

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Heavy Metals Toxicity Irritant poisons

Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge				
Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb
Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	
Rf	Rn	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Nh	Fl	Mc

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Objectives



- Definition of heavy metals
- General characters, mechanisms and treatment.
- Some toxic metals: Arsenic, Lead, Mercury, Cadmium.
- Sources, mechanism of action, diagnosis and treatment.

Types of elements

- Metals
- Non metals
- Metalloids
- **Metals:**
 - Metals differ from other toxic substances because, as elements, they are **neither created nor destroyed** by human endeavors.
 - Metals are certainly one of the oldest toxicants known to humans due to their very early use.

Heavy metals

- Heavy metals are naturally occurring elements that have a **high atomic weight** and a relatively **high density**; at least 5 times greater than that of water.
- Non degradable.
- They are toxic or poisonous at low concentrations.
- Application in various fields have led to their wide distribution in the environment; raising concerns over their potential effects on animal health. Their toxicity depends on several factors including the dose, route of exposure, age, gender, genetics and nutritional status of the exposed individuals.
- Because of their high degree of toxicity Cadmium (Cd), Lead (Pb), Arsenic (As) and Mercury (Hg) rank among the priority metals that are of great health significance. They are all systemic toxicants that induce multiple organ damage even at lower level of exposure.
- They are also classified as **human carcinogens** (known or probable) according to the U.S. EPA, and the International Agency for Research on Cancer.

• Essential heavy metals (trace elements)

- **P**erform physiological and biochemical functions in plants and animals. They are important constituents of many key enzymes and play important roles in various oxidation-reduction reactions.
- Metals such as Cobalt (Co), Copper (Cu), Iron (Fe), Magnesium (Mg), Manganese (Mn), Selenium (Se) and Zinc (Zn), although heavy, are essential nutrients that are required for various biochemical and physiological functions.
- ✓ Inadequate supply of these micro-nutrients results in a variety of **deficiency** diseases or syndromes.
- ✓ **Excess amount** of such metals produce cellular and tissue **damage** leading to a variety of adverse effects.

Heavy metals	
Essential elements (authorized in animal nutrition*)	Non-essential elements (undesirable**)
Co (cobalt)	As (arsenic)
Cr (chromium)	Cd (cadmium)
Cu (copper)	Hg (mercury)
Fe (iron)	Pb (lead)
Mn (manganese)	
Mo (molybdenum)	
Ni (nickel)	
Se (selenium)	
Zn (zinc)	

✓ General characters of irritant poisons

- 1- They have two actions: **local action**:(direct tissue damage)&**Systemic** or remote.
 - 2- They cause **irritation of the mm.** of the **GIT**. Symptoms appeared after latent period, **vomiting**, colic, diarrhea, or constipation in some cases of lead poisoning.
 - 3- The form of toxicity either acute or chronic.
 - 4- Their affinity to combine compounds containing thiol groups (-SH).
 - 5- Urine and feces are the primary routes of excretion for most ingested metals.
 - 6- Metals not affected or destroyed by putrefaction.
- ⑦ Thiosulphates, charcoal and tannic acid is a general antidote for this group.

General Mechanism of action of metals

- Interaction between the metal and **sulfhydryl (SH)** groups on the enzyme, this leads to **inhibition** of these enzymes.
- The metal may **displace** an essential **metal cofactor** of the enzyme. For example, **lead** may displace zinc in the **zinc-dependent enzyme** δ -aminolevulinic acid dehydratase (ALAD), thereby inhibiting the synthesis of heme, an important component of hemoglobin and heme-containing enzymes, such as cytochromes.

- **Mimicry**: Displacement of certain metals essential for cell by similar metal is another cause of toxicity. For example cadmium can substitute for the essential metal zinc in certain protein that requires zinc for their structure or function.
- **lead can substitute for calcium** in bone, and in other sites where calcium is required.
- **Oxidative stress**: Induction of free radical destructive activity. producing oxidative modification of biomolecules such as proteins or DNA. This may be a key step in the **carcinogenicity** of certain metals
- Metals in their **ionic form** can be very reactive and form DNA and protein adducts in biological systems.

General line of treatment of metals

1-Removal and Minimizing Absorption from the Gastrointestinal Tract: (emetics or gastric lavage).

2- Inactivation of the Poison in the Gastrointestinal Tract: egg white or milk will to precipitate the metal in the stomach. Activated charcoal will effectively absorb many poisons.

3- Diuresis: Elimination of the absorbed poison may be promoted by diuresis.

4-General Supportive Therapy.

✓ **5-Treatment by chelating agents:** BAL, Ca EDTA, DMSA, DMPS, D- penicillamin.

1- Arsenic (As)



12 IIB Zn Zinc 65.38	13 Al Aluminium 26.98153	14 Si Silicon 28.0855	15 P Phosphorus 30.97696	16 S Sulfur 32.06	17 Cl Chlorine 35.453	18 Ar Argon 39.948
30 Zn Zinc 65.38	31 Ga Gallium 69.723	32 Ge Germanium 72.63	33 As Arsenic 74.92160	34 Se Selenium 78.96	35 Br Bromine 79.904	36 Kr Krypton 83.798
48 Cd Cadmium 112.411	49 In Indium 114.818	50 Sn Tin 118.710	51 Sb Antimony 121.757	52 Te Tellurium 127.6	53 I Iodine 126.9044	54 Xe Xenon 131.293

- Arsenic (As) is a toxic and carcinogenic **metalloid** (has characteristics between metals and nonmetals).
- The word **arsenic** is from the Persian word **Zarnikh**, as translated to the Greek **arsenikon**, meaning “yelloworpiment” bright yellow.
- - Arsenic has been known as the ***Poison of Kings and the King of Poisons***.
- The major inorganic forms of arsenic include the trivalent arsenite and the pentavalent arsenate.
- - The organic forms are the methylated metabolites.
- **Organic compounds** : are less toxic than trivalent inorganic salts.
- NB: - Trivalent form is more toxic than pentavalent.
- - Inorganic form is more toxic than organic one.

