Heavy Metals Poisoning

Toxicology Lab.

4th Stage / 2nd semester

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Introduction:

- Heavy metals are naturally occurring elements with high atomic weight and a density 5 times higher than water
- **Heavy metal may be categorized into 2 types:**
  - Those that can be used for medicinal purposes [eg/ Zinc (Zn), Selenium (Se), Iron (Fe), Chromium (Cr), Copper (Cu), Bismuth (Bi)]
  - Those used for industrial purposes [eg/ Lead (Pb), Mercury (Hg), Arsenic (As), Cyanide (Cn), Cadmium (Cd) and more)
- Most of the heavy metals used for industrial purposes are **highly poisonous even in very low concentrations and carcinogenic with chronic exposure**
- Poisoning from other heavy metals most often occurs in individuals regularly exposed to the metals in their work environment

Introduction:

- **Sources of exposure to heavy metals:**
  - Medications
  - Food and drinking water
  - Occupational hazards
  - Environmental contamination

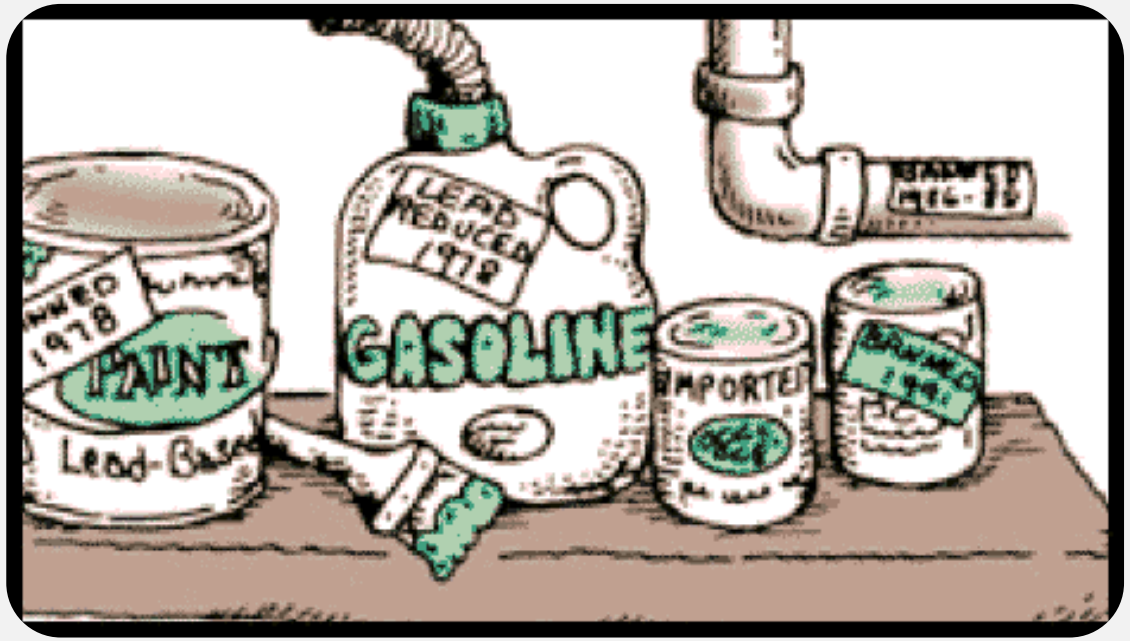
- **Common route of exposure to heavy metals:**
  - Ingestion
  - Inhalation
  - Skin contact

