
Former use:

Self-luminous paints - watches, nuclear panels, aircraft switches, clocks, instrument dials
Instrument dial painters - licked their brushes to give them a fine point - ingesting radium
Oral mucosal sores, anemia, bone cancer
Acts like calcium - deposited in bones - effects bone marrow
Radium Girls lawsuit - awareness of radioactive risk and protection
Additive - toothpaste, hair creams, and even food items
Nasal radium irradiation - administered to children to prevent middle-ear problems or enlarged tonsils (1940 - 1970s)

Current Use:

- Oncology - nasopharyngeal irradiation (delayed risk of brain cancer and pituitary dysfunction)
- Oncology - 223Ra Xofigo - FDA approved 2013 for metastatic bone cancer (prostate)
- Treatment: aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate
Radon (Rn-222)

- Naturally occurring radioactive gas
- Results from decay of Radium 226
- Emits alpha radiation - similar to plutonium
- Higher levels near spring waters and hot springs
- Tends to collect in basements and crawl spaces - poor ventilation
- Carcinogenic - highly
- 1000 times greater risk of death as any other EPA carcinogen
EPA action level = 4 pCi/L (Curie - unit of radioactivity)

Screening in seven states - 1 in 3 homes - levels over 4 pCi/L

1/15 U.S. homes - estimated to have elevated radon

Home level of 4 = 35x more than allowed level standing next to radioactive waste site - Nuclear Regulatory Comm

1000 times greater risk of death as any other EPA carcinogen

Action level DOES NOT EQUAL safe level

Ventilation lowers radon levels

#1 Cause of lung cancer among non-smokers
#2 Cause of lung cancer

21,000 lung cancer deaths every year
2,900 of these deaths occur among people who have never smoked

Treatment - ventilation / no conventional / Functional Med Tx - anti-oxidants
Cobalt 60 –
Radioactive Element - manufactured isotope - nuclear power plants / radiation therapy / irradiated food

Cobalt 27
Metal / compounds - manufacturing - pigments (dyes, tattoos, paints), medical device (metal implants)

Cobalt Organic - B12
Methylcobalmin / hydroxycobalamin / s-adenosylcobalain
methionine metabolism - Methionine aminopeptidase 2 - tissue repair
Cobalt 60 and 58 – Radioactive Element

Manufactured radioactive isotopes - produced in nuclear reactors
Ionizing radiation - gamma rays
Probable human carcinogen
Exposure - released to the environment
Result of nuclear accidents - water, air currents, soil
Radioactive waste dumping in the sea
Radioactive waste landfills
Nuclear power plant operations - contaminants in cooling water

Half life - moderately short-lived

- Co60 5 yrs
- Co 58 71 days

Occupational Exposure:

- Workers at nuclear facilities, irradiation facilities, or nuclear waste storage sites
- Sterilizing medical equipment and consumer products
- Radiation therapy for treating cancer patients - brain
- Food irradiation
Probable human carcinogen

Genotoxic - oxidative damage / inhibition of DNA repair
Associated cancers - lung, upper GI, bone cancer


National Toxicology Program, Department of Health and Human Services
Cobalt Metal and Cobalt Compounds That Release Cobalt Ions In Vivo

Reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals

Animal studies - rats and mice exposed to cobalt metal or cobalt compounds developed tumors at various tissue sites — lungs, adrenal glands, pancreas, and immune system
Cobalt - Co 27 - Metal and Compounds

Reasonably anticipated human carcinogen

Use / Exposure:

Rechargeable battery electrodes - smart phone and laptops

Cobalt nanoparticles
  - Medical application sensors
  - MRI contrast enhancement
  - Drug delivery

Cobalt compounds
  - Pigments for glass, ceramics, enamels, paints, dyes, tattoos
  - Driers for paints, varnishes, or lacquers
  - Adhesives
  - Trace mineral additives in animal diets

“Green” energy technology applications
Cobalt alloys - joint implants
Increasing exposure of a Reasonably anticipated human carcinogen
Excessive exposure / higher levels - cardiomyopathy, vision or hearing impairment, hypothyroidism, polycythemia

Urinary cobalt - higher in occupational exposure and failed hip implants

Cobalt ions may be released into the body throughout the lifetime of a cobalt-containing device (Sampson and Hart 2012, Devlin et al. 2013).

