

- Heavy metals are found in everyday existence and are frequently hard to avoid entirely. Most people can excrete toxic heavy metals from the body successfully. However, some people—especially those who suffer from chronic conditions—cannot excrete them efficiently enough and toxicity occurs
- The most hazardous heavy metals that humans are exposed to are arsenic (As), lead (Pb), mercury (Hg), cadmium (Cd), aluminum (Al) and iron (Fe)

- Acute heavy metal toxicity is an uncommon diagnosis.
- With the possible exceptions of acute iron toxicity from intentional or unintentional ingestion and suspected lead exposure, emergency physicians will rarely be alerted to the possibility of metal exposure.
- Yet, if unrecognized or inappropriately treated, heavy metal exposure can result in significant morbidity and mortality.

The toxicity of heavy metals depends on a number of factors.

- 1. the total dose absorbed**
- 2. the exposure was acute or chronic.**
- 3. The age of the person can also influence toxicity.**

For example, young children are more susceptible to the effects of lead exposure because they absorb several times the percent ingested compared with adults and because their brains are more plastic and even brief exposures may influence developmental processes.

4- The route of exposure is also important. Elemental mercury is relatively inert in the gastrointestinal tract and also poorly absorbed through intact skin, yet inhaled or injected elemental mercury may have disastrous effects.

- Exposure to metals may occur through the diet, from medications, from the environment, or in the course of work or play.

Pathophysiology

- The pathophysiology of the heavy metal remains relatively constant.
- For the most part, heavy metals bind to oxygen, nitrogen, and sulfhydryl groups in proteins, resulting in alterations of enzymatic activity.
- Nearly all organ systems are involved in heavy metal toxicity; however, the most commonly involved organ systems include the CNS, PNS, GI, hematopoietic, renal, and cardiovascular. To a lesser extent, lead toxicity involves the musculoskeletal and reproductive systems.

Clinical presentation

- Nausea, persistent vomiting, diarrhea, and abdominal pain are the hallmark of most acute metal ingestions.
- Dehydration is common. Metal salts are generally corrosive.
- Encephalopathy, cardiomyopathy, dysrhythmias, acute tubular necrosis, and metabolic acidosis are also commonly seen with acute, high-dose exposures to most metals.

- Patients with chronic metal toxicity tend to have more prominent involvement of the CNS and PNS.
- A classic presentation of chronic metal exposure includes anemia, Mees lines (horizontal hypopigmented lines across all nails), and subtle neurologic findings. These findings should prompt suspicion of heavy metal toxicity in any patient regardless of chief complaint.

Treatment

- Removal of the patient from the source of exposure is critical to limiting dose.

- **Decontamination**

Treatment may include whole-bowel irrigation with polyethylene glycol electrolyte solution if radiographic evidence of retained metal (toys, coins, paint chips) is present.

- **Resuscitation:** Good supportive care is critical. Ensure airway patency and protection, provide mechanical ventilation where necessary, correct dysrhythmias, replace fluid and electrolytes (significant fluid losses generally occur and require aggressive rehydration), and monitor and treat the sequelae of organ dysfunction.

Chelation

- Chelation regimens have been shown to enhance elimination of some metals, and thereby decrease the total body burden.
- These drugs supply sulfhydryl groups for the heavy metals to attach and, subsequently, may be eliminated from the body.
- Consideration of chelation therapy for patients with suspected or confirmed metal exposures should be made in conjunction with a medical toxicologist or the local poison control center.

The most useful chelators have

- a low order of toxicity,
- do not redistribute to other organs (ie.brain)
- are eliminated quickly without breakdown.

Contraindications

- Liver failure
- Glucose 6 phosphate dehydrogenase deficiency
- Peanut allergy
- During iron supplementation

(BAL) Dimercaptol

- Drug of Choice in the treatment of lead, arsenic, and mercury toxicity.
- Administered via deep IM injection only, q4h, mixed in a peanut oil base.
- Enhances fecal and urinary elimination
- Diffuses into brain and RBC's
- Chelates intracellular and extracellular lead and is excreted in urine and bile.
- May be given to patients with renal failure.

EDTA

- Second-line for lead toxicity. Most effective when given early in the course of acute poisoning.
- Chelates only extracellular lead and may induce CNS toxicity if BAL therapy not initiated first.
- Begin therapy 4 h after BAL is given. Only given IV, and continuous infusion is recommended.
- Not recommended with renal failure. Because of potential for renal toxicity, patient should be well hydrated.
- To prevent hypocalcemia, use only calcium disodium salt of EDTA for chelation in heavy metal toxicity.

Succimer (DMSA)

Dimercaptosuccinic acid (DMSA)

- More effective than BAL
- Can be used to chelate Hg, As, and Pb
- Wider therapeutic index than BAL
- Does not re-distribute Pb to brain
- May produce transient elevation of serum alanine transaminase

Penicillamine

- Metal chelator used in treatment of arsenic poisoning. Forms soluble complexes with metals that are subsequently excreted in urine.