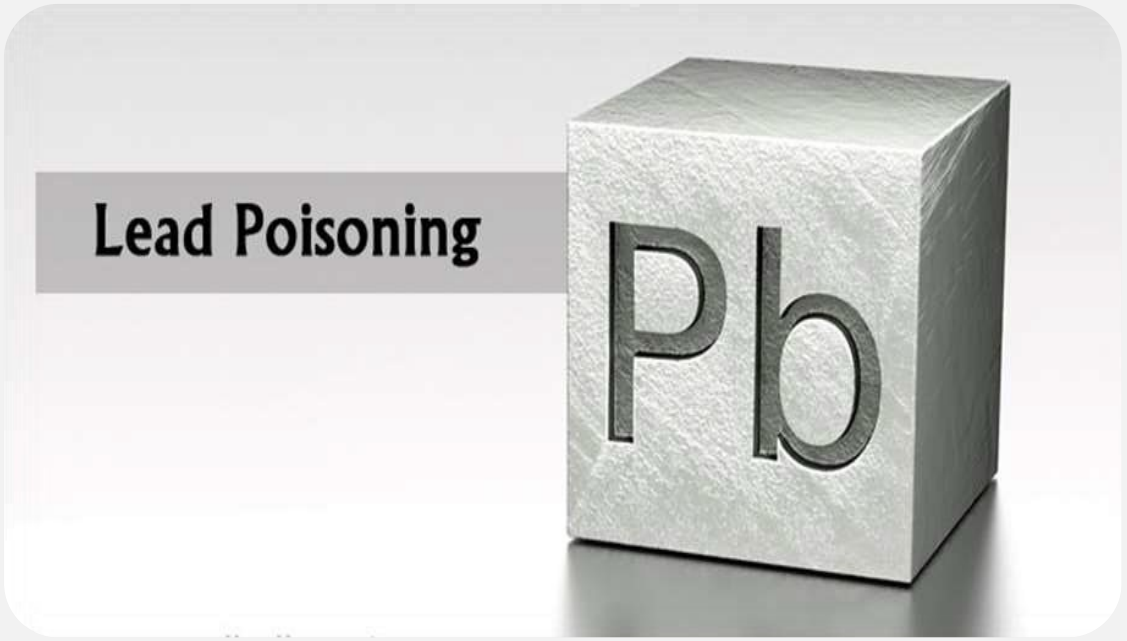
Introduction:

- **Why heavy metals are highly poisonous?**
  1. They can not be degraded by the biological system
  2. They tend to bio-accumulate overtime (which means an increase in the concentration of the chemical in a biological organism overtime compared to the chemical concentration in the environment)
  3. They exert their harmful effect by binding to one or more of the reactive groups (oxygen, nitrogen, and sulfhydryl) in cellular proteins and enzymes, causing alterations in their activity

- **Factors affecting toxicity with heavy metals:**
  - Exposure concentration
  - The exposure either chronic or acute
  - Age of the person
  - Route of exposure

Lead (Pb) Poisoning





Characteristics and Sources of Lead:

- **<u>Lead is available in 2 different compounds:</u>**
  - Organic lead / exp: tetraethyl lead & tetramethyl lead
  - Inorganic lead / exp: lead arsenate, lead carbonate, lead oxide, and lead sulphide

- Both of these lead compounds are toxic but organic lead is more toxic (why?)
- Route of exposure/ inhalation, ingestion, and skin contact

