Heavy Metals Toxicity

Heavy Metals include :

- Arsenic
- Cadmium
- Chromium
- Cobalt
- Lead
- Mercury
- Nickel
- Thallium

Essential metals :

- Iron
- Selenium
- Zinc
- Copper

- Metals are a unique class of toxicants that occur naturally and persist in nature, but their chemical forms may be changed because of physicochemical, and biological activities

- Their toxicity may be markedly altered as these elements assume different chemical forms.

- Most metals are of value to humans because of their varied use in industry, agriculture, or medicine.
- Some are essential elements, required in various biochemical / physiological functions.
- Others may pose health hazards to the public because of their presence in food, water, or air, and to workers engaged in mining, smelting, and a variety of industrial activities.

- The toxicity of heavy metals depends on a number of factors :

1. *The total dose absorbed*
2. *The exposure whether acute or chronic.*
3. *The age of the person*
4. *The route of exposure*
5. *The chemical form of metal*

Chemical forms of heavy metals

- All heavy metals have 3 chemical forms :

1. Elemental state
2. Organic compounds
3. Inorganic compounds

Mechanism of heavy metal toxicity

- Most heavy metals have relatively the same mechanism with many differences :

- They bind to *oxygen, nitrogen, and sulfhydryl groups in proteins, resulting in alterations of enzymatic activity*
- *Displacement of essential metal from their site of activity*
- *Blocking of enzyme synthesis*
- *Specific mechanism of toxicity for each heavy metal*

Biological biomarkers

- The presence of metal in blood and urine indicate a recent exposure
- The level of metals in hair and nail indicate past exposure

Acute vs. chronic heavy metal toxicity

- Acute toxicity :
  - N / V / D and abdominal pain are the hallmark of most acute metal ingestions
  - Encephalopathy
  - Renal problems
  - Cardiac problem

- Chronic toxicity :
  - Involvement of the CNS (children) and PNS (adults)
  - Anemia (basophilic stippling)
  - Mees lines (horizontal hypopigmented lines across all nails)

Specific Metal Toxicity

Lead Toxicity

- Lead has no physiologic role in biological systems
- It interferes with a number of body functions
- Acute toxicity is related to occupational exposure and is quite uncommon.
- Chronic toxicity is much more common
- Pediatric lead poisoning is a problem.

Mechanisms of Toxicity

- Interferes with many enzymes :

- SOD and catalase and bind with GSH lead to ROS generation

- 5 – aminolevulinic acid dehydratase (ALAD) leading to hemoglobin oxidation resulting in red cell hemolysis

- It replaces Ca+2 in many organs especially in the bones

Toxicokinetic

- Bind to RBC
- Has t1/2 about 30 days in blood
- Stored in bone with t1/2 for several decades
- Redistributed from bone to blood
- Excreted by urine and bile
- Organic lead has high lipid solubility penetrating to brain

Toxic effects of lead

Neurological	• In children : behavioral effects, hyperactivity, language delay, lower IQ • PNS toxicity in adults • Convulsion, delirium, and encephalopathy in severe toxicity
Hematological	• Anemia mostly in adults due to impaired synthesis of heme
Renal	• Acute nephropathy manifests with tubular defects, include : phosphaturia, glucosuria and amino aciduria (Fanconi's syndrome) • Chronic lead nephropathy is characterized histologically by chronic interstitial nephritis and is frequently associated with hypertension and gout
Bone	• Lead can interfere with bone development, leading to the formation of lead lines at bone metaphyses • Lead interferes with the conversion of 25-hydroxy vitamin D to 1,25-dihydroxy vitamin D and causes rickets or osteomalacia

Diagnosis

Blood lead level (BLL)	• Symptoms are associated with BLL • Low BLL is asymptomatic (10 – 25 mcg / dL) • Moderate BLL leading to different symptoms (> 25 mcg / dL) • High BLL leading to severe toxicity causing encephalopathy
Blood tests	• Hypochromic microcytic anemia • Basophilic stippling of red blood cells
Bone X – ray	• Metaphyseal lines in long bones

