



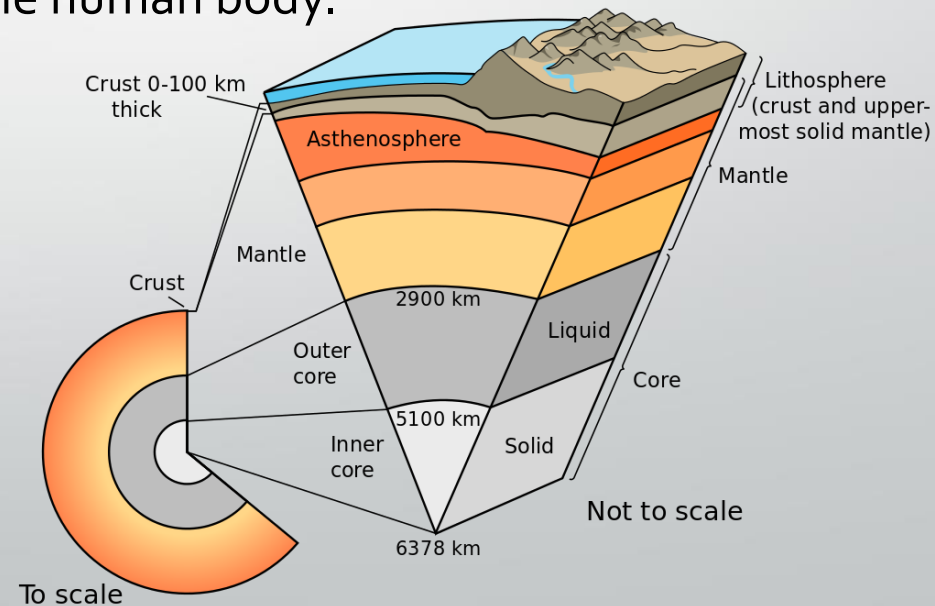
Arsenic & Mercury: Toxicity effects

Introduction

- ❖ A “heavy metal” refers to its atomic weight, not its toxicity
- ❖ Heavy metals are those whose specific gravity is more than water (atleast five times)
- ❖ Many metals are essential or play a normal role in biology
- ❖ Like all chemicals, all metals are toxic at high enough doses
- ❖ Like all chemicals, all metals are non-toxic at very low doses

Arsenic

- ❖ Arsenic is a semi-metal with an atomic number of 33.
- ❖ Twentieth most abundant element in earth's crust.
- ❖ It is odorless and tasteless, and is naturally occurring in rocks and soil.
- ❖ Most common oxidation numbers of arsenic are +5, +3 and -3, in which the element is able to form both inorganic and organic compounds both in the environment and within the human body.



General Chemical Forms (As+3 or As+5)

❖ Inorganic forms:

1. Arsenic trioxide $\text{As}^{\text{III}} \text{2O}_3$,
2. Arsenic pentoxide $\text{As}^{\text{V}} \text{2O}_5$,
3. Sodium arsenite $\text{NaAs}^{\text{III}}\text{O}_2$,
4. Sodium arsenate $\text{Na}_2\text{HAs}^{\text{V}}\text{O}_4$,
5. $\text{As}^{\text{III}}(\text{OH})_3$,
6. $\text{As}^{\text{V}}\text{O}(\text{OH})_3$

❖ Organic forms:

1. Monomethylarsonic acid (MMAV) $\text{CH}_3\text{H}_2\text{AsO}_3$
2. Dimethylarsonic acid (DMAV , cacodylic acid) $(\text{CH}_3)_2\text{As}(\text{O})\text{OH}$,
3. Arsenobetaine (fish) $(\text{CH}_3)_3\text{AsVCH}_2\text{CO}_2$

Arsenic Pollution

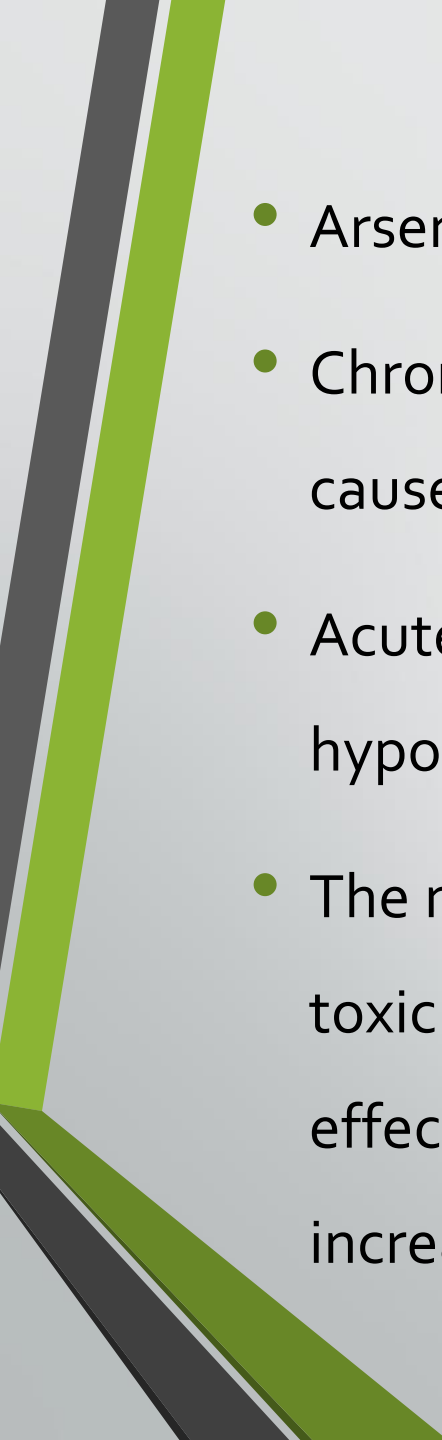
- **Introduction in soil and groundwater:**
 - Weathering of rocks and minerals followed by subsequent leaching and runoff
 - Anthropogenic sources
 - Combustion of fossil fuels also pollutes the environment with arsenic through atmospheric deposition when water from rains brings the arsenic to the ground.