Desferrioxamine (DFO)

- it has natural origin (a derivative of the iron-bearing metabolite, ferrioxamine B, from *Streptomyces pilosus*) & used for Iron poisoning, and aluminum poisoning.

Lead toxicity

- Lead is ranked 2nd on “the Top Hazardous Substances”



- Lead is a ubiquitous toxicant in the environment. It is one of the oldest chemical toxins and lead poisoning is probably the most important chronic environmental illness affecting modern children.

- It has no physiologic role in biological systems
- Despite efforts to control it and despite apparent success in decreasing incidence, serious cases of lead poisoning still appear
- In children, virtually no organ system is immune to the effects of lead poisoning. Perhaps the organ of most concern is the developing brain

Mood of Exposure

- Lead exists in the environment in various forms, organic and inorganic compounds.
- Inorganic lead compounds are less toxic and poisoning could happen mainly by direct ingestion of lead compounds or items contaminated with them.

Sources of Exposure

Occupational exposure

- Battery makers
- Cable makers
- Glass makers/polishers
- Gunshot/gun barrel makers
- Jewelers
- Lead burners
- Painters
- Pigment makers
- Pipe cutters
- Printers

Non-occupational exposure

- Battery burning
- Bullet retention
- Cooking in leaden pots
- Target shooting
- lead containing herbal medicines
- Ingestion of paints
- still used as additives in gasoline in several countries
- Exists in cigarette smoke.
- surface paints on the toys.
- stagnant water in pipes.

Absorption

1. GI Tract

- **Children are at greater risk for lead absorption than adults.**
- **Lead absorption is dependent on several factors, including the physical form of lead, the particle size ingested, the GI transit time, and the nutritional status of the person ingesting.**
- **Increased with Fe, Ca, Zn deficiency**
- **decreased if phosphorus, riboflavin, vitamin C, and vitamin E are in the diet.**
- **Adults: 11% - 16%**
- **Children : 40% - 50%**

Absorption (contiuene)

2. Lungs

- 50% - 70% if $< 1 \mu\text{m}$

3. Skin

- Inorganic lead is non-absorbable
- Organic lead is readily absorbed

Distribution

- Absorbed lead is exchanged primarily among the following 3 compartments:
 1. Blood
 2. Soft tissue (liver, kidneys, lungs, brain, spleen, muscles, and heart)
 3. Mineralizing tissues (bones and teeth)
- Lead readily crosses the placenta and exists in breast milk, with the fetus retaining lead cumulatively throughout gestation.
- Specific health problems, such as malnutrition and iron deficiency, may result in higher lead absorption in the mother. Elevated maternal lead levels subsequently result in higher lead distribution to the fetus.

- Lead entering the intravascular space binds quickly to red blood cells.
- Lead has a half-life of approximately 30 days in the blood, from where it diffuses into the soft tissues.
- Lead then diffuses into bone and is stored there for a period that corresponds to a half-life of several decades. Increased bone turnover with pregnancy, menopause, lactation, or immobilization can increase blood lead levels.
- Estimations of blood lead levels are more useful for diagnosing acute lead poisoning, whereas the extent of past lead exposure can be estimated by determining the body burden of lead on the basis of results from the edetate calcium disodium (CaNa_2EDTA) lead mobilization test.

Elimination

- 1. Kidney is responsible for 65% of lead's elimination**
 - Process is dependent on glomerular filtration rate and renal plasma flow
- 2. Biliary excretion is responsible for 35% of lead's elimination**