• **Uses:**

- Several arsenic-containing compounds are produced **industrially**, and have been used to manufacture products with agricultural applications such as:
 - insecticides, herbicides, fungicides, algicides, **sheep dips** and wood preservatives.
 - **In veterinary medicine** used for the eradication of **tapeworms** in sheep and cattle.
 - **Thiacetarsamide**, has been used for heartworm (filariasis) **therapy in dogs**.
 - **Yellow arsenic, Arsenic sulphide**; used as insecticide and paints.
- **Fowlers solution**(1% potassium arsenite or sodium arsenite and used as tonic.
- **Arsine gas (AsH₃)** is an industrial gas or product of the charging of storage batteries.

Exposure

- **Accidental** exposure of livestock to old pesticides.
- Arsenic **contaminated soil and water** around mining or smelting sites.
- Contamination of water and herbage by lead or calcium arsenates
- Therapeutic use in dog or following **dipping in sheep**,
- over dosage or extended use of **organic arsenical feed additives** in poultry.
- The ingestion of arsenical **rat poisons**.
- **Burning of wood** products treated with arsenical preservatives.
- **Homicidal**.
- **Inhalation** - arsenic **fumes** and dust from smelting.
- **Animal sensitivity**: Cats may be more sensitive followed by horses, cattle, sheep, swine and birds.

Toxicokinetics

	Absorption	Detoxification	Storage	Excretion
ARSENIC	GIT	Methylation in liver	Liver, kidney, GI, spleen, lung and ✓ <u>keratinized tissues</u> such as <u>hair and hoof</u>	Urine, feces, (Trivalent arsenic is excreted into the intestine via the bile.) sweat and milk (can be toxic to human)

Inorganic trivalent arsenite (As^{III}) is 2–10 times more toxic than pentavalent arsenate (As^V) •

Mechanism of action:

1- It combines with **thiol or sulfhydryl (SH)** groups on proteins, causing inactivation of various enzymes system (As (III) can inactivate over 200 enzymes):



• Reduced oxidative phosphorylation through competitive substitution (mimicry) of arsenate for **inorganic phosphate** in the formation of **adenosine triphosphate** (decreased production of adenosine triphosphate ATP).

2- **Organic arsenical** (e.g. feed additives) produce **demyelination and axonal degeneration due to interference with B vitamins**, which is essential for maintenance of nerve tissues.

3- Arsine gas :

rapidly attacks the red blood cells, producing irreversible cell-membrane damage,

- At low levels, arsine is a potent **hemolysin**, causing dose-dependent intravascular hemolysis lead to **hemolytic anemia** followed by **acute renal failure** (due to precipitation of Hemoglobin in kidneys).
- At high levels, arsine produces direct multisystem cytotoxicity.

✓ 4- In addition, several mechanisms have been proposed for arsenic toxicity and **carcinogenicity**:

- Arsenic and its metabolites have been shown to produce **oxidants and oxidative DNA damage**,
- alteration in DNA methylation status (mechanism that regulates gene expression) and genomic instability,
- impaired DNA damage **repair**, and enhanced cell proliferation





Clinical signs

- A) **Peracute** : may lead to sudden death so rapidly that illness is never observed. When symptoms do manifest themselves they include intense abdominal pain, a staggering gait, collapse, paralysis and death.

B) **Acute arsenic toxicity**: The onset is rapid and signs are usually seen within minutes to hours after acute ingestion.

1- Gastrointestinal (GI) effects: hemorrhagic gastroenteritis with bloody diarrhea as a presenting symptom.

Severe abdominal pain, (nausea, vomiting??), and **bloody rice-water diarrhea**, ataxia and recumbancy.

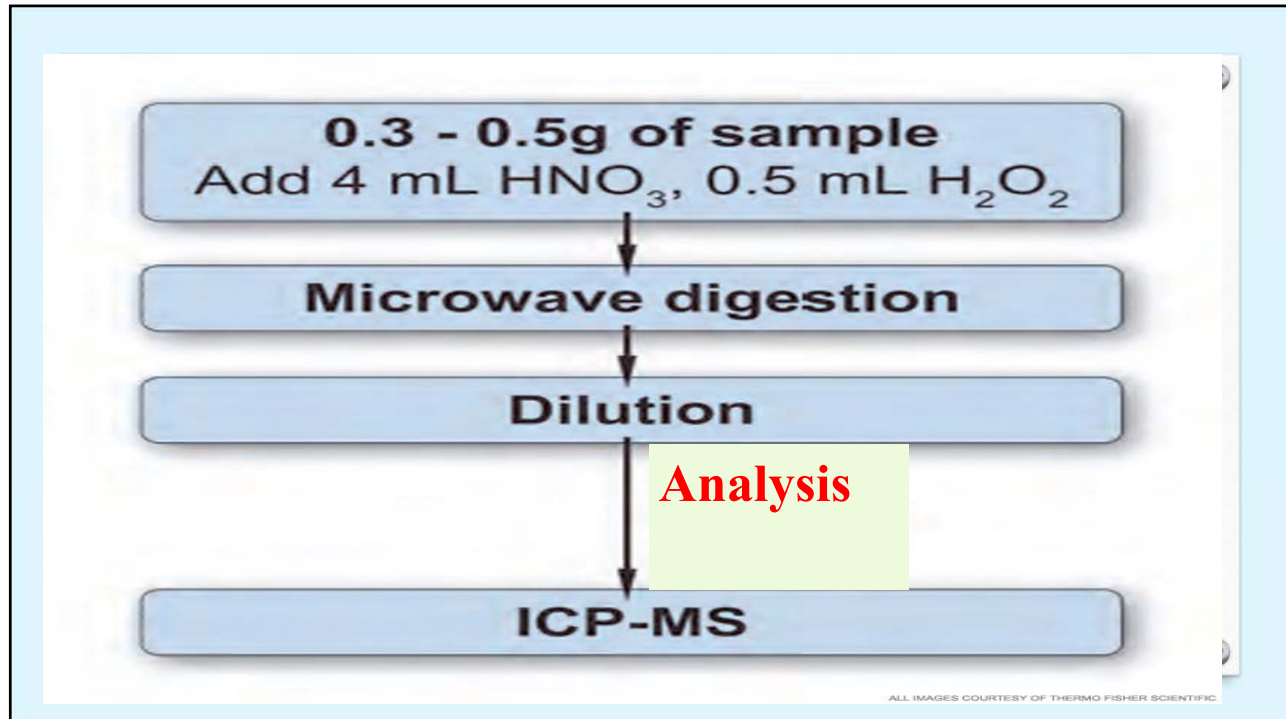
2- Hepatic and renal effects: Toxic hepatitis and elevated liver enzyme levels, hematuria, oliguria, and proteinuria.

