LEAD POISONING

By

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INTRODUCTION

- Lead is the commonest metal involved in chronic poisoning.
- It was one of the first metals known to man and has been widely used during the last two thousand years for domestic, industrial, and therapeutic purposes.
- Lead is abundant in soil, being distributed throughout the earth's crust.

SOURCE

- The main use of Pb is in the production of storage batteries and in sheathing electric cables.
- It is also useful as protective shielding from x-rays and radiation from nuclear reactors.
- Certain folk medicines (eg, the Mexican remedies and some Indian Ayurvedic preparations) may contain high amounts of lead salts.

SOURCE

- Lead acetate (sugar of lead) has been used in therapeutics,
- lead carbonate (white lead) is still used in paints,
- lead oxide (litharge) is essential for glazing of pottery and enamel ware, and Tetraethyl lead is mixed with petrol as an antiknock to prevent detonation in internal combustion engines.
- Among cosmetics, lead tetroxide is the most common compound in "Sindoor" and lead sulfide in "Surma"

SUMMARY OF SOME OF THE COMMON SOURCES OF PB:

- Candle with lead-containing wicks
- Ayurvedic medicines
- Paint
- Retained bullets
- Ink
- Automobile storage battery casing; battery repair shops
- Ceramic glazes
- Lead pipes
- Silver jewellery workers
- Renovation/modernisation of old homes.

MECHANISM OF TOXICITY

- Pb toxicity affects virtually all organs and systems of the body

- The proposed mechanism of Pb toxicity involves its ability to inhibit or mimic the action of cations such as calcium, zinc, and iron, and to interfere with vital proteins by binding to sulfhydryl, amine, phosphate, and carboxyl groups.

- Pb increases intracellular levels of Calcium in brain capillaries, neurons, hepatocytes, and arteries that trigger smooth muscle contraction, thereby inducing hypertension

MECHANISM OF TOXICITY

- Pb interferes with **heme biosynthesis** by interfering with ferrochelatase, ALAS (aminolevulinic acid synthetase), and ALAD (aminolevulinic acid dehydrase). Therefore, decreased hemoglobin and anemia results in individuals exposed to excessive Pb

- Lead increases haemolysis as a result of which immature red cells are released into circulation such as **reticulocytes** and **basophilic stippled cells** (the result of aggregation of ribonucleic acid due to inhibition of the enzyme pyrimidine-5-nucleotidase which normally eliminates degraded RNA)

MECHANISM OF TOXICITY

- In the nervous system, Pb substitutes for Ca as a secondary messenger in neurons, blocking voltage-gated Ca channels, inhibiting influx of Ca and subsequent release of neurotransmitter. The result is an inhibition of synaptic transmission.

- Pb inhibits glutamate uptake and glutamate synthetase activity in astroglia, thus inhibiting the regeneration of glutamate, a major excitatory neurotransmitter

- This leads to decreased nerve conduction, increased psychomotor activity, lower IQ, and behavioural/learning disorders.

MECHANISM OF TOXICITY

- Lead also has deleterious effects on the CVS (hypertension and myocarditis), kidney (nephritis), and reproductive organs (infertility).

- In addition, lead can decrease uric acid renal excretion, thereby raising blood urate levels and predisposing to gout

LETHAL DOSE

This is not really relevant to lead since acute poisoning is very rare.

The average lethal dose is said to be 10 gm/70 kg for most lead salts, while it is 100 mg/kg for tetraethyl lead.

- Today the accepted upper level for blood lead (BL) is fixed as 35 mcg/100 ml.
- However there are reports that adverse effects especially on the haematopoietic system can occur at levels as low as 10 mcg/100 ml.

LETHAL DOSE

- Neurobehavioural disorders in children can occur at BL as low as 25 mcg/100 ml.

- Hence, the currently even levels as low as 10 mcg/100 ml as unacceptable, especially in children.

TOXICOKINETICS

Absorption

Lead is absorbed through all portals of entry

- Occupational exposure results mainly from inhalation, while in most other situations the mode of intake is ingestion.
- Tetraethyl lead can be absorbed rapidly through intact skin.
- About 5–15% of ingested lead is absorbed by adults with less than 5% retained.
- Children, however, absorb approximately 50% of ingested lead and retain about 30%.