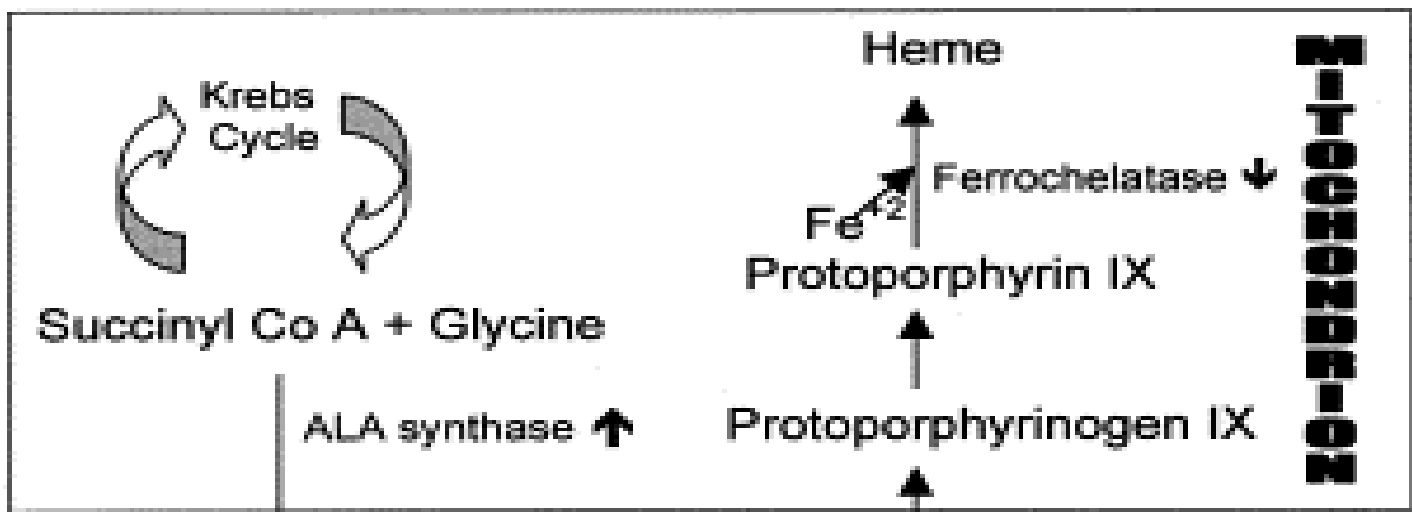
Pathophysiology

- Lead interferes with a variety of body processes and is toxic to many organs and tissues. The heart, bones, teeth, intestines, kidneys, thyroid gland reproductive and nervous systems represent its main targets.
1. Lead perturbs multiple enzyme systems. As in most heavy metals, any ligand with sulfhydryl groups is vulnerable.

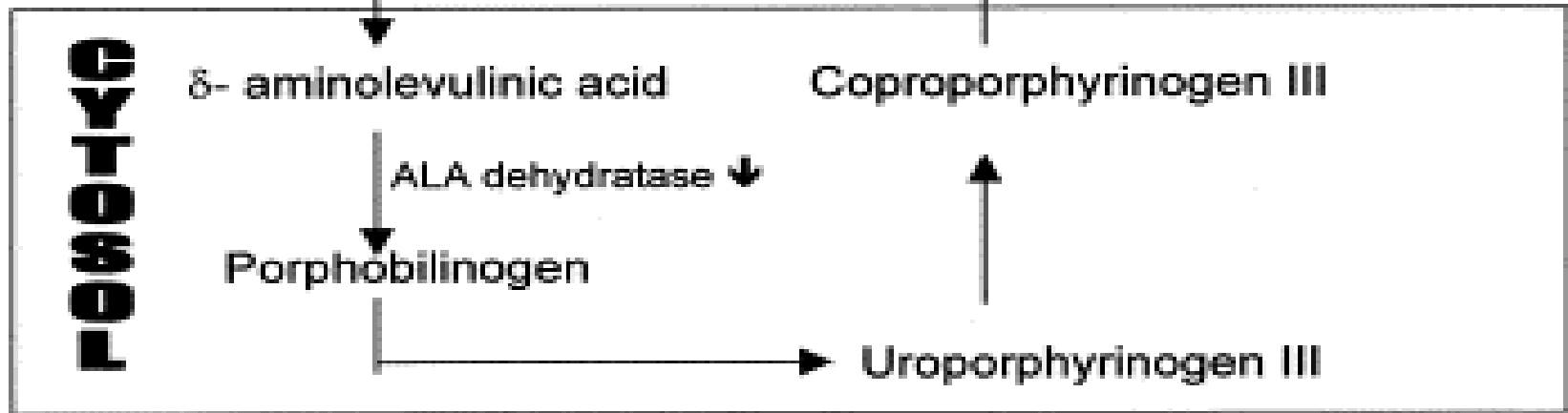
- Perhaps the best-known effect is that on the production of heme. The enzymes **delta-aminolevulinic acid dehydratase**, which catalyzes the formation of the **porphobilinogen ring**, and **ferrochelatase**, which catalyzes the incorporation of iron into the **protoporphyrin ring**, both are compromised by lead. the result is a decrease in heme production.

-

- zinc is substituted for iron and zinc protoporphyrin concentrations increase. The major consequence of this effect is the reduction of circulating levels of hemoglobin. Basophilic stippling of erythrocytes may be present.
- Because heme is essential for cellular oxidation, deficiencies have far-reaching effects.



20-00000-02



2. Substitutes as calcium interfering with calcium dependent processes.
- **Pb²⁺ disturbs this intracellular Ca²⁺ homeostasis.**
 - **Pb²⁺ interacts with a number of Ca²⁺ - dependent effector mechanisms, such as calmodulin, protein kinase C, Ca²⁺ - dependent K⁺ channels and neurotransmitter release.**

3. The effects of lead poisoning on the brain include delayed or reversed development, permanent learning disabilities, seizures, coma, and even death.

The long-term effect of lead exposure is maximal during the first 2 or 3 years of life, when the developing brain is in a critical formative

- The microvasculature of a child's developing brain is uniquely susceptible to high-level lead toxicity, characterized by cerebellar hemorrhage, increased blood-brain barrier permeability, and edema.**

4. Lead toxicity has been associated with **decreased fertility**, and increased miscarriage.
5. **The Burton line** or gingival lead line is a dark blue line along the gums, signifying lead poisoning. It occurs typically when lead poisoning is associated with poor oral hygiene.