Management of lead toxicity

BLL	Treatment
Less than 10 mcg / dL	Preventive
Less than 20 mcg / dL	Nutritional and educational intervention
More than 20 mcg / dL	Medical evaluation and environmental intervention
Equal to 45 mcg / dL	Chelation therapy by Succimer or D – Penicillamine
More than 50 mcg / dL	For lead encephalopathy a combination of dimercaprol and EDTA or CaNa2 EDTA IV

Mercury Toxicity

Mercury has 3 forms :

1. Elemental mercury
2. Inorganic salts
3. Organic compounds

Toxicokinetics

- The most deadly form of mercury is methyl mercury.
- Only 2-10% of the ingested mercury is absorbed from the gut, and ingested elemental mercury is not absorbed at all
- About 90% of any methyl mercury ingested is absorbed into the bloodstream from the GI tract

Elemental Mercury

- Present as liquid form
- It is easily vaporized
- Poor GI absorption
- Well absorption if inhaled
- Penetrate to RBCs as target and converted to an inorganic divalent or mercuric form by catalase in the erythrocytes.
- Elemental mercury as a vapor has the ability to penetrate the central nervous system (CNS), where it is ionized and trapped, attributing to its significant toxic effects.

Inorganic Mercury

- Occurs in several forms:
  - *Mercurous mercury (Hg1+)*
  - *Mercuric mercury (Hg2+)*
- It is highly toxic and corrosive
- It gains access to the body orally or dermally and is absorbed at a rate of 10% of that ingested.
- Accumulates mostly in the kidney, causing significant renal damage.
- Excretion of inorganic mercury, as with organic mercury, is mostly through feces

Organic Mercury

- Mostly methyl mercury
- Organic mercurials are absorbed more completely from the GI tract than inorganic salts
- Methyl mercury is readily absorbed in the GI tract (90-95%) and remain stable in its initial forms.
- Methyl mercury has high lipid solubility and is distributed uniformly throughout the body, accumulating in the brain, kidney, liver, hair, and skin.
- It crosses the blood – brain barrier and placenta and penetrate erythrocytes, producing neurologic symptoms, teratogenic effects

Mechanism of toxicity

1. *Covalent binding to sulfur,* replacing the hydrogen ion in the body's sulfhydryl groups.
2. Reacts with *phosphoryl, carboxyl, and amide groups,* resulting in widespread dysfunction of enzymes, transport mechanisms, membranes, and structural proteins.
3. Necrosis of the GI mucosa and proximal renal tubules which occurs shortly after mercury salt poisoning, is thought to result from *direct oxidative effect of mercuric ions.*

SPECIFIC TOXIC EFFECTS OF MERCURY

- *Elemental mercury*

- Symptoms of acute elemental mercury inhalation occur within hours of exposure and consist of *cough, chills, fever, and shortness of breath.*
- GI complaints include nausea, vomiting, and diarrhea accompanied by a metallic taste, dysphagia, salivation, weakness, headaches, and visual disturbances.
- Chest radiography during the acute phase may reveal interstitial pneumonitis and both patchy atelectasis and emphysema.
- Symptoms may resolve or progress to acute lung injury, respiratory failure, and death.
- Thrombocytopenia may also occur during the acute phase.

SPECIFIC TOXIC EFFECTS OF MERCURY

- Inorganic mercury
- The hallmarks of severe acute mercuric salt ingestion :

- Hemorrhagic gastroenteritis
- Massive fluid loss resulting in shock
- Acute tubular necrosis
- Proximal tubular necrosis
- GI symptoms consist of a metallic taste and burning sensation in the mouth, loose teeth and gingivo-stomatitis, hypersalivation (ptyalism), and nausea.
- The neurologic manifestations of chronic inorganic mercurialism include tremor, as well as the syndromes of neurasthenia and erethism.
- An idiosyncratic hypersensitivity to mercury ions is thought to be responsible for acrodynia, or "pink disease," which is an erythematous, edematous and hyperkeratotic induration of the palms, soles, and face, and a pink papular rash

Specific toxic effects of mercury

Organic mercury :

- Methyl mercury produces an almost purely *neurologic disease due to its lipophilic property* and slower elimination, but acute GI symptoms, tremor, respiratory distress, and dermatitis may occur.
- *Electrocardiographic (ECG) abnormalities (ST segment changes) and renal tubular dysfunction* are associated with this poisoning.
- Characteristically, clinical manifestations occur after the initial poisoning *by a latent period of weeks to months.* Consequently, the lethal dose of methyl mercury is difficult to determine.