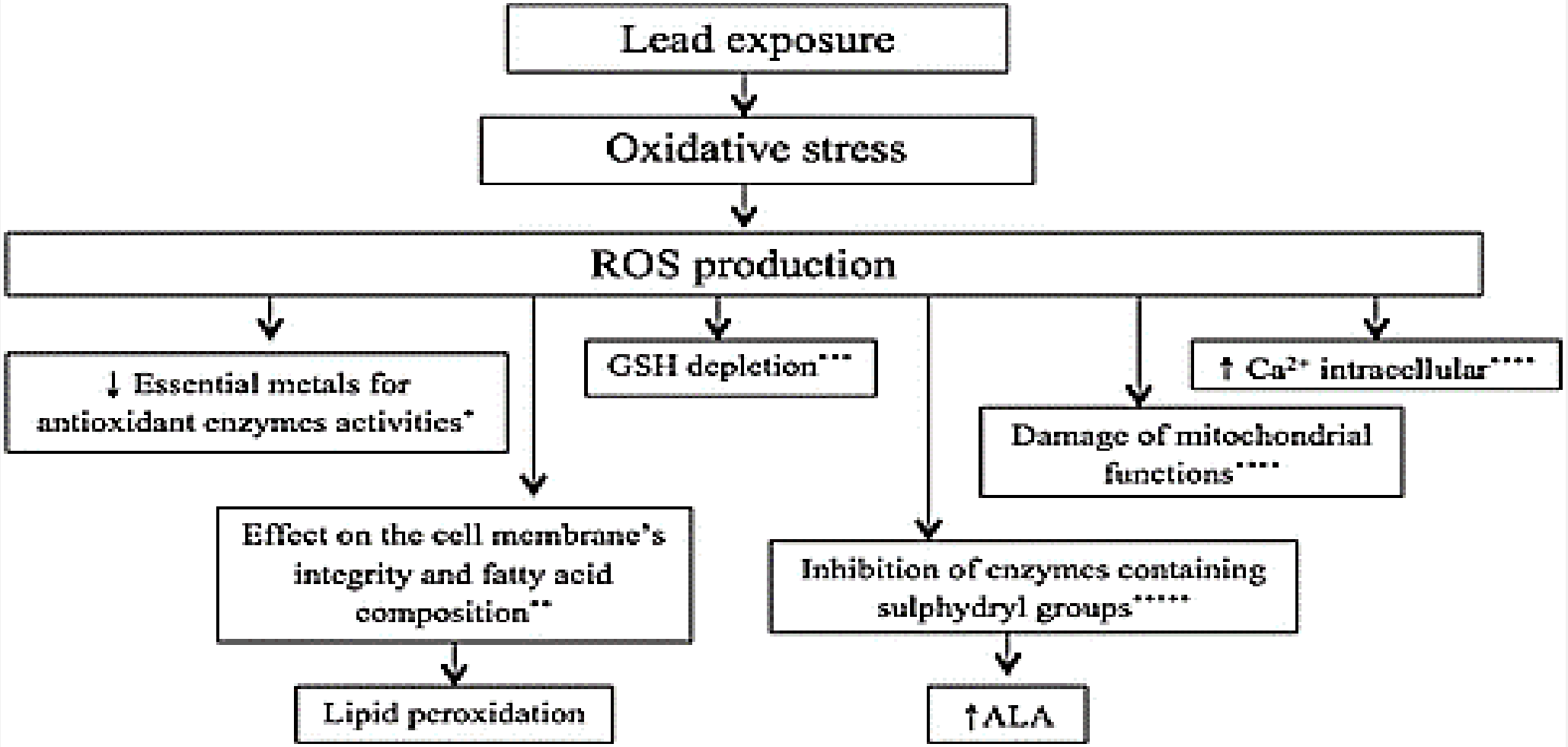
- **<u>Common sources of lead poisoning:</u>**
  1. Occupational exposure: gas stations, (found in gasoline), miners, plumbers, construction workers
  2. Lead found in paints, and considered the main source of toxicity in children
  3. Water pipes made of lead
  4. Some traditional home remedies and cosmetics
  5. Lead is found is low conc.in soil
  6. Cigarettes & exhaust of vehicles

What is Lead poisoning?

- Is a medical condition caused by increased by increased levels of the heavy metal (lead) in the body, and this can interfere with different body processes and causes toxicity to many organs and tissues
- After absorption, lead is precipitated in blood, soft tissues, and bones and teeth
- 90% of the lead is precipitated in bones and teeth, where the half-life takes several years

- **Lead toxicity can be classified into:**
  - Acute toxicity/ intense exposure of short duration
  - Chronic toxicity/ repeated low-level exposure of prolonged period

Pathogenesis (mechanism of toxicity):