Symptoms

- Mortality related to lead toxicity is rare today. However, morbidity remains common. Because lead is an enzymatic poison, it perturbs multiple essential bodily functions, producing a wide array of symptoms and signs.
- With exposure to high levels of lead (acute) , patients develop Abdominal pain, loss of appetite, vomiting, constipation, headache, ataxia, somnolence, lethargy, seizures, stupor, coma
- Acute lead nephropathy is usually completely reversible with chelation therapy.
- Deaths may result from the elevated intracranial pressure (ICP) associated with lead encephalopathy.

Chronic toxicity (from repeated low-level exposure over a prolonged period)

Depend on amount and duration

- Lead poisoning (also known as *plumbism*), is a medical condition caused by increased levels of the lead in the body.
- **Early symptoms manifested as:**
 - Diffuse muscle weakness, and paresthesias
 - General fatigue/lethargy
 - Attention deficiency and confusion/ irritability
 - Joint and muscle pain
 - Unusual metallic taste in mouth

Symptoms of Chronic Lead Toxicity:

- Then complicated with
 - Intermittent abdominal cramping, vomiting, and constipation
 - Loss of appetite and diminished libido
 - Weight loss and anemia and increase in systolic blood pressure.
 - Tremors and peripheral neuropathy in extensor surfaces that manifested as wrist drop and/or foot drop (most common neurological symptom in adults)
 - Short-term memory loss
 - Depression and Insomnia
 - Cerebral edema (headache, incoordination, and sometimes seizures)



Symptoms of chronic Lead Toxicity

- Renal insufficiency
 - bluish black edging to the teeth
- are another features of chronic lead poisoning
- **Children *plumbism*** is characterized by loss of appetite, abdominal pain, vomiting, weight loss, constipation, anemia, diminished renal function, irritability, lethargy, and confusion. Also, Lead interfere with the growth rate and development of the nervous system causing potentially permanent learning disability and behavior disorders.
 - Children may also experience hearing loss, aggression and delayed growth.

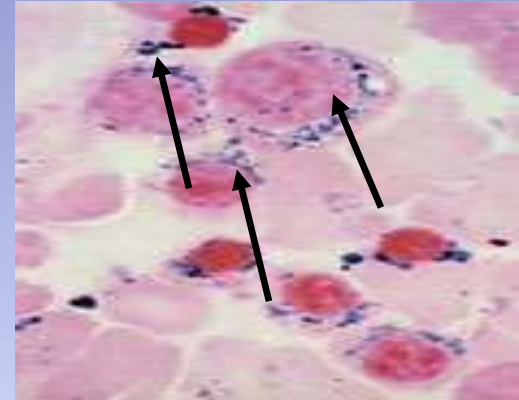


Treatment

- The signs of lead poisoning are difficult to distinguish , they may look so general, and confusing with other conditions. Good treatment depends on good diagnosis.
- Diagnosis includes determining the clinical signs and the medical history, with inquiry into possible routes of exposure.
- The main tool in diagnosing and assessing the severity of lead poisoning is laboratory analysis of the blood lead level (BLL), CBC, and sometimes concentration of lead in bones (X-ray fluorescence, XRF)- to asses the whole body burden.

Treatment

CBC examination may reveal basophilic stippling of red RBCs, as well as the changes normally associated with iron-deficiency anemia (microcytosis and hypochromasia).



- a blood lead level of $9 \mu\text{g}/\text{dL}$ or above is a cause for concern; however, lead may impair development and have harmful health effects even at lower levels, and there is no known safe exposure level.
- Radiographic examination of the abdomen in cases of acute poisoning.

Free erythrocyte protoporphyrin level

Lead interferes with the enzyme ferrochelatase, blocking the incorporation of iron into the protoporphyrin molecule; thus, an FEP level may be useful in demonstrating the degree of biologic abnormalities that exist.

FEP can also be used to help distinguish recent acute lead exposure from chronic exposure. If FEP is normal in the context of high blood lead levels, the exposure is more likely acute; if both are elevated, the exposure is more likely chronic. FEP elevation lags behind the blood lead elevation that causes it.

- Succimer is a water-soluble, oral chelating agent that is appropriate for use with BLLs higher than 45 $\mu\text{g}/\text{dL}$.
- Edetate calcium disodium (CaNa_2 EDTA) is a parenteral chelating agent. It should never be used as the sole agent in patients manifesting with lead encephalopathy, because it does not cross the blood-brain barrier and can potentially lead to exacerbation of lead encephalopathy; dimercaprol, which does cross the blood-brain barrier, should be administered first.

- Dimercaprol (also referred to as British antilewisite [BAL]) is another parenteral chelating agent recommended as an agent of first choice for patients with lead encephalopathy. With high BLLs (ie, > 70 $\mu\text{g}/\text{dL}$), it is used in conjunction with CaNa_2EDTA .