- **3- Hematologic effects:** anemia, leukopenia, thrombocytopenia, and disseminated intravascular coagulation.
- **4- Cardiovascular and respiratory effects:** Weak rapid pulse with signs of shock is common, hypotension, ventricular arrhythmia, congestive heart failure, and pulmonary edema and garlic odor on the breath.
- **5- Neurologic effects:** weakness, lethargy, delirium, encephalopathy, convulsions, coma and sensorimotor peripheral neuropathy.
- **C) Chronic toxicity:** Chronic cases are rare and characterized by wasting, poor condition, thirst, skin changes, anemia, neuropathy and hepatotoxicity within a few weeks to months. Arsenic is a known carcinogen. Chronic arsenic dust inhalation may be accompanied by upper respiratory symptoms.
- Skin affection in human: hyperpigmentation and keratosis
- **Organic arsenical toxicity in birds:** Organic arsenicals are marketed as feed additives for turkeys and chickens. Accidental overdoses can occur. **Clinical signs includes;** ataxia, diarrhea, dullness, increased mortality in flocks of birds, lack of growth or weight gain, neck weakness, paresis and paralysis of the legs in birds.

Diagnosis

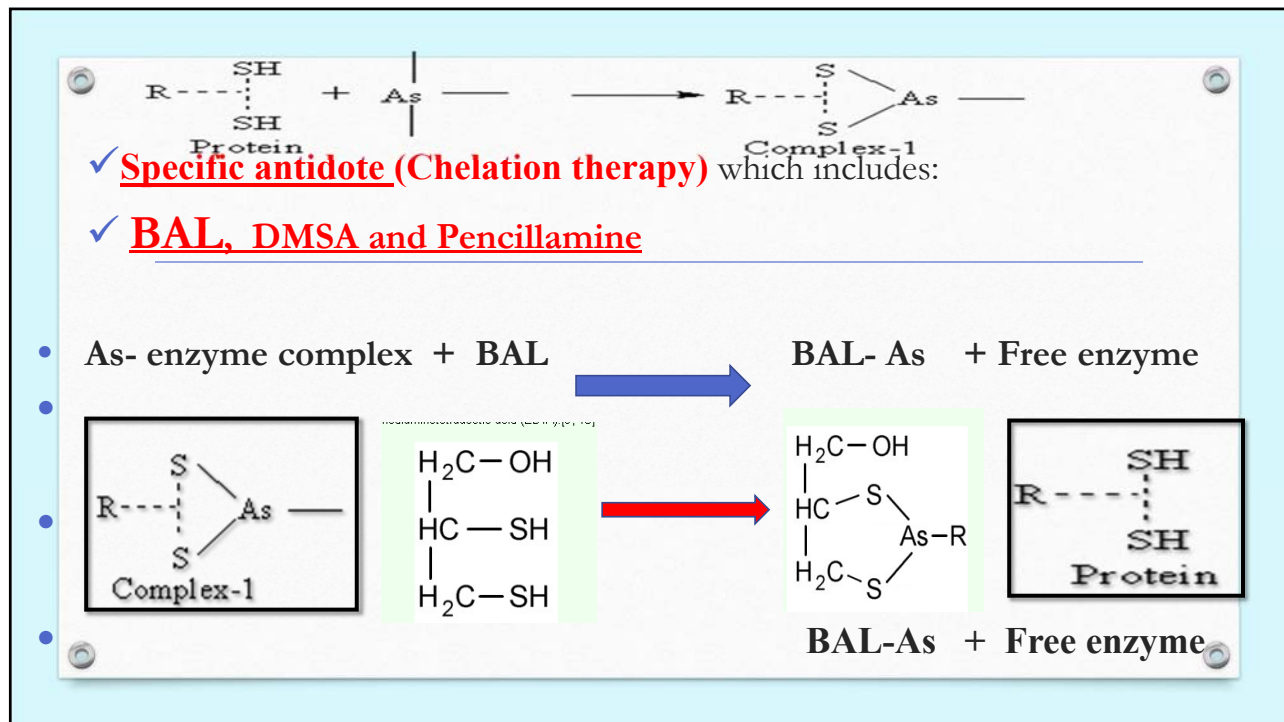
- **1- Case history**
- **2- Clinical signs** (sudden onset with severe gastroenteritis)
- **3- PM lesions:** In all species:-Severe hemorrhagic gastritis, enteritis, extensive inflammation and necrosis of the mucosa and submucosa of the stomach and intestine. Diffuse inflammation of the liver and kidneys .
- **4- Chemical analysis :** Urine, blood, stomach contents or tissues for detection of arsenic by using atomic absorption spectrophotometer (AAS) or ICPE





Treatment

- In severe poisoning by inorganic arsenic compounds, once the first symptoms have occurred, The treatment of animals is **hopeless** and has no economic justification.
- In less severe cases, where most of the poison has not been absorbed, the following therapeutic procedure may be followed:-
 - **Emetics (in animals have the ability to vomit), activated charcoal or gastric lavage** may be employed if ingestion is recent.
 - In large animals, **sodium thiosulphate** may be used orally or IV
 - 20-30g orally in about 300 ml water and 8-10 g, 10-20% sol. IV).
 - Small ruminants should be given 1/4 of the mentioned dose.