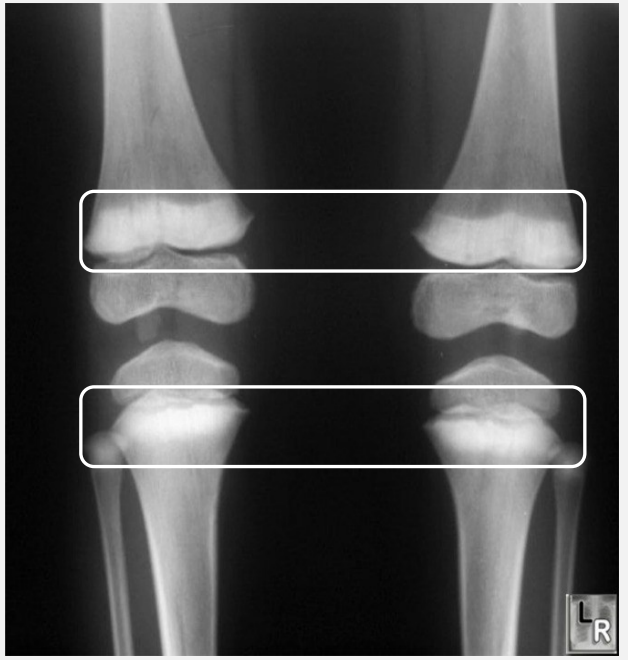


Harmful Effects of Lead:

- It interferes with the normal synthesis of vitamin D3
- It interferes with normal homeostasis of calcium causing it to build up within cells
- It interferes with the metabolism of bones and teeth, resulting in deposition of lead in them
- It interferes with the immune system, alternating between increasing the inflammatory mediators or decreasing the activity of PMN leukocytes
- It interferes with the normal integrity cellular membrane and RBC synthesis
- It interferes with the release of neurotransmitters, mainly (glutamate)

Diagnosis of lead poisoning:

- Patient history
- Clinical examination
- Lab. Tests:
  - Blood lead level (BLL) is the main tool for diagnosing and assessing the severity of lead poisoning [normal value/ adult (>20mcg/dl), children (>10mcg/dl)]
  - Free erythrocytes protoporphyrin (FEP)/ specific to determine the time period of exposure (exp/ if BLL is high and the FEP is normal, then the exposure is recent)
  - CBC/ microcytic anemia, leukocytosis, basophilic stippling of RBCs
  - **Radiodensity of long bone** reveals deposition of lead (lead lines), an indication of chronic toxicity
  - Urinalysis and Fecal analysis
  - Examination of the hair and nails



Clinical Manifestations:

Acute Toxicity:

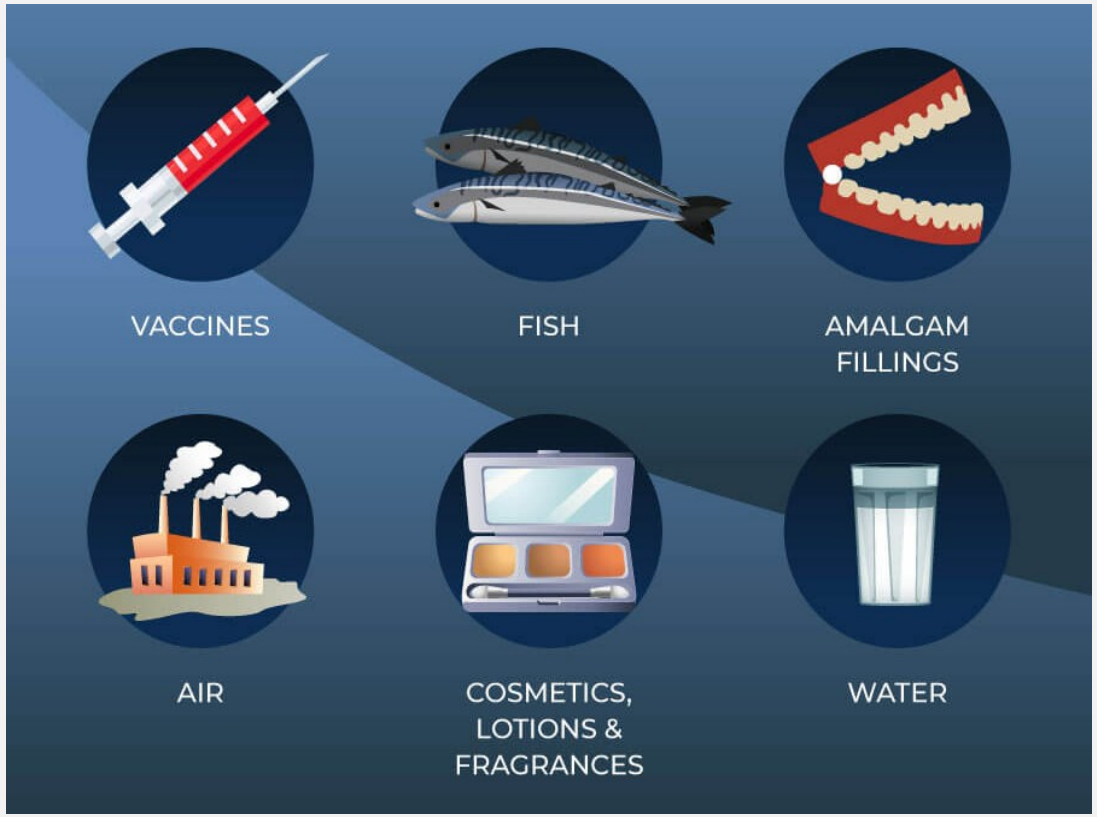
- Neurological (CNS) signs/ pain, muscle weakness, and convulsion
- GIT signs/ metallic taste, poor appetite, abdominal pain, diarrhea, vomiting
- Hematological signs/ acute hemolytic crisis >>> severe anemia >>> circulatory shock
- Renal damage from hemolytic anemia and shock
- Such toxicity is very rare and depends on the intensity of exposure