- Several nations in the world such as Argentina, Australia, Bangladesh, China, Hungary, India, Mexico, Peru, Thailand, and the U.S. have shown concentrations higher than the guideline value of **10 ug/L** of the WHO.
- Highly contaminated areas (India, South America) can contain as much as 1800 ppb (180 times the WHO standard).

Routes of Exposure to As

- When air containing arsenic dusts is breathed in, the majority of the dust particles settle onto the lining of the lungs/gills.
- Very little internal exposure to arsenic occurs via the material passing through the skin into the body, and so there is little risk posed by this route.
- Majority of arsenic enters the body in the trivalent inorganic form As(III) via a simple diffusion mechanism.
- Small amount of pentavalent inorganic arsenic can cross cell membranes via an energy-dependent transport system, after which it is immediately reduced to trivalent arsenic.

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- Arsenic is most sensitive to kidney
 - Chronic arsenic exposure affects the vascular system and causes hypertension and cardiovascular disease.
 - Acute arsenic toxicity may cause cardiomyopathy and hypotension.
 - The most common neurological effect of long-term arsenic toxicity is peripheral neuropathy and the gastrointestinal effects are manifested by toxic hepatitis accompanied by increased levels of liver enzymes.

Toxicity of trivalent As

- ✓ Inhibits pyruvate dehydrogenase by binding to the sulfhydryl groups of dihydrolipoamide, resulting in a reduced conversion of pyruvate to acetyl coenzyme A (CoA).
- ✓ Citric acid cycle activity and production of cellular ATP are decreased.
- ✓ Inhibits numerous other cellular enzymes through sulfhydryl group binding.
- ✓ Inhibits the uptake of glucose into cells, gluconeogenesis, fatty acid oxidation and further production of acetyl CoA.
- ✓ Inhibits the production of glutathione, which protects cells against oxidative damage.

Disease Caused by As

- ✓ Lung cancer
- ✓ Bladder cancer
- ✓ Skin cancer
- ✓ Prostate cancer
- ✓ Kidney cancer
- ✓ Nasal cancer
- ✓ Liver cancer
- ✓ Stillbirths
- ✓ Post neonatal mortality
- ✓ Ischemic heart disease (heart attack)
- ✓ Diabetes mellitus
- ✓ Nephritis (chronic inflammation of the kidneys)
- ✓ Nephrosis (degenerative kidney diseases)
- ✓ Hypertension
- ✓ Hypertensive heart disease
- ✓ Bronchitis
- ✓ Lymphoma (tumors in the lymph)
- ✓ Black-foot disease



Mercury

- Mercury is found in the environment in three basic states:
 1. Elemental mercury or mercury vapor,
 2. Inorganic mercury,
 3. Organic mercury- ethyl-, methyl-, alkyl, -phenyl mercury

Safety dose/concentration of Hg

- The Bureau of Indian Standards (BIS) has laid down safety limits for drinking water at 0.001 mg of mercury per litre
- According to EPA maximum containment level was set at 2 parts per million

Sources of Hg into the environment

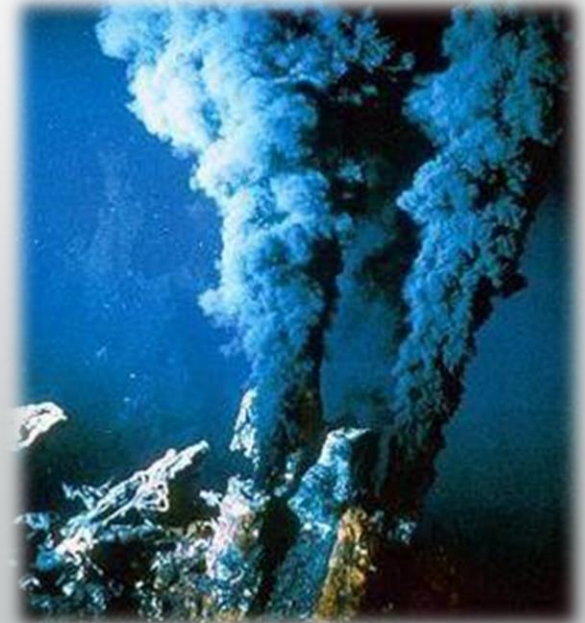
1. Anthropogenic Sources:

- ❖ Burning of fossil fuels – Coal fired power plants contributes 65% of anthropogenic emissions
- ❖ Metal mining operations – gold and silver
- ❖ Metal smelting and refining
- ❖ Cement manufacture
- ❖ Chemical manufacture
- ❖ Disposal of Hg-waste – Municipal landfill



2. Natural Sources:

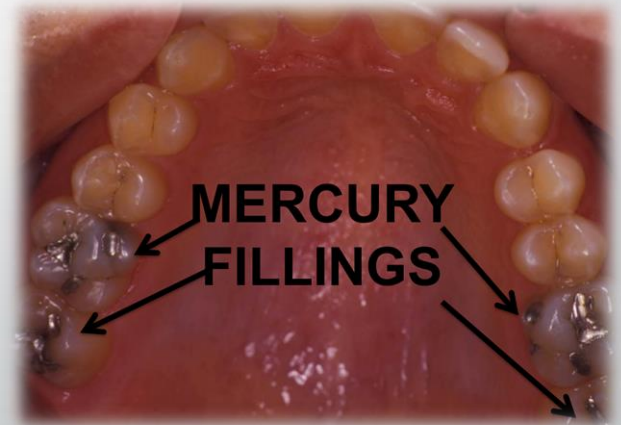
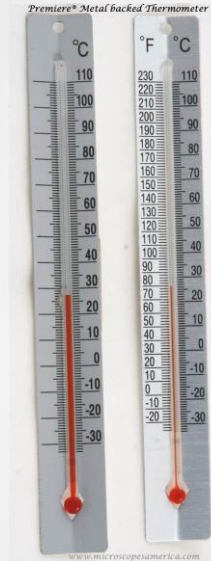
- ❖ Volcanoes
- ❖ Deep-sea vents
- ❖ Terrestrial hot springs



Different state of Hg

❖ Elemental Hg:

1. Thermometers
2. Thermostats
3. Dental amalgams
4. Hg added to latex paint, eventually enters a vaporized state



❖ Inorganic Hg

- ✓ Cosmetic products,
- ✓ Laxatives
- ✓ Teething powders
- ✓ Diuretics
- ✓ Antiseptics
- ✓ Inorganic mercury can be formed from the metabolism of elemental mercury vapor or methylmercury



Elemental Mercury

- Eighty percent of inhaled elementary mercury vapor is absorbed and can cross the blood-brain barrier or reach the placenta.
- Mercury vapor in the gastrointestinal tract is converted to mercuric sulfide and excreted in the feces.
- Mercury vapor in the kidneys is carried to all parts of the central nervous system as a lipid soluble gas.
- Mercury vapor can also be oxidized to inorganic mercury by catalase and can attach to the thiol groups in most proteins – enzymes, glutathione, or almost any structural protein.
- Elemental mercury can also be methylated by microorganisms in soil and water and potentially the human gastrointestinal tract, where it can then be transformed into organic methylmercury, the form found in fish, fungicides, and pesticides

Inorganic Mercury

- Although inorganic mercury does not normally reach the placenta or cross the blood-brain barrier, it has been found in the neonatal brain due to the absence of a fully formed blood brain barrier.
- Inorganic mercury is complexed with glutathione in the liver and secreted in the bile as a cysteine mercury or glutathione-mercury complex.

Organic Mercury

- Methylmercury is almost completely absorbed (95-100 percent) in the human gastrointestinal tract, 90% of which is eventually eliminated through the feces.
- Methylmercury is present in the body as a water-soluble complex, mainly with the sulfur atom of thiol ligands, and crosses the blood-brain barrier complexed with L-cysteine in a molecule resembling methionine.

Bioaccumulation of methyl-Hg

- Accumulates in tissues over time
- Concentrates in the muscle tissue of fish
- Accumulates in the envelopes of nerve cells
- 100x more toxic than Hg⁰ and Hg²⁺
- Destroys muscle proteins and enzymes essential to cell function

Hg poisoning

- 1. Enzyme inhibition:-** inhibits catalysis of general metabolic reactions.
- 2. Cellular disfunctions :-** bound to protein of cell membrane resulting in alteration of distribution of ions, change electrode potential & interfere in movements of fluids.
- 3. Neurological disorder:-** brain is target organ of methylHg damaging nervous cells.
 - Symptoms are loss of sensation at extremities of hands & feet & areas around mouth.

4. Erethism :-

- ❖ Psychic disorder result from Hg poisoning.
- ❖ Characterized by self consciousness, lack of concentration, depression. Severe poisoning causes blindness, coma & death.

5. Teratogenic effects:-

- ❖ CH_3HgCl readily penetrates through placenta and effects foetus.
- ❖ The conc. of Hg in foetus brain & blood is about 20% higher than mother.