- **Magnesium oxide and magnesium hydroxide** can be used as antidote to produce insoluble arsenate.
- **Supportive therapy: fluid, electrolyte replacement, blood pressure support** (dopamine)
- **Thioctic acid (lipoic acid)** alone at a dosage 50 mg/Kg as a 20% sol. IM, 3 times a day or in combination with BAL.
- For **organic arsenical** compounds, there is **no specific treatment** or antidote but supportive therapy can be used.

Antimony (Sb): Sb (from Latin: stibium)

- Antimony (Sb) is a **metalloid** that belongs to the same periodic group as arsenic.
 - **Antimony compounds are chemically, pharmacologically and toxicologically similar to arsenic compounds**
 - **Mechanisms: Inhibition of SH-group containing enzymes and substrate**
- .Diagnosis and Symptoms - same as for Arsenic**

Mercury (Hg), quick silver

- The symbol Hg was derived from the Latinized Greek *hydrargyrum*, meaning “water” and “silver.”
- metallic mercury is in liquid state at room temperature.
- **Forms of mercury:**
 - Elemental mercury** e.g. mercury vapor, mercury metal Hg^0 in thermometers.
 - Inorganic mercury** such as mercuric (divalent) chloride and oxide, etc. (Hg^+ mercurous, Hg_2Cl_2 ; Hg^{2+} , mercuric; HgS , $HgCl_2$). Mercuric salts are more toxic than mercurous (monovalent) salts.
 - Organic mercury** salts; Includes alkyl forms such as ethyl, methyl, propyl, dimethyl, etc., used as fungicides and aryl forms of mercury, such as phenyl mercuric acetate.



• The 1971 Iraq poison grain disaster :

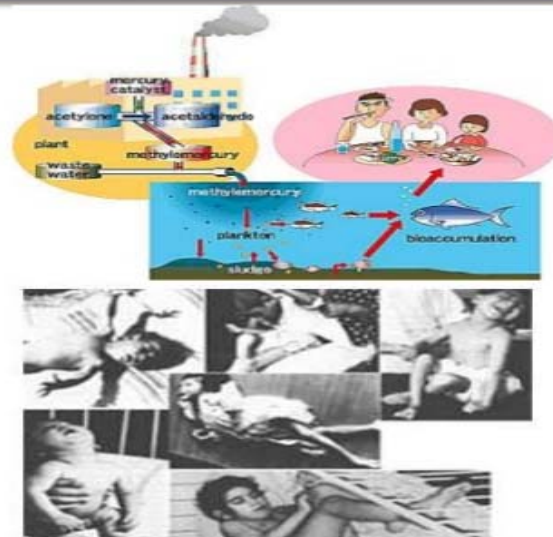
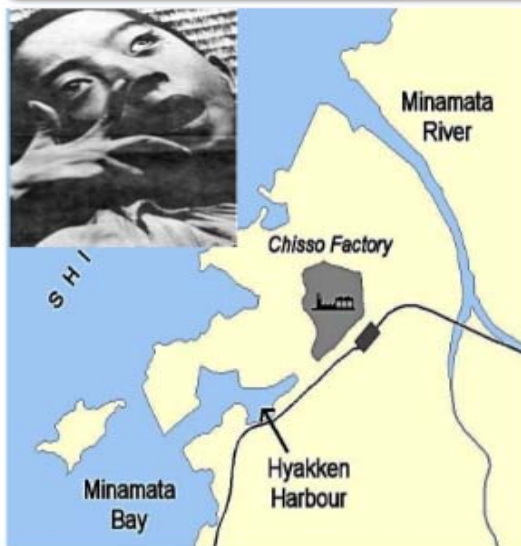
- It was a **mass methylmercury poisoning** incident that began in late 1971. Grains treated with a **methylmercury** fungicide and never intended for human consumption was imported into **Iraq** as seed grain from Mexico and the United States.