TOXICOKINETICS

Distribution

- lead is distributed among three compartments: blood, soft tissues and the mineralizing tissues (bones and teeth).
- Lead is distributed to those areas of the skeleton which are growing most rapidly.
- These include the radius, tibia, and femur, which are the most metabolically active
- it is stored in the bones as phosphate and carbonate.

TOXICOKINETICS

- In children about 70% of total body lead is skeletal, while in adults over 95% is in osseous tissues.

- Significant amounts of skeletal lead are released from bone into the blood stream periodically resulting in symptoms of toxicity.

- The conditions favouring this include acidosis, fevers, alcoholic intake, and even exposure to sunlight.

Elimination

- Excreted primarily in the urine (about 65%) and bile (about 35%).

CLINICAL PRESENTATION

Acute poisoning

- This is rare. Many reported cases of acute poisoning may actually be exacerbations of chronic lead poisoning when significant quantities of lead are suddenly released into the bloodstream from bone.

- Symptoms include metallic taste, abdominal pain, constipation or diarrhoea (stools may be blackish due to lead sulfide), vomiting, hyperactivity or lethargy, ataxia, behavioural changes, convulsions, and coma.

CLINICAL PRESENTATION

Chronic Poisoning

- Subacute or chronic exposure is more common than acute poisoning
- Constitutional effects include fatigue, malaise, irritability, anorexia, insomnia, weight loss, decreased libido, arthralgias, and myalgias.
- Hypertension may be associated with lead exposure in susceptible populations
- Gastrointestinal effects include crampy abdominal pain (lead colic), nausea, constipation, or (less commonly) diarrhea.

CLINICAL PRESENTATION

- Central nervous system manifestations range from impaired concentration, headache, diminished visual-motor coordination, and tremor to overt encephalopathy (a life-threatening emergency characterized by agitated delirium or lethargy, ataxia, convulsions, and coma).

- Chronic low-level exposure in infants and children may lead to decreased intelligence and impaired neurobehavioral development, stunted growth, and diminished auditory acuity

- Peripheral motor neuropathy, affecting mainly the upper extremities, can cause severe extensor muscle weakness ("wrist drop")

CLINICAL PRESENTATION

- **Hematologic effects** include normochromic or microcytic anemia, which may be accompanied by basophilic stippling. Hemolysis may occur.

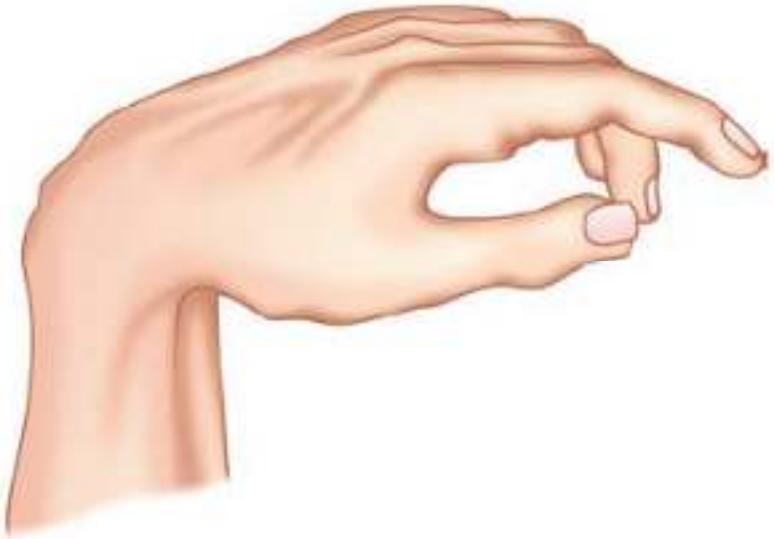
- **Nephrotoxic effects** include reversible acute tubular dysfunction and chronic interstitial fibrosis. Hyperuricemia and gout may occur.

- **Adverse reproductive outcomes** may include diminished or aberrant sperm production, increased rate of miscarriage, preterm delivery, decreased gestational age, low birth weight, and impaired neurologic development.