- **Patients with chronic lead nephropathy, in the absence of marked interstitial fibrosis and with only minimal impairment in kidney function, may respond to chelation therapy.**
- **The diet should be adequate in energy (caloric) intake and replete in calcium, zinc, and iron.**
- **Data suggests that low dietary intake of vitamin D may increase accumulation of lead in bones, whereas low dietary intake of vitamin C and iron may increase lead levels in blood in subjects who range in age from middle-aged to elderly.**

MERCURY TOXICITY

Sources

- **Mercury is ranked 3rd on the Top Hazardous Substances.**
- **Mercury is generated naturally in the environment from the degassing of the earth's crust, from volcanic eruption.**
- **Occurs in three forms (elemental, inorganic salts, and organic mercurial compounds).**
- **Contamination results from mining, smelting, and industrial discharges.**
- **Atmospheric mercury is dispersed across the globe by winds and returns to the earth in rainfall, accumulating in soil and food chains and fish in lakes .**
- **the effects that are most toxic occur in the brain and nervous system, renal and GIT of humans**

Sources

- Mercury compounds were added to paint as a fungicide (these compounds are now banned) however, old paint supplies and surfaces painted with these old supplies still exist).
- Mercury continues to be used in thermometers, thermostats, fluorescent light bulbs, disc batteries, electrical switches, manometers and dental amalgam.
- Medical substances, such as antiseptics (mercurochrome and merthiolate), and some vaccines are still available.

Mood of Exposure

- Elemental
 - Liquid at room temperature that volatizes readily
 - Inhalation is the main source of intoxication, rapid distribution in body by vapor, poor in GI tract. Can affect CNS. Skin contact may also considered.
- Inorganic
 - Poorly absorbed in GI tract, but can be caustic
 - Dermal exposure has resulted in toxicity
- Organic
 - Lipid soluble and well absorbed via GI, lungs and skin. Cross BBB and affects CNS
 - Can cross placenta and into breast milk

The organic form is readily absorbed in the GIT (90-100%); lesser but still significant amounts of inorganic mercury are absorbed in the GIT(7-15%). Target organs are mostly the nervous system and kidneys

- Industrial mercury pollution is often in the inorganic form, but aquatic organisms and vegetation in waterways such as rivers, lakes, and bays convert it to deadly methylmercury. Fish eat contaminated vegetation, and the mercury becomes biomagnified in the fish.
- Fish protein binds more than 90% of the consumed methyl mercury so tightly that even the most vigorous cooking methods (eg, deep-frying, boiling, baking, pan-frying) cannot remove it.

- **Minamata disease** is an example of organic toxicity. In Minamata Bay, a factory discharged inorganic mercury into the water. The mercury was methylated by bacteria and subsequently ingested by fish. Local villagers ate the fish and began to exhibit signs of neurologic damage, such as visual loss, extremity numbness, hearing loss, and ataxia. Babies exposed to the methylmercury in utero were the most severely affected. Furthermore, because mercury was also discovered in the breast milk of the mothers, the babies' exposure continued after birth.

Elemental Mercury

- At high concentrations, vapor inhalation produces acute necrotizing bronchitis, pneumonitis, and death may occur at very high dose. Skin, and nose irritation or even burns may occur
- Long term exposure affects CNS.
 - Early: insomnia, impaired memory, anorexia, mild tremor
 - Late: progressive tremor and erethism (red palms, emotional lability (characterized by irritability, excessive shyness, confidence loss, and nervousness),
 - Salivation, excessive sweating, renal toxicity (proteinuria, or nephrotic syndrome)



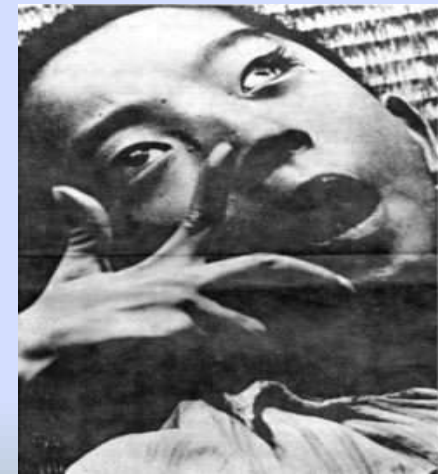
Inorganic Mercury

- Gastrointestinal ulceration or perforation and hemorrhage are rapidly produced, followed by circulatory collapse.
- Breakdown of mucosal barriers leads to increased absorption and distribution to kidneys (proximal tubular necrosis and anurea).
- **Acrodynia** (**Pink disease, erythroedema, or Feer's disease**) usually from dermal exposure
 - The fingertips, toes and nose turn pink, maculopapular rash with pus-filled skin eruptions, swollen and painful extremities with hands and feet turn deep pink with bluish patches, peripheral neuropathy, hypertension, and renal tubular dysfunction.