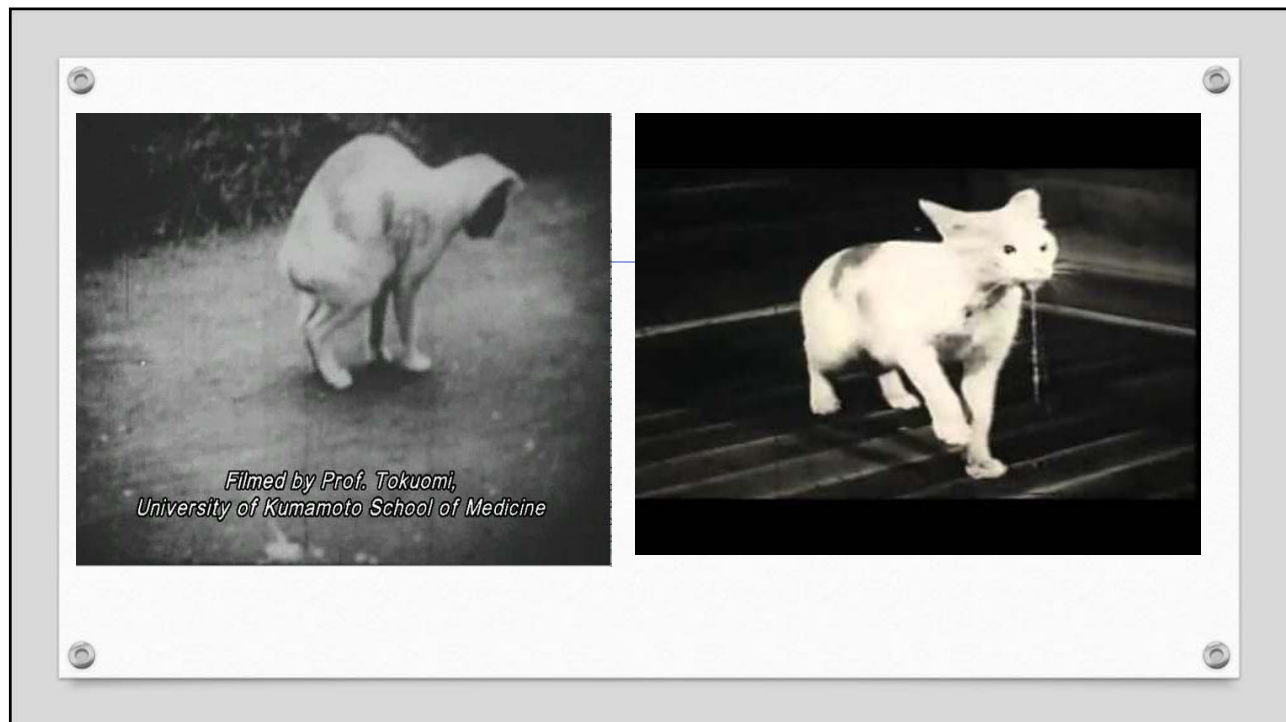


- **Minamata disease** (1956) and Niigata (1965), was a **neurological syndrome** described in humans, birds, and **cats** that were exposed to methylmercury-contaminated fish in the **Minamata** area of Japan. The animal effects were severe enough in cats that they came to be named as having "**dancing cat fever**".



Minamata (1953--60) & Niigata(1964--65) disease in Japan





Sources of exposure:

**Broken thermometers,
mercurial diuretics,
algaecides,
antiseptics,
fungicides,
germicides,
industrial waste,
insecticides,
mercurochrome,**

**paints,
ointment,
seafood's (especially tuna and
swordfish),
sewage disposal,
tattooing,
water (contaminated),
wood preservatives.**

Toxicokinetics

Absorption	Distribution	Storage	Excretion	
			Inorgani	Organic
Metallic: low Inorganic: poor Organic: via all routes including dermal .It readily penetrates the placenta. Vapor: quick	These compounds initially bind to erythrocytes, become distributed throughout body, and eventually bioaccumulate primarily in brain and to some extent in kidney and muscles.	Inorganic:- primarily in:- Kidney, Liver, Muscles, Hair . Methyl mercury: primarily in:- Brain, Kidney, Muscles, Hair .	primarily via the urine Excretion of mercury is slow, the half-life being 70 days.	Bile, Feces, less than 10% appears in the urine, Eggs (Methyl mercury is the principle tissue residue form in eggs , regardless of the mercury compound ingested by a bird.)

Mechanism of action:

- Inorganic mercurials combine with **sulphydryl (SH-)** or disulphide groups thereby causing interference with the functioning of glutathione.
- Hg vapor readily diffuses across the alveolar membrane and is lipid soluble, so that it has affinity for RBC and CNS.
- **Organic alkyl mercurials (methyl mercury)** target the **brain**. Mercury may irreversibly inhibit voltage-gated K^+ channels in the early developing nervous system. This may help explain **neurologic teratogenicity**.

Clinical Signs:

- Onset is usually after a period of several days or longer.
- Acute signs: corrosive effects on the GI mucosa with resultant vomiting, diarrhea, colic, and fluid and electrolyte loss. Also neurologic, GI, renal and dermal effects.
- **In birds** it reduced hatchability and birds producing eggs without shells.
- **in cattle:**
 - 1)- Weakness, anorexia, emaciation, prostration, stomatitis, salivation, loose teeth, gastroenteritis.
 - 2)- Nasal discharge, bronchopneumonia, dyspnea.
 - 3)- Dermatitis, pustules, skin ulceration, depilation, hyperkeratinization.

- 4)- CNS depression, ataxia, stumbling, hyperesthesia, convulsions.
- 5)- Hematuria, bloody feces, non regenerative anemia.
- 6)- High fever, hemorrhage.
- 7)- Low total protein, low globulin, proteinuria.

All give poor prognosis.

Diagnosis:

- Case history, - clinical signs and
- postmortem lesions,
- confirmation of Hg poisoning may set upon the **detection of Hg by chemical** analysis.
- Kidney (especially cortex) Hg usually 10 - 15 ppm or more, liver, stomach contents, blood, urine and suspected feed.

Treatment

- Treatment of acute oral exposures includes:
 - 1- Gastric lavage and administration of proteinaceous liquids (milk, **egg white**, etc.) are recommended as first aid.
 - ✓ (Egg white PPT mercury as mercury albuminate).
 - 2- **Activated charcoal** and saline cathartic or sorbitol.
 - 3- **Sodium thiosulfate** orally also safe to bind Hg.
 - 4- **Leishka solution:**
 - 500 ml skim milk-
 - 50gm glucose –
 - 20 gm sod. bicarbonate –
 - three egg white and
 - boiled barley water

- ✓ **5- Chelation therapy:**
 - With inorganic mercurials, DMSA > BAL > DMPS at increasing urinary excretion.
 - D-penicillamine orally, but only after gut is free of significant ingested mercury and only if renal function is present, otherwise is dangerous.
 - BAL
 - DMSA and DMPS are less toxic and have greater water solubility than BAL but have limited lipid solubility.
 - They are effective when given orally.
 - DMSA (Di Mercapto Succinic Acid) is preferred.

Lead: Pb (from the Latin plumbum)



- In veterinary medicine, lead is one of the most common causes of metallic poisoning in dogs and cattle.
- Lead is widely used for commercial purposes in the past and is persisted in the environment.
- **Chemical compounds:**
 - 1- Metallic lead.
 - 2- Lead oxides, sulphides.
 - 3- Lead tetroxide (red lead).
 - 4- Lead carbonate (white lead).
 - 5- Lead arsenate, garden sprays
 - 6- Tetraethyl lead found in leaded petroleum products.

Sources of lead

- Lead objects such as batteries, fish sinker, shot
- Farm machinery and automotive supplies;
- Lubricants (grease, motor oils), lead plates in automotive batteries.
- Industrial: motor and vehicle emissions, lead mine, sewage sludge, smelters, white paint, glass manufacture, pottery, brass and bronze
- Pesticides: e.g. lead arsenate.