Chronic Toxicity:

- The signs & symptoms of chronic lead poisoning is called (plumbism)
- CNS signs are the early signs and most predominant (vertigo, insomnia, headache, restlessness, irritability, neuromuscular signs, and impaired cognitive function)
- GIT signs/ anorexia, metallic taste, weight loss, abdominal pain, vomiting, constipation or diarrhea
- Nephropathy and Fanconi syndrome
- Reproductive system effects/ abnormal sperms, miscarriages or low birth weight

Note: children are highly prone to lead poisoning than adults

Mercury (Hg) Poisoning



Characteristics & Sources of Mercury:

- It has a bright silvery appearance
- Found in liquid form
- <u>It is available in different compounds:</u>
  - Elemental mercury (Hg)
  - Organic mercury / methyl Hg & ethyl Hg
  - Inorganic mercury / mercuric oxide, mercuric sulfide, mercuric chloride, ammoniated Hg

- Route of exposure/ inhalation & ingestion
- Ingestion of liquid Hg is non-toxic and excreted in bile
- Inhalation of Hg vapors is very toxic and can distribute through out all body tissues

Sources of mercury poisoning :

- Air pollution from burning of coal and fuel oil
- As mercury – based preservative in some flu vaccines (its use was banned in 1999)
- Some types of fish (sword fish, shark, tuna)
- Dental amalgam fillings
- Contaminated drinking water with municipal wastes
- added to cosmetics and fragrances
- Part of industrial and electrical products, and batteries

The different form of Mercury:

Elemental

- Liquid and silvery appearance
- Non-poisonous if swallowed, not absorbed through the GIT
- Volatile at room temp. and vapors of Hg is very toxic
- Vapors of Hg are lipid soluble and can cross the blood brain barrier
- Sources/ dental amalgams, jewelry, batteries, thermometers and sphygmomanometer