Arsenic Toxicity

Arsenic and sources of exposure :

- Arsenic considered one of the hazardous metals
- Arsenic is released into the environment by the smelting process of copper, zinc, and lead, as well as by the manufacturing of chemicals
- Arsine gas is a common byproduct produced by the manufacturing of pesticides that contain arsenic.
- 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)*

Arsenic Compounds

- Arsenic exists in the environment in major three forms :

- Organic arsenic compounds
- Inorganic arsenic compounds
- Arsine gas

- Organic arsenic is 500 times less harmful than inorganic arsenic.
- Organic arsenic exposure can occur by eating food especially seafood.

Inorganic arsenic compounds

- Two forms of inorganic arsenic :

- *Reduced (trivalent As (III))*
- *Oxidized (pentavalent As (V))*

Unlike the organic form, inorganic arsenic is quite harmful even in minute quantities

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 mucocillary clearance.
- After the absorption of arsenic compounds, it accumulate 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

TOXICOKINETICS

- Inorganic arsenic is reduced non – enzymatically from pentoxide to trioxide, using glutathione (GSH)
- Reduction of arsenic pentoxide to arsenic trioxide increases its toxicity and bioavailability
- 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 toxicity

- 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
  - Inhibits cellular glucose uptake, gluconeogenesis, fatty acid oxidation
  - Inhibition of DNA repair and alterations in the status of DNA leading to carcinogenic effect.

Mechanism of toxicity

As^{+5}

- It can replace phosphate in many reactions, and can replace the stable phosphate ester bond in ATP and produce an arsenic ester stable bond which is not a high energy bond

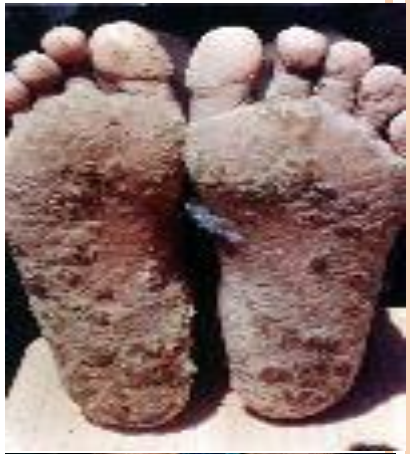
Specific Arsenic toxic effects

- 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
- 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.

Specific arsenic toxic effects

- ***Repeat exposure to arsenic compounds lead to the development of multiple organ dysfunctions problems like neural, cardiac, respiratory, renal and GIT problems***
- ***Specific toxic effects due to repeated exposure include :***

- **Skin abnormalities:** **darkening of the skin and the appearance of small "corns" or "wart" on the palms, soles (palmar keratosis)**



Thallium Toxicity

THALLIUM

- Thallium, a bluish white heavy elemental metal
- Exists in two oxidative states, *+3 (thallic),* and the more common and stable *+1 (thallous)*
- Thallium is present in the environment as a result of natural process and from man – made sources.

TOXICOKINETICS

- Exposures usually occur via one of three routes: *inhalation of dust, ingestion, and absorption through intact skin.*
- Thallium is rapidly absorbed following all routes of exposure. Bioavailability is greatest after ingestion and *exceeds 90%.*
- Volume of distribution about *3.6 L / kg.*
- Thallium can be distributed to all organs, but it is distributed unevenly, with the highest concentrations found in the large and small intestine, liver, kidney, heart, brain, and muscles.

TOXICOKINETICS

- The toxicokinetics of thallium can be described in the following three-phase model:

- *The first phase :* occurs within the 4 hours after exposure during which thallium is distributed to a central compartment and to well perfused peripheral organs such as the kidney, liver, and muscle.
- *The second phase :* which may last between 4 and 48 hours, thallium is distributed into the central nervous system (CNS).
- *The third phase (elimination phase) :* usually begins within 24 hours after ingestion.