Commonly used in industry for:

- **Plumbing** (lead water pipes)
- Printing - Painting
- Pottery - Projectiles
- Batteries

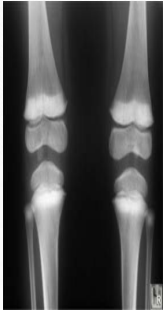


- In the past, lead salts were used as coloring agents in various foods.
- Soundproofing in industry building.
- **Exposure:**
- **Licking or chewing** on batteries and peeling paint or lead contaminated dust.
- **Vegetation grown** in lead smelter areas.
- **Feeding on crops sprayed with lead insecticides.**
- **Waterfowl ingest lead shot**, mud in lacks or marshes.

Toxicokinetics

- Lead absorption can be enhanced by low dietary **iron and calcium**,
-
- Lead in **blood** is primarily (99%) in erythrocytes bound to **hemoglobin**, only 1% of circulating lead in serum is available for tissue distribution
 - Lead is initially distributed to soft tissues such as kidney and liver, and then redistributed to **skeleton** and **hair**.

Toxicokinetics

	Absorption	Detoxification	Storage	Excretion
Lead	<p>Oral: slow and incomplete</p> <p>Enhanced by:-</p> <ul style="list-style-type: none"> -acidic diets, -diets deficient in calcium, zinc or protein 	<p>Deposition in bone</p> 	<ul style="list-style-type: none"> -In Soft tissues as diphosphate or triphosphate -In active bone growth (epiphysis). 	<ul style="list-style-type: none"> -By active transport in bile where it is reabsorbed -In milk by 5% ratio from blood

Toxicity

- The toxic effects range from **inhibition of enzymes** to the production of severe pathology or death.
- Effects on the **nervous system**
- Other target tissues include the gastrointestinal, immune, skeletal and reproductive systems.
- Effects on the **heme biosynthesis**.

Mechanism of action

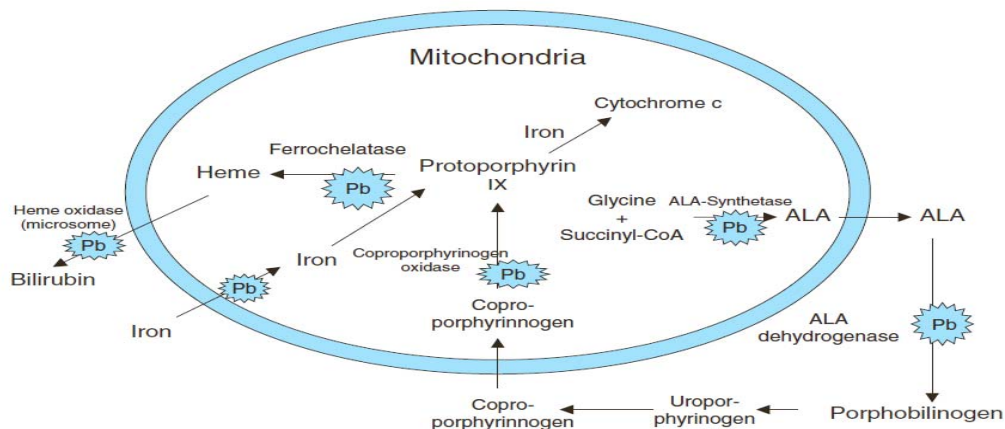
- Bind with **SH-containing enzymes**
- Compete with or **replace Ca and Zn** in some enzymes
- Crosses the placenta** and accumulates in the fetus → developmental defects
→ abortion or stillbirth

✓ Inhibition of key enzymes in heme synthesis :

1- Inhibition of delta-aminolevulinic acid dehydratase (ALA-D), → **Elevated δ -aminolevulinic acid (ALA)** in serum & urine

2- Inhibition of ferrochelatase: Results in increases in **Ferrochelatase** in serum and Accumulation of **protoporphyrin IX** in RBCs.

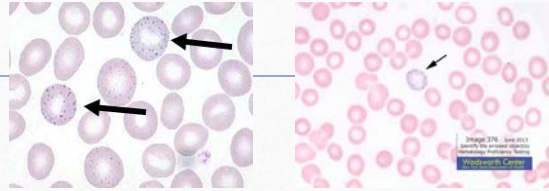
Heme synthesis



Lead has multiple hematologic effects, ranging from increased urinary porphyrins, coproporphyrins, δ -aminolevulinic acid (ALA), and zinc-protoporphyrin to anemia. Microcytic and hypochromic anemia, as in iron deficiency.

✓ **Lead** causes retention of nucleic acid fragments and ribosomes which results in **basophilic stippling** (is the presence of numerous basophilic granules that are dispersed through the cytoplasm of erythrocytes in a peripheral blood smear)

- and increase **fragility of RBCs**.