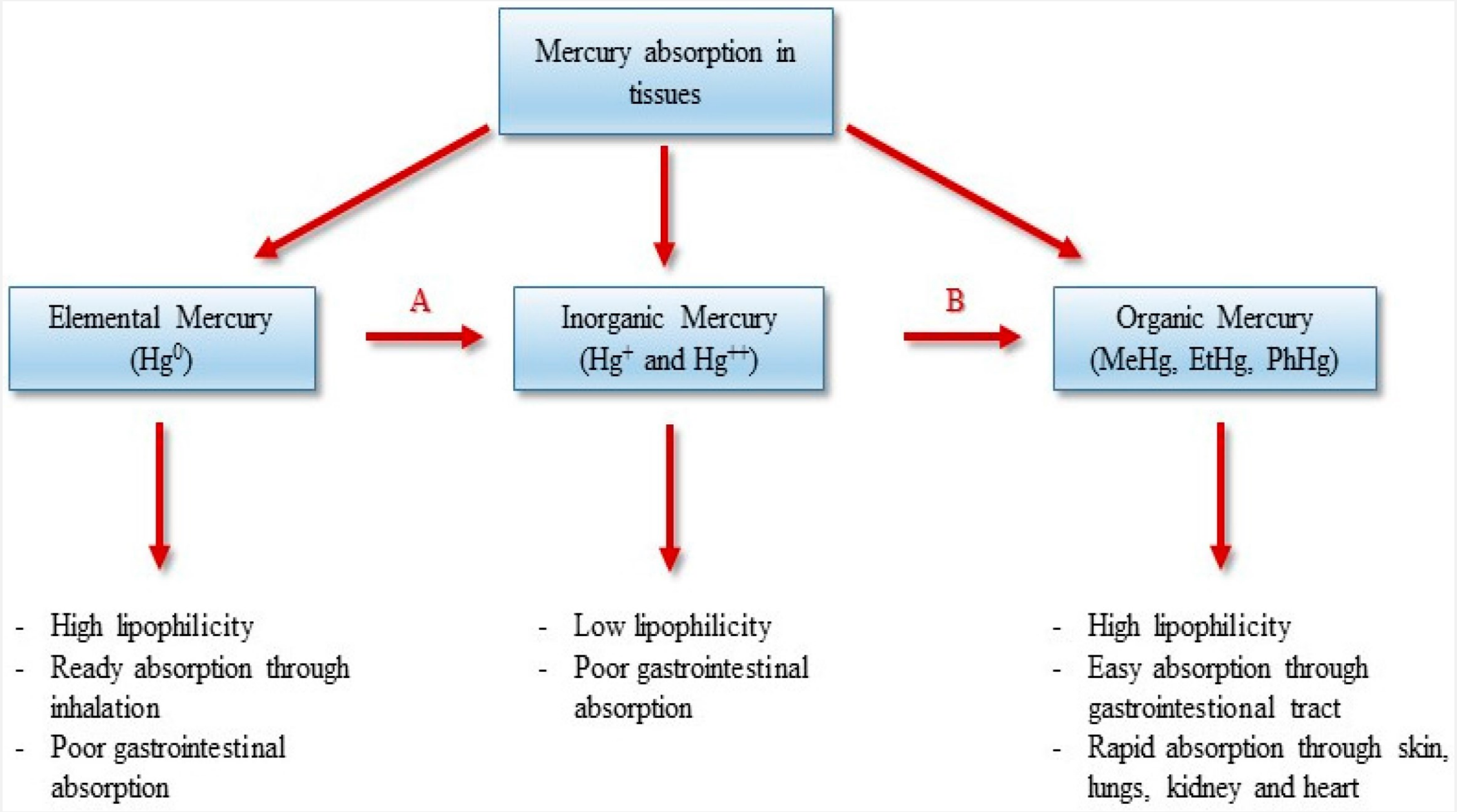
Organic

- The most toxic form of Hg
- High lipid solubility that can be distributed through out all body parts
- Can cross BBB, placenta and breast milk and cause serious fetal toxicities
- Sources/ preservatives, some mercury – based preservatives in vaccines, and aquatic fish

Common Mercury Exposure Routes			
	Elemental	Inorganic	Organic
Inhalation	High	Low	Low
Oral	Low	Med	High
Dermal	Low	Med	Low