Organic Mercury

- Toxicity occurs with long term exposure (especially methylmercury, dimethylmercury and ethylmercury) and effects the CNS (**Minamata disease**)
 - Signs progress from paresthesias to ataxia, in hand and feet followed by generalized muscle weakness, narrowing of the field of vision and talking and hearing impairment, tremor and muscle spasticity In extreme cases, paralysis, coma and death follow within weeks of the onset of symptoms.
- Teratogen with large chronic exposure
 - Asymptomatic mothers with severely affected infants
 - Infants appeared normal at birth, but psychomotor retardation, blindness, deafness, and seizures developed over time (**congenital Manimata disease**).



- Mercury binds to sulfhydryl groups and inactivates key enzymes involved in the cellular stress response, protein repair, and oxidative damage prevention.
- Methylmercury also inactivates sodium-potassium adenosine triphosphatase (Na^+/K^+ -ATPase), which leads to membrane depolarization, calcium entry, and eventual cell death. Several pathways may be simultaneously activated converging in apoptosis

Treatment

- Diagnosis is made by history of exposure, physical findings, and an elevated body burden of mercury. Lab analysis of elemental and inorganic mercury can be measured in urine collection (plasma concentration is not useful that mercury's short half-life in the blood); while for organic mercury whole-blood (blood mercury concentrations limit is $< 6 \mu\text{g/L}$) or hair analysis is more reliable than urinary mercury levels.
- The most important and effective treatment is to identify the source and end the exposure

- Gastric lavage is recommended for organic ingestion, especially if the compound is observed on an abdominal radiograph series.
- Activated charcoal is indicated for GI decontamination because it binds inorganic and organic mercury compounds to some extent.
- Whole bowel irrigation may be used until rectal effluent is clear and void of any radiopaque material. However, its effectiveness in decreasing the GI transit time of elemental mercury is doubtful because of the high density of elemental mercury and the low density of the whole bowel irrigant solutions.

- Hemodialysis is used in severe cases of toxicity when renal function has declined. The ability of regular hemodialysis to filter out mercury is limited because of mercury's mode of distribution among erythrocytes and plasma. However, hemodialysis with L-cysteine compound as a chelator has been successful.
- Older literature indicates that neostigmine may help motor function in methylmercury toxicity as this toxicity may lead to acetylcholine deficiency

- Chelating therapy for acute inorganic mercury poisoning can be done with DMSA, DPCN, or BAL. Only DMSA is approved for treating mercury poisoning in children, organic mercury poisoning, and poisoning due to mercury vapor
- Exchange transfusion has been used as a treatment of last resort. Because mercury-chelating agent complexes are large molecules, they may fail to be filtered out by standard hemodialysis membranes, rendering conventional hemodialysis ineffective.
- Because of the high morbidity and mortality rates associated with methyl mercury poisoning, especially in utero, pregnant women and nursing mothers should avoid consuming larger fish, because their mercury concentrations tend to be higher than those in smaller fish.

Arsenic toxicity

- Arsenic and many of its compounds are especially potent poisons.
- Arsenic is the **most common cause of acute heavy metal poisoning** in adults and is **number 1 on the Top Hazardous Substances**.
- Arsenic is released into the environment by the smelting process of copper, zinc, and lead, as well as by the manufacturing of chemicals, galvanization and glasses.
- Arsine gas is a common byproduct produced by the manufacturing of pesticides that contain arsenic.
- Arsenic may also be found in water supplies worldwide, leading to exposure of fishes.
- Other sources are paints, pesticides (herbicides, insecticides, fungicides, rodenticides, wood preservatives), tobacco smoke, and wallpaper paste .
- Target organs are the blood, kidneys, and central nervous, digestive, and keratinized tissues (skin, hair and nails)