- Unlike many other metals, thallium does not have a major anatomic reservoir. For this reason, reported elimination half-lives are as short as 1.7 days in humans with thallium poisoning

Mechanism of toxicity

- Thallium is similar to potassium leading to disruption of potassium – dependent processes
- Riboflavin sequestration
- Interference with cysteine residues
- Ribosomal inhibition
- Myelin sheath injury

Specific thallium toxic effects

- Acute thallium poisoning is primarily characterized by gastrointestinal, neurological, and dermatological symptoms
- Neurologic findings predominate with chronic exposure and tend to progress, even despite decreasing blood thallium levels. These symptoms usually appear 2-5 days post exposure and include :
- Severely painful
- Rapidly progressive
- Ascending peripheral neuropathies.

- *Ocular symptoms:*

- Diplopia, abnormal color vision, and impairment of visual acuity may develop.
- Loss of the lateral half of the eyebrows, skin lesions on the lids, ptosis, seventh nerve palsy, internal and external ophthalmoplegia, and nystagmus.

Management

- Decontamination measures
- Antidote therapy by using *Prussian blue (ion exchanger for univalent cations)*
- *Multiple dose activated charcoal* if Prussian blue is not available
- *Forced diuresis with potassium* loading to enhance thallium elimination

Copper Toxicity

- Metallic copper, although not in itself poisonous, may react in acidic environments to release *copper ions*.
- Local copper ion release is responsible for the occasional case of *dermatitis that occurs after skin exposure* to copper metal.
- Ingestion of large amounts of metallic copper; for example, as coins : *may rarely produce acute copper poisoning*. Poisoning under these circumstances is a result of the release of large amounts of copper ion from copper alloy by the acidic gastric contents.

Copper Toxicity

- Inhalation of finely divided metallic copper dust or bronze powder, which is used in industry and for gilding, may produce life-threatening bronchopulmonary irritation, presumably as a consequence of the local release of ions
- The majority of patients with acute copper poisoning have been exposed to ionic copper. In copper sulfate, also known as cupric sulfate, the copper atom is in the +2 oxidation state.

Mechanism of copper toxicity

- *Redox reactions :* Copper is an active participant in redox reactions. In particular, participation in the *Fenton reaction and Haber-Weiss cycle* which lead to generation of oxidative stress and inhibition of several key metabolic enzymes
- Cupric ion *inhibits sulfhydryl groups* on enzymes in important antioxidant systems, including *glucose-6-phosphate dehydrogenase and glutathione (GSH) reductase* leading to generation of excessive quantities of oxidants, the depletion of GSH augments peroxidative membrane damage of erythrocytes leading to hemolysis

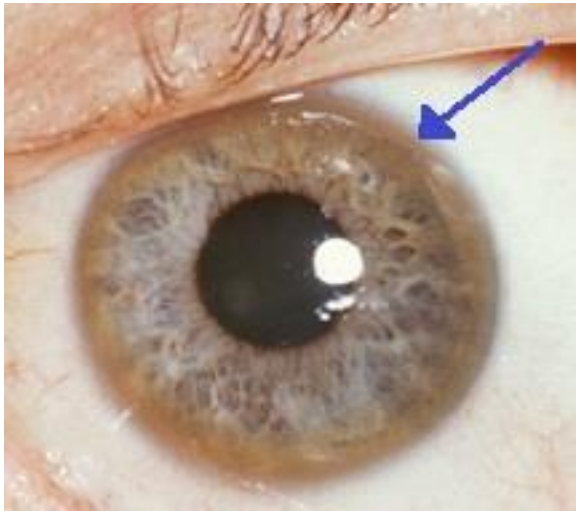
Wilson's Disease

- Is a genetic disorder in which copper builds up in the body.
- Occur due to inhibition of the function of *ATP7B* enzyme in the liver
- ATP7B links copper to *ceruloplasmin* and releases it into the bloodstream, as well as removing excess copper by secreting it into bile
- Copper accumulates in the liver tissue; ceruloplasmin is still secreted, but in a form that lacks copper and is rapidly degraded in the bloodstream