CHRONIC POISONING CLINICAL PRESENTATION

Mild Toxicity (BL 40 to 60 mcg/100 ml):	Moderate Toxicity (BL 60 to 100 mcg/100 ml) :	Severe Toxicity (BL more than 100 mcg/100 ml) :
Myalgia Paraesthesia Fatigue Irritability Abdominal discomfort	–Arthralgia (especially nocturnal) – Muscular exhaustibility – Tremor – Headache – Diffuse abdominal pain – Anorexia, metallic taste, vomiting – Constipation – Weight loss – Hypertension.	–Lead palsy: wrist drop) or foot drop. – A bluish black lead line on gums (Burton's line) – Lead colic: intermittent severe abdominal cramps. – Lead encephalopathy: It is more common in children and is often associated with organic lead toxicity, especially tetraethyl lead or TEL.

WRIST DROP



CLINICAL PRESENTATION

- TEL is more lipid soluble and is distributed widely in lipophilic tissues such as the brain

- TEL is metabolised to triethyl lead which is the major toxic compound which leads to sudden onset of vomiting, irritability, headache, ataxia, vertigo, convulsions, psychotic manifestations, coma, and death.

- Mortality rate is around 25%. Even if recovery occurs, there is often permanent brain damage manifesting as mental retardation, cerebral palsy, optic neuropathy, hyperkinesis, and periodic convulsions.

DIAGNOSIS

- FEP and Znp levels (>50 mcg/100 ml)—An elevated FEP level indicates impairment of the haeme biosynthetic pathway and may result from lead poisoning or iron deficiency.
- In order to confirm whether it is due to the lead poisoning, the BL must be estimated
- Today ZnP levels are more commonly studied than FEP
- Urine levels of aminolaevulinic acid (ALA) can also serve as a sensitive indicator of lead poisoning.
- Complete blood count and peripheral smear-include low haematocrit and haemoglobin values, peripheral smear may either be normochromic or hypochromic, Basophilic stippling and microcytic.
- Hypochromia and basophilic stippling are strongly suggestive of lead intoxication

DIAGNOSIS

- Blood lead levels reflect recent exposure or exposure over a period of up to 3 to 5 weeks.

- In individuals with high or chronic past exposure, BL usually underrepresents the total body burden because most lead is stored in the bone and may be found at normal levels in the blood.

- The recommended methods of estimating blood lead level (BL) include
  - Atomic absorption spectroscopy (AAS)
  - Electrothermal atomic absorption spectroscopy (EAAS),
  - Anodic stripping voltammetry (ASV)
  - Inductively coupled plasma atomic emission spectroscopy (ICPAES)
  - X-ray fluorescence spectroscopy.
  - Fast neutron activation analysis (FNAA)
  - Mass spectrometry (MS), and microwave plasma detection

DIAGNOSIS

- EAAS and ASV are the methods of choice.

- In recent years, ICP-AES has become the technique of choice owing to superior specificity and sensitivity