Mood of Exposure

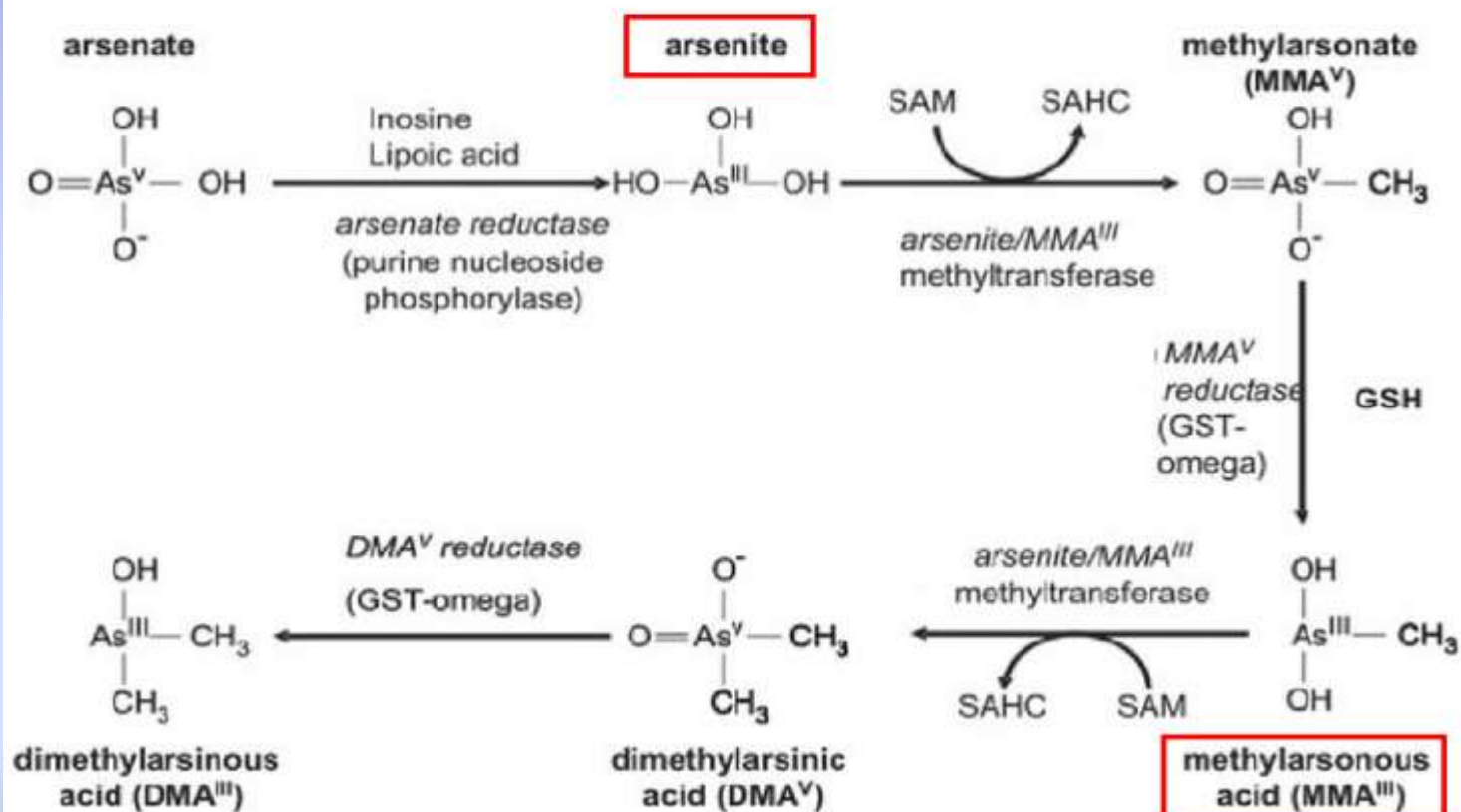
- Arsenic exists in the environment in major three forms, **organic** and **inorganic arsenic compounds** in addition to Arsine gas.
- **Organic arsenic is 500 times less harmful than inorganic arsenic.**
- Organic arsenic exposure can occur by eating food especially seafood.
- Two forms of inorganic arsenic, reduced (trivalent As (III)) and oxidized (pentavalent As(V)) are existed. Unlike the organic form, inorganic arsenic is quite harmful even in minute quantities.
- Inorganic arsenic poisoning can be related to human activities such as mining and smelting but is more often associated with dissolved solids naturally in ground water and soil.

Toxicokinetics

- Many arsenic compounds (especially inorganic arsenic) are readily absorbed through the GI tract when delivered orally in humans
- Absorption within the lungs is dependent upon the size of the arsenic compound, and it is believed that much of the inhaled arsenic is later absorbed through the stomach after (respiratory) mucociliary clearance.
- After the absorption of arsenic compounds, it accumulates in tissues and body fluids.
- The primary areas of distribution are the liver, kidneys, lung, spleen, aorta, and skin. Arsenic compounds are also readily deposited in the hair and nails
- In the liver, the metabolism of organic arsenic involves enzymatic and non-enzymatic methylation, the most frequently excreted metabolite ($\geq 90\%$) in the urine of mammals is dimethylarsinic acid (DMA(V)).

Toxicokinetics

- Inorganic arsenic is reduced nonenzymatically from pentoxide to trioxide, using glutathione (GSH).
- Reduction of arsenic pentoxide to arsenic trioxide increases its toxicity and bioavailability .
- Reduction is followed by series of methylation occurs through methyltransferase enzymes. Resulting metabolites are monomethylarsonous acid (MMA(III)) and dimethylarsinous acid (DMA(III)).
- Methylation had been regarded as a detoxification process. While in fact reduction from As^{+5} to As^{+3} may be considered as a bioactivation and increase toxicity instead.
- Methylation accelerates renal excretion.