Blood cobalt > 10 μg/L Mayo Clinic (2015)
Recommended - further clinical investigation and action

Review of the Health Hazards Posed by Cobalt
Radioactive hydrogen
Produced naturally in upper atmosphere when sunlight interact with nitrogen
Most common form in water

Use:

Produced during nuclear weapons explosions
Byproduct in nuclear reactors
Government weapons production plants
EXIT signs - self luminating

Exposure:

Released as steam / leak into the underlying soil and groundwater
Improper disposal / handling of EXIT signs
Treatment: water diuresis - 3 to 4 liters daily * 3 weeks
Cesium 133 - stable

Naturally occurring metal

By product of mining

Cesium 134 and 137 - radioactive metal isotopes

From nuclear processing / degradation of uranium / nuclear accidents and explosions

Transported though air - 1000s of miles - then settles in water and soil - then food

Cesium 137 half life = 30 yrs
RadioActive Elements – Public Health and Environmental Contamination

2011 Fukushima nuclear power plant accident
Radiation leaked into sea and ground water
300 tons of radiation still leaking
Leak irreparable due to high temperatures

I-131 - 8 days
Ce 134 - 2 yrs
Ce 137 - 30 years
Strontium 90 - 20 yrs

Concern: Cesium 137 and 134

spread in air currents - globally
distributed in water, soil, fish, plant life
fish, produce, herbs transported internationally

Cesium-134 2 yr half life
Western U.S. offshore water
Canadian salmon

Cesium 137 30 yr half life
Recently detected higher levels on U.S. and Canadian west coast
Radiation levels are predicted to continue rising
RadioActive Elements – Public Health and Environmental Contamination

2011 Fukushima nuclear power plant accident

2014 radiation levels on West coast - increased by 300 to 500 percent

Pacific ocean 5-10x more radioactive than after nuclear bombs of WWII era
Fukushima Pacific Radiation picture
Exposure:

Air, water, soil, food
Food - considered greatest exposure
Nuclear plants - waste and accidents

Effects:

Ce 133  GI symptoms, cardiac arrhythmias, including prolonged QT syndrome, neurological, infertility

Ce134/137 Cancer - Leukemia

Acute radiation syndrome (vomiting, nausea, and diarrhea)
Skin and ocular lesions, compromised immune function, neurological signs, irrational behavior,
Circulatory system collapse, neuromuscular incoordination, followed by convulsions and death

Treatment: Conventional - Prussian blue
1-3 grams 3x daily * 30-60 days - insoluble ferric hexacyanoferrate

Functional - combination antioxidants
RadioActive Elements
Strontium 90

Exposure - nuclear power plants and accidents

20 yr half life

Risk - bone cancer and hyperparathyroidism

Treatment - high exposure - conventional: aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate

IV Calcium gluconate

Functional: combination antioxidants

Treatment - low exposure - combination antioxidants
Iodine 131 and 129 – Radioactive Metal Isotopes

I 131 - occurs naturally - but short lasting

I 131 and 129 - by product nuclear processing of uranium and plutonium

Half life

131    8 days    Medical use, Nuclear by-product

129    1.6x10^7 year    Nuclear by-product

Use / Exposure:

Accidental release from nuclear accidents
Contamination water from nuclear power plants
Occupational - medical, laboratory, nuclear facilities
Patients undergoing medical nuclear imaging
Imaging - pheochromocytoma and neuroblastoma
Thyroid conditions - hyperthyroid, nodule, and cancer
Patients undergoing medical treatment of thyroid conditions I 131 capsules
Family members (children) of patients undergoing I131 treatment

Treatment:

Conventional - Potassium iodine (KI) 12 - 150 mg * weeks / months
Functional - combination antioxidants
Highly radioactive element (alpha particles) and chemically toxic

Decay product of radioactive Lead Pb 210

Increasing levels of Lead Pb 210

- Calcium phosphate fertilizers
- Drinking water
- Tobacco and plants

Polonium in cigarette smoke - cancer in laboratory animals


Treatment: Functional - combination anti-oxidants
ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

Department of Radiation Oncology, University of Rochester Medical Center

The ability of antioxidants to reduce the cytotoxic effects of radiation - 50 years

Sulfur-containing antioxidants - most beneficial therapeutic ratio

Capable of both scavenging oxygen radicals

Affecting chemical repair of some forms of DNA damage

Prevention of immediate radiation-induced genotoxicity requires that an antioxidant be present at the time of irradiation.
Immediate Radioprotective Effects

- By scavenging of radicals ROS
  - Caffeine, melatonin, flavonoids, polyphenols

Chronic Radioprotective Effects by Antioxidants

1. Increasing an-ox mechanisms
   - Glutathione peroxidase
   - Glutathione reductase
   - Increasing the synthesis of glutathione (GSH)
   - Reducing levels of oxygen radicals and peroxides in cells