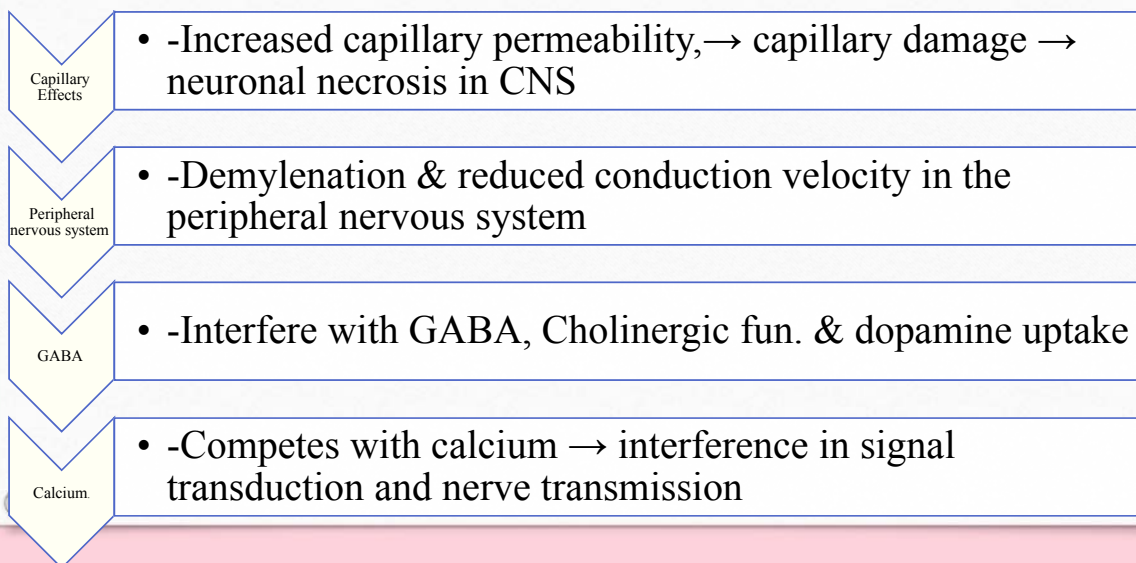


- **Bone Effects:**

- Lead has an extremely long half-life in bone,
- Lead can affect bone by interfering with metabolic and homeostatic mechanisms including parathyroid hormone, calcitonin, vitamin D, and other hormones that influence calcium metabolism
- Lead substitutes for calcium in bone.

✓ **Lead can affect nearly every organ and system in the body.**

Neurologic effects



Toxicity:

- **Acute toxicity:** Rare; nonspecific; related to GI inflammation.

✓- **Chronic Toxicity (Plumbism):**

characterised by several toxic effects including:

1- Gastrointestinal:

Abdominal pain, anorexia, vomiting, severe abdominal cramping (lead colic), constipation, **Dark gray-blue lines** (Burton's line) of **lead sulfide** in the **gums**






2- Hematologic – Anemia, **basophilic stippling**.


3- CNS – neurobehavioral abnormalities, **encephalopathy**

characterized by: seizures, tremors, blindness and depression.




Lead	GIT	Bone	Neurologic
Clinical Signs In cattle Acute	More common in calves Sudden death of some animals,		Blindness, head pressing, stiffness, champing, staggering, rolling of eyes, excitability, tonic-clonic convulsions, opisthotonus, muscle tremor especially head and neck
Subacute	More common in adult. Abdominal pain, ruminal atony, constipation .		Blindness, dullness, inappetence, incoordination, circling, muscle tremors,
Horses	Not common Anorexia, mild to moderate colic,	Epiphysial enlargement (lead line). 	Blindness, head pressing, knuckling of fetlocks, roaring, pharyngeal paralysis, regurgitation through nostrils, paralysis, convulsions.
Dogs	Vomiting, anorexia, colic, constipation appear early, abdominal pain Mild anemia, basophilic stippling, nucleated RBCs, elevated zinc protoporphyrin.		Range from depression and inactivity to hysteria, barking, seizures and behavioral changes.
Cats	Colic and vomiting		Depression, seizures and hysteria are rare
Birds	In some cases anemia, emaciated, green diarrhea .		Derangement such as ataxia, depression, paralysis of wings or convulsions.

LEAD POISONING: CLINICAL SIGNS



Cattle : show head pressing behaviour.



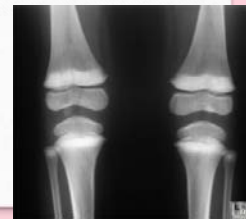
Cattle: advanced stages of lead poisoning, become frenzied, bellow, stagger and crash into obstacles

- Gastrointestinal signs include colic, constipation for several days followed by diarrhoea.
- Abortion (mid or late gestation), opisthotonos, salivation, lacrimation and paralysis may also be observed.
- Death may occur within several hours or days. *(O.M.Radostits et al. 10th Ed.)*

Lead PM	GIT	Bone	Neurologic
Lesions	Gastroenteritis, solid black feces of offensive odour -Renal tubular degeneration & necrosis	Epiphyseal enlargement (lead line) Metaphyseal sclerosis	-Cerebral cortical necrosis and poliomalacia -Neuronal necrosis and hyaline changes in arterioles
Diagnosis	<p>-In acute cases may have no specific lesions.</p> <p>-In subacute toxicity, gastroenteritis, brain edema - cerebrocortical softening, yellow discoloration, cavitations are the main characteristic lesions in brain.</p> <p>-In chronic toxicity cattle may have pale musculature.</p> <p>Lead objects, paint chips, or motor oil may be visible in the GIT</p>		

Diagnosis

- Case history
- Clinical signs
- **Laboratory diagnosis:**
- **A) Blood analysis:**
 - The blood **lead level** is elevated in all affected species (more than 0.4 ppm).
 - **Plasma porphyrins** are fluorescence under UV light are characteristic in cattle.
 - Blood **zinc protoporphrin** level is increased.
- **B) Hematology:**
 - blood smears for nucleated erythrocytes and/or **basophilic stippling**
- **C) Urine analysis :** - ALA (δ -aminolevulinic acid).
- **D) Radiography: X rays,** Presence of **metaphyseal sclerosis** as a result of chronic lead exposure especially in puppies and foals.