Wilson's Disease

- When the amount of copper in the liver overwhelms the proteins that normally bind it, *it causes oxidative damage through a process known as Fenton reaction;* this damage eventually leads to chronic active hepatitis, fibrosis and cirrhosis.
- The liver also releases copper into the bloodstream that is not bound to ceruloplasmin. This free copper precipitates throughout the body *but particularly in the kidneys, eyes and brain.*

Kayser – Fleischer rings (KF rings)



It is pathognomonic sign occur due to deposition of copper in a ring around the cornea

Cadmium Toxicity

- Cadmium occurs in nature mainly in lead and zinc ores, and is thus released near mines and smelters of these metals.
- Cadmium is used as a pigment (such as in ceramics), in electroplating, and making alloys and alkali storage batteries.
- Most foods contain trace amounts of cadmium. Grains and cereal products usually constitute the main source of cadmium.
- Humans may be exposed to cadmium through cigarette smoking: a pack a day may double the metal intake.

Toxicokinetic of Cadmium

- There is no known biologic role for cadmium. The bioavailability of elemental cadmium is unknown. Orally ingested cadmium salts are poorly bioavailable (5%–20%). However, inhaled cadmium fumes (cadmium oxide) are readily bioavailable (up to 90%).
- After exposure, cadmium is absorbed into the bloodstream, where it is bound to α 2 -macroglobulin and albumin. It is then quickly and preferentially redistributed to the liver and kidney.
- Cadmium enters target organs by three mechanisms:
  - Zinc and calcium transporters
  - Uptake of cadmium–glutathione or cadmium–cysteine complexes by transport proteins
  - Endocytosis of cadmium–protein complexes.

Toxicokinetic of Cadmium

- After incorporation into the liver and kidney, cadmium is complexed with metallothionein, an endogenous thiol – rich protein that is produced in both organs. Metallothionein binds and sequesters cadmium. Slowly, hepatic stores of the cadmium–metallothionein complex (Cd-MT) are released. Circulating Cd-MT is then filtered by the glomerulus.
- A significant amount is reabsorbed and concentrated in proximal tubular cells. This in part explains why the kidney is the principal target organ in cadmium toxicity.
- Cadmium has a large Vd
- The slow release of cadmium from metallothionein – complexed hepatic stores accounts for its very long biologic half-life of 10 or more years.