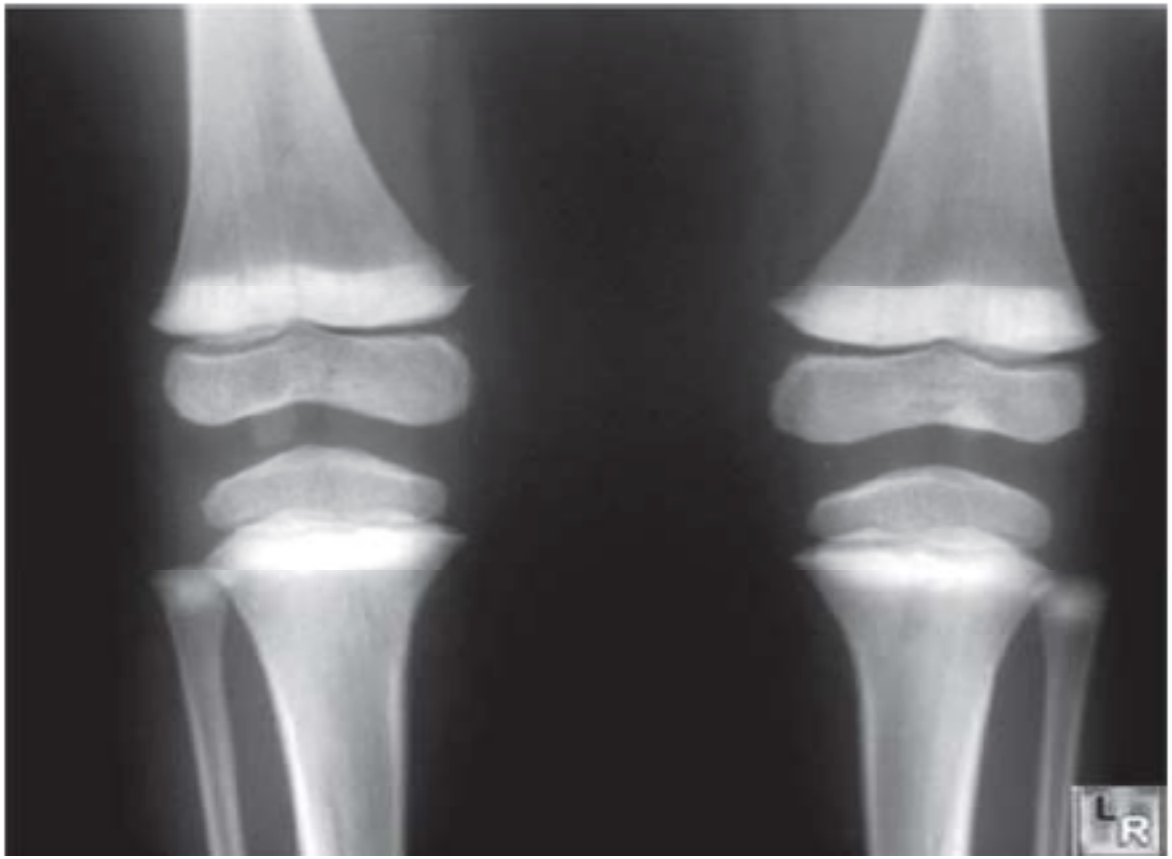
URINE

- ALA in urine
- Urine lead level : If this is above 150 mcg /litre it is a significant finding, but it is unfortunately not very reliable
- Calcium disodium EDTA mobilisation test : This test is done mainly in children to find out whether a child whose BL is between 25 and 41 mcg/100 ml will respond to chelation therapy with a brisk lead diuresis..

DIAGNOSIS

- Children whose BL is more than 45 mcg/100 ml should not receive this provocative test.
- An 8 hour *CaNa2 EDTA chelation provocative test* is considered positive if the lead excretion ratio is more than 0.6 (though some clinicians use a cut-off of 0.5).
- Urine porphyrin
- X-Ray
- Radiography-lead lines in long and flat bones.

LEAD LINES



TREATMENT
EMERGENCY AND SUPPORTIVE MEASURES

- Treat seizures and coma if they occur.

- Provide adequate fluids to maintain urine flow (optimally 1–2 mL/kg/h) but avoid over hydration, which may aggravate cerebral edema

- Patients with increased intracranial pressure may benefit from corticosteroids (eg, dexamethasone, 10 mg IV) and mannitol (1–2 g/kg IV).

TREATMENT

- Treatment with chelating agents decreases blood lead concentrations and increases urinary lead excretion.

Severe acute poisoning with encephalopathy

- BAL 4 mg/kg immediately (in children)
- CaNa2 EDTA 75 mg/kg/day IV infusion

Severe acute poisoning without encephalopathy

- BAL 12 mg/kg/day.
- EDTA 50 mg/kg/day.

Moderate poisoning:

- EDTA50 mg/kg/day

Mild poisoning

- D-Penicillamine 30 mg/kg/day

DECONTAMINATION

Acute ingestion

- Administer activated charcoal (although efficacy is unknown).
- If lead-containing material is still visible on abdominal x-ray after initial treatment, consider whole-bowel irrigation.
- Consider endoscopic or surgical removal of lead foreign bodies that exhibit prolonged gastrointestinal retention

ENHANCED ELIMINATION

- There is no role for dialysis, hemoperfusion, or repeat-dose charcoal.