Mechanism of action

- As⁺³ :
 - Binds to SH- containing proteins thus reacts with a variety of structural and enzymatic proteins leading to inhibition of their activity (like glutathione reductase and thioredoxin reductase)
 - Inhibit the Krebs cycle (inhibit pyruvate dehydrogenase) and oxidative phosphorylation. These lead to inhibition of ATP production
 - Trivalent arsenic inhibits cellular glucose uptake, gluconeogenesis, fatty acid oxidation,
- As⁺⁵
 - It can replace phosphate in many reactions can replace the stable phosphate ester bond in ATP and produce an arsenic ester stable bond which is not a high energy bond
- Arsenic has very high carcinogenic potential. The mechanisms responsible for this may be inhibition of DNA repair and alterations in the status of DNA. Due to inactivation of DNA-binding proteins, transcription factors and DNA-repair proteins by interaction of arsenic with –SH group.
- Arsenic has irritant effect and has the ability to induce endothelial damage, loss of capillary integrity, and capillary leakage .

- Arsenic trioxide has been shown to cause a significant prolongation of cardiac action potential duration at many levels of repolarization producing conduction delay and increased triangulation.
- It also has been associated with inducing/accelerating atherosclerosis, increasing platelet aggregation and reducing fibrinolysis

Symptoms of toxicity:

Acute toxicity:

- Acute exposure to arsenic compounds can cause nausea, anorexia, vomiting (hematemesis), abdominal pain, muscle cramps, diarrhea (rice-water stool), Garlic-like breath, malaise, thirst and metallic taste, fatigue and burning of the mouth and throat.
- In most severe cases, tachycardia, hypotension acute encephalopathy, acute renal failure, congestive heart failure, stupor, convulsions, paralysis, coma and even death can occur.

Arsenic acute toxicity

- In addition **contact dermatitis**, skin lesions and skin irritation are seen in individuals whom come into direct tactile contact with arsenic compounds.
- Arsine gas exposure manifests with an acute hemolytic anemia and striking chills.

Symptoms of acute arsenic poisoning

Bodily system affected	Symptoms or signs	Time of onset
Systemic	Thirst Hypovolemia, Hypotension	Minutes Minutes to hours
Gastrointestinal	Garlic or metallic taste Burning mucosa Nausea and vomiting Diarrhea Abdominal pain Hematemesis Rice-water stools	Immediate Immediate Minutes Minutes to hours Minutes to hours Minutes to hours Hours
Hematopoietic system	Hemolysis Hematuria Lymphopenia Pancytopenia	Minutes to hours Minutes to hours Several weeks Several weeks
Pulmonary (primarily in inhalational exposures)	Cough Dyspnea Chest Pain Pulmonary edema	Immediate Minutes to hours Minutes to hours Minutes to hours
Liver	Jaundice Fatty degeneration Central necrosis	Days Days Days
Kidneys	Proteinuria Hematuria Acute renal failure	Hours to days Hours to days Hours to days

Arsenic symptoms of Toxicity

Chronic toxicity:

- Repeat exposure to arsenic compounds have been shown to lead to the development of multiple organ dysfunctions problems like
 - **Neuronal** :peripheral neuropathy, encephalopathy, dementia, cognitive impairment, hearing loss
 - **CVS**: peripheral vascular disease, ECG abnormalities, hypertension, myocardial infarction, anemia and leukopenia
 - **Respiratory**: pharyngitis, laryngitis, pulmonary insufficiency
 - **GIT**: severe abdominal cramping and hematoemesis.
 - **kidney and liver damage**
 - **Skin abnormalities**: darkening of the skin and the appearance of small "corns" or "wart" on the palms, soles (palmar keratosis).

Also, whitish lines (Mees lines) that look much like traumatic injuries are found on the fingernails.



Arsenic chronic Toxicity

- **Reproductive system:** higher percentage of spontaneous abortions , lower birth weights and birth defects.
- **Carcinogenic:** cancers of the skin, liver, respiratory tract, kidney, bladder and gastrointestinal tract are well documented in regards to arsenic exposure.

Treatment

- Diagnosis includes determining the clinical signs and the medical and occupational history.
- 1. The main tool in diagnosing and assessing the severity of arsenic poisoning is **laboratory analysis of urinary and whole blood arsenic measurements**. In addition to analysis of arsenic contents in hair and fingernails
- Normal values
 - Spot urine= ~11 mcg/L
 - Whole blood= <1mcg/L (usually is elevated in acute intoxication)

2. Complete blood count.

- As with all heavy metals, microcytic hypochromic anemia is common
- Acute hemolytic anemia is common with arsine exposure.

3. **Serum electrolytes**, including calcium and magnesium: Particularly in patients with severe vomiting and diarrhea

- Hemodynamic stabilization is of primary importance, and large amounts of electrolytes solutions may be required because of significant GI losses (ie, vomiting, diarrhea).
- In the face of acute blood loss, consideration of the use of blood products may be critical in sustaining the life of the victim
- For acute arsenic ingestions, orogastric lavage is recommended if the patient presents rapidly or plain radiography indicates that arsenic is present in the stomach.
- Activated charcoal does not adsorb arsenic appreciably and is not recommended for patients in whom co-ingestants are not suspected.
- Whole bowel irrigation with polyethylene glycol may be effective to prevent GI tract absorption of arsenic.