Mechanism of cadmium toxicity

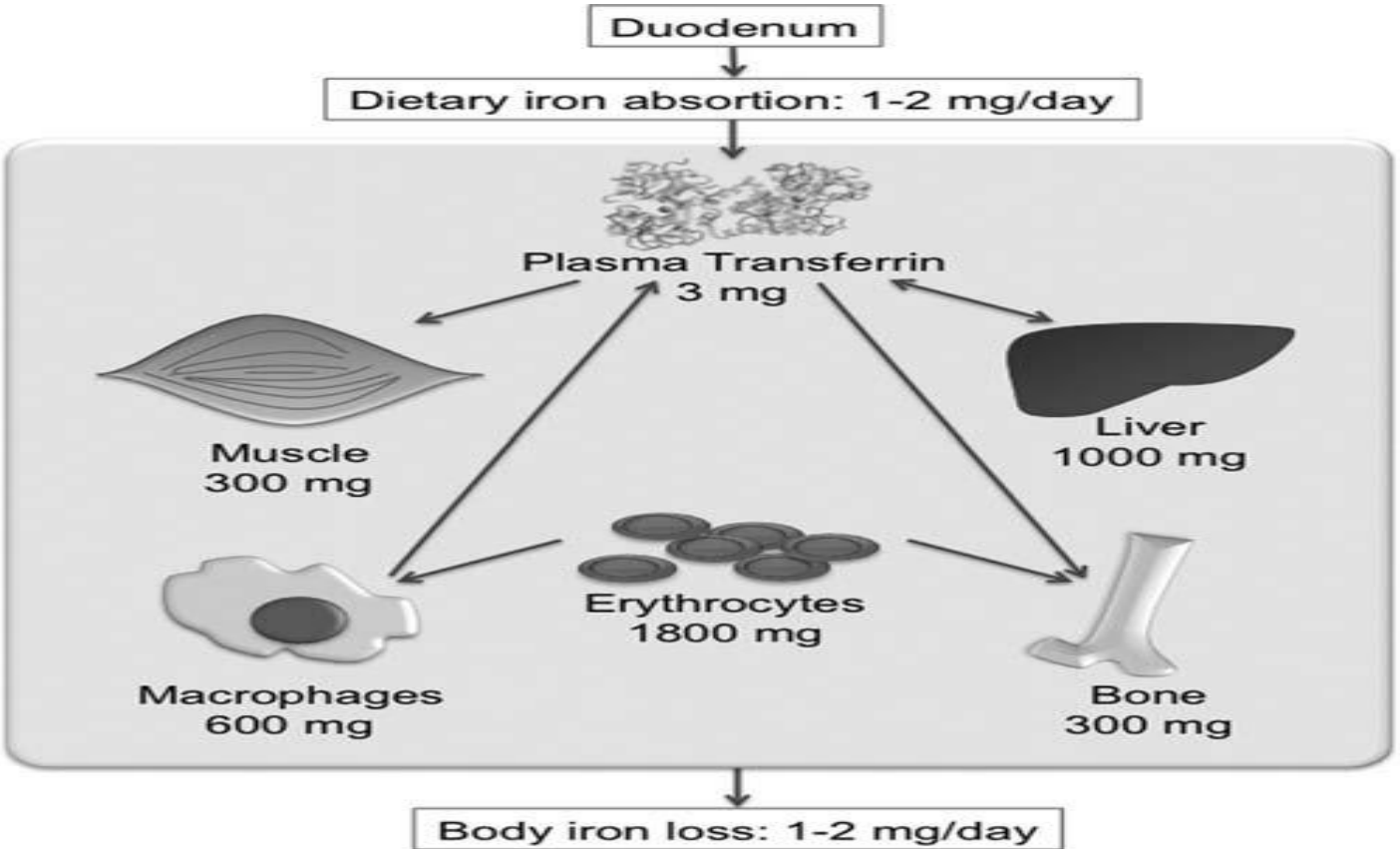
- Cadmium toxicity results from interaction of the free cation with target cells. There are several mechanisms by which cadmium interferes with cellular function :
  - Binds to sulfhydryl groups
  - Denaturing proteins
  - Inactivating enzymes
- The mitochondria are severely affected by this process, which may result in an increased susceptibility to oxidative stress.
- Interference of cadmium with calcium transport mechanisms might lead to *intracellular hypercalcemia* and, ultimately, apoptosis

Specific Cadmium toxic effects

- *The renal damage caused* by cadmium develops over years. Proteinuria is the most common clinical finding, and correlates with proximal tubular dysfunction, which manifests as urinary loss of low – molecular – weight proteins such as β 2 -microglobulin and retinol binding protein. Cadmium also produces hypercalciuria, possibly also via damage to the proximal tubule
- *Cadmium – induced osteomalacia* is a result of abnormalities in calcium and phosphate homeostasis, which, in turn, result from renal proximal tubular dysfunction
- *Acute cadmium pneumonitis* is characterized by infiltrates on chest radiograph and hypoxia

Iron toxicity

IRON DISTRIBUTION WITHIN THE BODY



- Iron preparations are available most commonly in the form of iron salts. The amount of elemental iron in each preparation varies depending upon the salt form

TABLE 1 **Iron Salts and the Percentage of Elemental Iron***

Form of Iron	Elemental Iron (%)
Ferric hydroxide	63
Ferrous carbonate (anhydrous)	48
Ferric phosphate	37
Ferrous sulfate (anhydrous)	37
Ferric chloride	34
Ferrous fumarate	33
Ferric pyrophosphate	30
Ferrous lactate	24
Ferrous sulfate (hydrate)	20
Peptonized iron	17
Ferroglycine sulfate	16
Ferric ammonium citrate	15
Ferrous gluconate	12
Ferrocholinate	12

*Source: References 1-3.