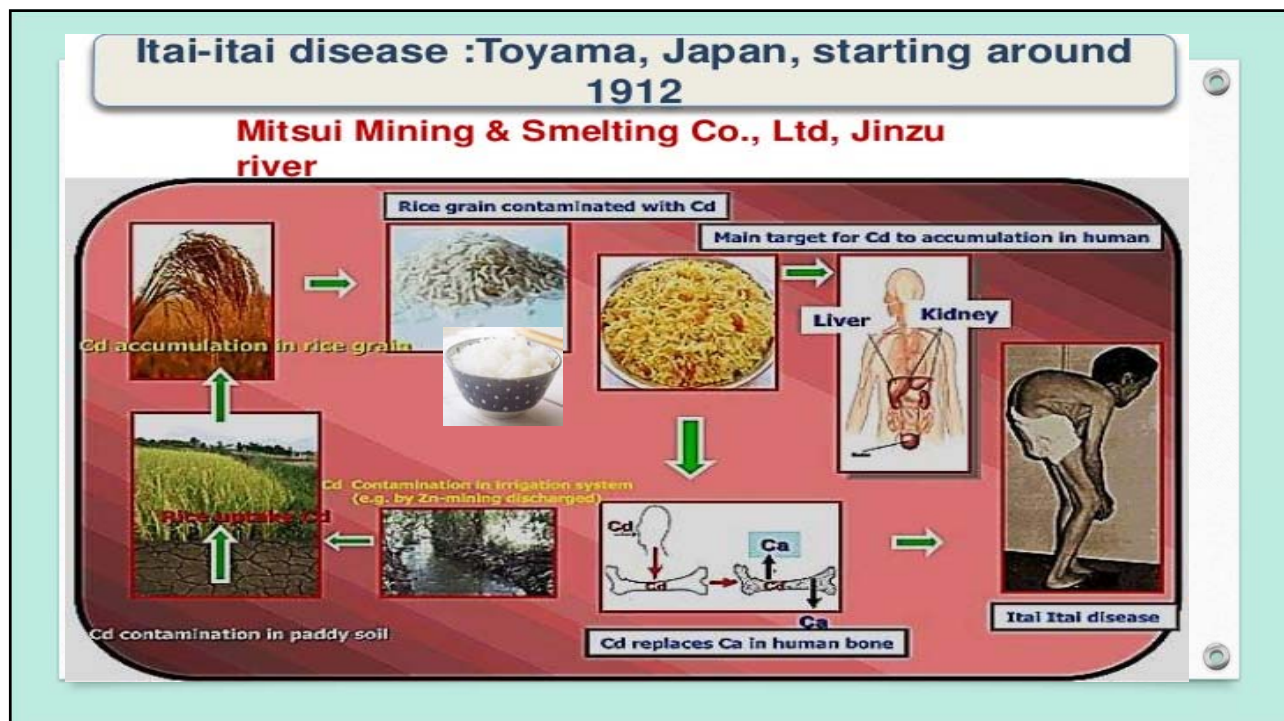


Treatment:

- 1- Prevent further exposure.
- 2- Decontamination of the GIT:
 - A- Saline cathartic, sodium sulfate or magnesium sulfate
 - B- Gastric lavage
- **3- Chelation therapy:**
 - ✓ **Ca disodium EDTA.**
 - BAL
 - DMSA.
 - Penicillamine: It is contraindicated when lead is still present in the gastrointestinal tract.

Cadmium (Cd)

- Cadmium (Cd) is a toxic transition metal, (the Latin name is *cadmia*).
- **Sources of Cadmium**
 - Cadmium is used as an electrode in “nickel” batteries.
 - Cadmium is used as a pigment in paints (yellow color).
 - It is also used in photovoltaic devices and in TV screens.
 - **Cigarette smoking** is a major nonoccupational source of cadmium exposure
 - Fertilizers and pesticides.
 - Food is the major source of cadmium for the general population (Cereal grains such as rice and wheat, and Shellfish)



Toxicokinetics

- Cadmium absorption can be increased by dietary deficiencies of calcium or iron and by diets low in protein.
- Once absorbed, cadmium is very poorly excreted,
- It is rapidly taken up by tissues and is primarily **deposited** in the liver and to a lesser extent in the kidney.
- In the liver, kidney, and other tissues, cadmium induces the synthesis of **metallothionein** (MT), a low-molecular-weight, high affinity metal-binding protein.
- Cadmium– MT may be released from the liver and transported via blood to the kidney, where it is reabsorbed and degraded in the lysosomes of the renal tubules. This releases cadmium to induce more cadmium–MT complex or cause renal toxicity.

Toxic effects:

- **Renal effect:** renal damage, proteinuria, calcium loss and tubular lesion.
- **Skeletal Effects:** The long-term consumption of cadmium contaminated rice caused *Itai-Itai* disease characterized by severe **osteomalacia** (bone softness) and osteoporosis, resulting in bone deformities and concomitant renal dysfunction.
- Cadmium affects calcium metabolism, through renal dysfunction, and excess excretion of
- calcium often occurs in the urine. The skeletal changes are probably related to calcium loss and interference with the actions of parathyroid hormone and vitamin D.
- Cadmium may also act directly on bone

Treatment:

- Immediate gastric wash
- **Chelation therapy:**

 - 1- **DTPA (Diethylen triamine penta acetic acid)**
 - 2- Penicillamine and sulfur containing compounds not used because it increase Cd conc. in the kidneys causing **nephrotoxicity**.
 - 3- **BAL, is contraindicated**, BAL-Cd complex is nephrotoxic.
- Symptomatic treatment.
- Ca, Fe, Zn, Se decrease Cd absorption.

Flourine

- **Exposure:**

- The widespread prevalence of fluorine in the soil, water and rock results in the presence of fluorides in **drinking water** and vegetation.
- Fluorides are emitted from **industries** involved in the manufacture of aluminum, steel, phosphate fertilizer etc



Toxicokinetics:

Absorption	Storage	Excretion
GIT	Bone and teeth. Soft tissues, kidneys contain the greatest concentrations	Primarily in the urine

Toxicity:

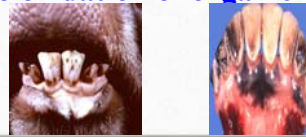
Acute: is rare , **Gastro-enteritis**, hypocalcemia, convulsions and weakness

Chronic, fluorosis (Osteomalacia): Developing teeth : Mottling, staining, pitting, hypoplasia, chalky, wearing of deciduous teeth.

Mature teeth : brown or black discoloration due to oxidation of organic materials in areas where the enamel is defective.

- **Lameness**, hemorrhage and anemia.

No specific treatment.



Thank you