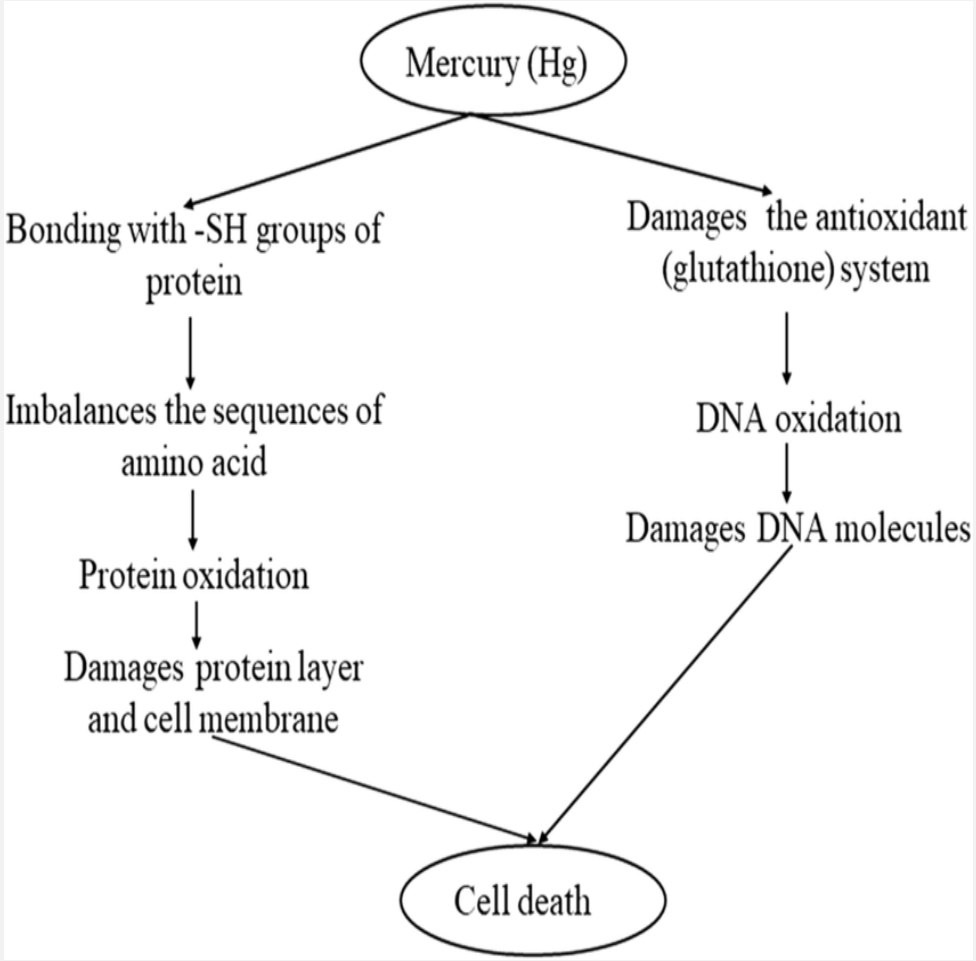
Inorganic

- Available in different salts forms
  - Water soluble/ mercuric chloride and ammoniated mercuric chloride
  - Water insoluble/ mercurous chloride
- Usually in powder formulation
- This form of mercury is the least toxic because of low lipid solubility and limited GI absorption
- Sources/ cosmetics, medicinal preparations for skin disorders, and certain chemical formulations used in taxidermy


Mercury absorption in tissues
Elemental Mercury (Hg^0)
A
Inorganic Mercury (Hg^+ and Hg^{++})
B
Organic Mercury (MeHg, EtHg, PhHg)
- High lipophilicity
- Ready absorption through inhalation
- Poor gastrointestinal absorption
- Low lipophilicity
- Poor gastrointestinal absorption
- High lipophilicity
- Easy absorption through gastrointestional tract
- Rapid absorption through skin, lungs, kidney and heart

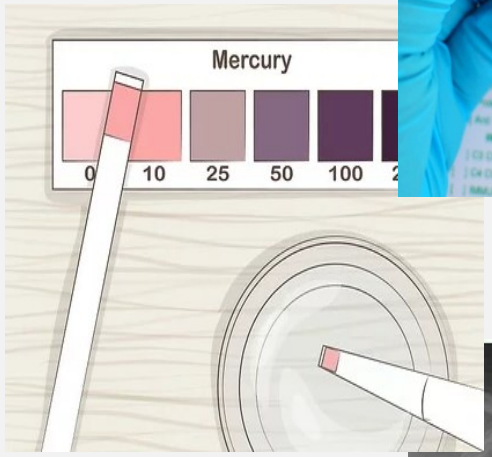
Pathogenesis (Mechanism of Toxicity):