Iron Absorption in Overdose

- Iron absorption is a highly regulated process
- How these processes are affected in overdose is unknown.
- Supra – therapeutic doses of iron are well absorbed after ingestion
- Peak serum iron level is achieved within several hours of ingestion
- It is unclear whether very high doses lead to delayed absorption and peak level; however in many reported cases, children became toxic soon after ingestion.

Mechanism of toxicity

- Iron has the ability to produce oxygen free radicals under aerobic conditions, which turns it into a potential harmful component
- Free radicals are generated within the cell as part of normal cellular mechanisms
- However, the overproduction of reactive oxygen species (ROS), such as superoxide (•O2−) and hydroxyl (•OH) radicals may lead to cellular damage

IRON LEVELS AND TOXICITY

- No clinical signs of toxicity are expected in those ingesting less than *20 mg/kg of elemental iron*
- Those ingesting between *20 and 60 mg/kg* of elemental iron can develop mild clinical signs
- Greater than *60 mg/kg*, serious clinical signs can develop.
- Death from iron toxicity has been reported from a wide range of *doses from 60 to 300 mg/kg.*

Stages Of Acute Iron Toxicity

- *Stage I:* Local gastrointestinal effects
- *Stage II:* Quiescent phase
- *Stage III:* Systemic toxicity
- *Stage IV:* Recovery
- *Stage V:* Gastrointestinal obstruction

Stage I: Gastrointestinal Toxicity

- Nausea, vomiting, and diarrhea *(5 mg Fe+2/kg)*
- Gastrointestinal bleeding may lead to hematemesis or bloody diarrhea
- This is attributed to the direct local corrosive effects of iron
- Occur early, usually within several hours

Stage II: Quiescent phase

- There is *resolution of gastrointestinal* symptoms with apparent clinical improvement
- Patients had resolution of gastrointestinal symptoms, and *became critically ill after 24 hours and died.*
- This stage would rarely be seen today. because children with *significant early gastrointestinal symptoms would receive fluid resuscitation and chelation therapy soon after presentation.*

Stage III: Systemic Toxicity

- Clinically manifest as shock with associated signs *of hypoperfusion (pallor), cold extremities, tachycardia, tachypnea, hypotension (late finding).*
- ***Hypovolemic shock and acidosis*** are the primary determinants of this shock state, but diminished cardiac function contributes.
- *Cardiac problems* can occur in case of severe toxicity
- Hepatic necrosis (high ferritin)

Stage IV: Clinical Recovery

- Begin soon after the initiation of fluid and antidotal therapy.
- For severely poisoned patients recovery will be marked by resolution of acidosis and other signs of shock, *usually within 3 to 4 days of the acute poisoning*
- Full recovery may take longer.

Stage V: Gastrointestinal Obstruction

- Late onset of gastric and pyloric strictures, which may occur 2 to 8 weeks after the initial injury.
- These strictures occur in mucosa in which there was previous damage, and they *frequently require surgical therapy*

LEVELS OF IRON TOXICITY

- Less than *350 mcg/dL* : Minimal toxicity.
- Between *350 and 500 mcg/dL* : Mild to moderate GI symptoms (rarely develop serious complications).
- Greater than *500 mcg/dL* : Serious systemic toxicity.
- Greater than *1000 mcg/dL* : Significant morbidity and mortality

Treatment of Heavy Metal Toxicity

- Removal of the patient from the source of exposure is critical
- *Decontamination :*

  Treatment may include *whole – bowel irrigation with polyethylene glycol electrolyte solution* if radiographic evidence of retained metal is present.
- *Resuscitation:*

  Good supportive care is critical. Ensure airway patency and protection, provide mechanical ventilation where necessary, correct dysrhythmias, replace fluid and electrolytes 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

DIMERCAPROL (BAL)

- 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 hypocalcaemia, use only calcium disodium salt of EDTA for chelation in heavy metal toxicity.

DIMERCAPTOSUCCINIC ACID (DMSA) " SUCCIMER "

- 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.
- It forms soluble complexes with metals that are subsequently excreted in urine.

Deferoxamine (DFOA) " Desferal "

- Used for Iron poisoning and aluminum poisoning.
- It can cause anaphylaxis and hypotension
- *Vin rose urine* occur after administration (pinkish red urine)