2. Activation of the redox-sensitive nuclear transcription factor, NFκB
   Subsequent expression of the antioxidant enzyme, manganese superoxide dismutase (MnSOD)

3. Protection of membranes
   Decreased lipid radical and peroxides
   
   Pretreatment - flavonoid, luteolin, reduced lipid peroxidation

4. Fold reduction in lipid peroxidation
Anti-oxidant Protection / Detoxification of Radiation


ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

4. Mitochondrial protection / preservation
   - Melatonin - effective at protecting mitochondria
   - Increasing the efficiency of oxidative phosphorylation
   - Reducing the leakage of electrons from the electron transport chain
   - Decreases the formation of ROS from these electrons
   - Induces the levels of antioxidant enzymes GPx
   - Increases GSH levels within the cell

5. Inhibition ROS related apoptosis
   - SOD, green tea polyphenol, (-)-epigallocatechin

6. Protection against - reperfusion injury - ROS

7. Modulation of inflammatory response - cytokines
   - Epicatechin, trans-resveratrol, and theaflavin
   - NAC

8. Reducing ROS and inflammation in late radiation-induced tissue injury (scarring / fibrosis)
   - MnSOD, a-tocopherol
ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

HBOT - most effective treatment for many chronic radiation-induced soft tissue injuries

HBOT mechanisms of action - attributed to:
- Induction of SOD and antioxidant systems
- Inhibition of inflammation
- Improved tissue vascularization

Prevention of immediate radiation-induced genotoxicity requires that an antioxidant be present at the time of irradiation

In vitro and in vivo studies - antioxidants given in combination result in GREATER radioresistance than when given individually
RadioActive Elements - Protection / Detoxification Treatment

<table>
<thead>
<tr>
<th>Turmeric</th>
<th>Spirulina</th>
<th>Green Tea</th>
</tr>
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<tbody>
<tr>
<td>Astaxanthin</td>
<td>Chlorella</td>
<td>Melatonin</td>
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<tr>
<td>NAC</td>
<td>ALA</td>
<td>GSH</td>
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<tr>
<td>Potassium iodide</td>
<td>Vit C</td>
<td>Zinc</td>
</tr>
<tr>
<td>Selenium</td>
<td>Vit D₃</td>
<td>Melatonin</td>
</tr>
<tr>
<td>SOD</td>
<td>Vit E</td>
<td></td>
</tr>
</tbody>
</table>
Radioactive Elements - Chernobyl Nuclear Accident

Radiation sickness
145k children
160k workers

Spirulina 5 grams daily

Reduced radiation sickness
Increased urinary excretion of radionuclides

Spirulina- natural sorbent of radionuclides Sep 1993. Research Institute of Radiation Medicine, Minsk, Belarus. 6th Int'l Congress of Applied Algology

ALA and Vit E - helped lower the amount of radioactivity found in the urine (Korkina, 1993)
Protective Effects of Vit C in Radiation Exposure

Mice study

Vit C therapy starting before radiation exposure vs starting after, and later bone marrow replacement

Pretreatment - 40% survival

Delayed treatment - 0% survival

Yanagisawa A: Orthomolecular approaches against radiation exposure.

1. Vitamin C - Radioprotector against iodine-131 in vivo

2. Combination of anti-oxidants (ALA, C, E, Se, NAC, CoQ10)
   Improved the survival of mice after total body irradiation
   Antioxi-dant diet supplementation starting 24 hours after exposure reduces radiation lethality
Astazanthin

Strongest carotenoid antioxidant

- $54 \times > C$
- $14 \times > E$
- $500 \times > E$ for singlet oxygen free radicals
- $11 \times > B$-Carotene for singlet oxygen free radicals

Crosses BBB and BRB (blood retinal barrier)

Anti-inflammatory
Toxic Metals and RadioActive Elements - summary points

Toxic Metals are UBIQUITOUS

Exposure is UNAVOIDABLE

Low Level Exposure - ACCUMULATION

METAL TOXICITY - subtle and non-specific

Effects of toxic metals - DEPLETING, INFLAMMATORY, DEGENERATIVE

MINIMIZING body burden = one of HIGHEST PRIORITIES of Preventive/Functional Med

OPTIMIZING nutrient levels is ESSENTIAL to protection / detoxification

Metal Detoxification with Pharmaceutical/Nutraceuticals - SCIENTIFIC, SAFE, EFFECTIVE