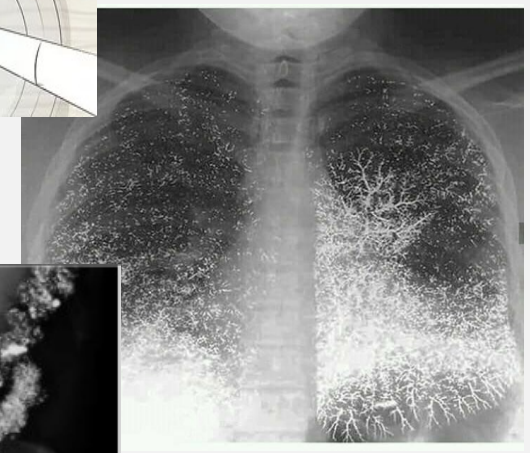
- Binding to sulfhydryl group in different proteins, and causing enzyme inhibition
- Protein oxidation and imbalance in amino acids sequence
- Depletes the antioxidant system
- Oxidation of the phospholipids bilayer membrane
- DNA oxidation leading to DNA damage
- Finally cell death (necrosis or apoptosis)



Diagnosis of Mercury poisoning:

- **Blood Hg analysis:**
  - Useful in acute Hg poisoning
  - Normal Hg level less than 10 mcg/L
  - Symptoms start to appear at blood Hg level 150 – 200 mcg/L
- **Urine Hg level:**
  - Is the most reliable indicator for both (acute and chronic poisoning)
  - Normal urine level less than 10 mcg/L
  - Symptoms appear with urine level of 100 – 150 mcg/L
- **Radiology Test**: in case of ingestion or aspiration of Hg





Clinical Manifestations:

Acute Toxicity:

- Inhalation of elemental Hg vapors or organic hg
  - Respiratory signs/ chemical pneumonia, pulmonary edema, gingivostomatitis, increased salivation
  - CNS signs/ ataxia, restricted vision, delirium, neuropathy, paresis
- Ingestion of organic Hg
  - GIT signs/ metallic taste, hoarsening of the voice, difficulty swallowing and breathing, abdominal pain, blood in stool
- Other signs/ bone marrow suppression, irregular heart beat, renal involvement

Chronic Toxicity:

- Excessive salivation and swollen salivary gland
- Foul breathing, inflamed and ulcered gum
- Necrosis of the jaw
- Acrodynia (pink disease)/ generalized body rash, erythematous and eczematous popular skin lesions mostly in hands and feet
- Mad Hatters syndrome (hatter shake)/ tremors and jerky movements resulted from inhaling the vapors of inorganic mercuric nitrate
- Minamata disease/ results from consumption of contaminated fish causing CNS symptoms

Management of Heavy Metal poisoning:

- Remove the patient from the source of exposure
- Identify the toxic agent
- Decontamination
- Suppurative care (ABC)
- Assess the metabolic activities, and other organ functions
- Administer antidotes (if exist)
- Heavy metal poisoning >>> the antidote is (a chelating agent)
- **Chelating agent**/ are chemical antagonists and organic compounds with 2 or more electronegative groups that form stable bond with cationic metals, used in heavy metal poisoning which make the metal readily excreted out of the body

Chelator	Use
Dimercaprol(BAL)	•acute arsenic poisoning •acute mercury poisoning •lead poisoning (in addition to EDTA)
Dimercaptosuccinic acid (DMSA)	•lead poisoning •arsenic poisoning •mercury poisoning
Dimercapto-propane sulfonate (DMPS)	•severe acute arsenic poisoning •severe acute mercury poisoning
Penicillamine	Mainly in: copper toxicity Occasionally adjunctive therapy in: •gold toxicity •arsenic poisoning •lead poisoning •rheumatoid arthritis
Ethylenediaminetetraaceticacid (EDTA)	•lead poisoning
Deferoxamine and Deferasirox	•acute iron poisoning •iron overload

Thank You For Your Patience

Best Of Luck In The Upcoming Examinations