Practical General Toxicology

Toxic Effects of Metals

Lab. 8

4th Year

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Arsenic

Cadmium

Lead

Liquid mercury

Lab objectives:

Objectives of this lab are to determine:

- some toxic effects associated with arsenic (As), cadmium (Cd), lead (Pb), & mercury (Hg) which are major toxic metals.

- how to assess exposure to metals.

Arsenic:

Sources of exposure:

- Environmental arsenic exposure mainly occurs from arsenic-contaminated drinking water.
- Manufacture of pesticides, & herbicides.
- Smelting industries.

Arsenic poisoning from groundwater in West Bengal:

In India arsenic contamination in ground water was first reported in West Bengal in 1978.

Unsafe tubewells have been marked with red paint.

Some effects of arsenic poisoning:

- Acute poisoning:
  - Hair loss
  - Transverse bands of opacity in nails (Mees' lines) (Fig. 1)
  - Fatty degeneration of liver

- Chronic poisoning:
  - Melanosis (neck, eyelids)
  - Hyperkeratosis (Fig. 2)
  - Hyperpigmentation (with rain drop pattern) (Fig. 3)
  - Skin cancer (Fig. 4)

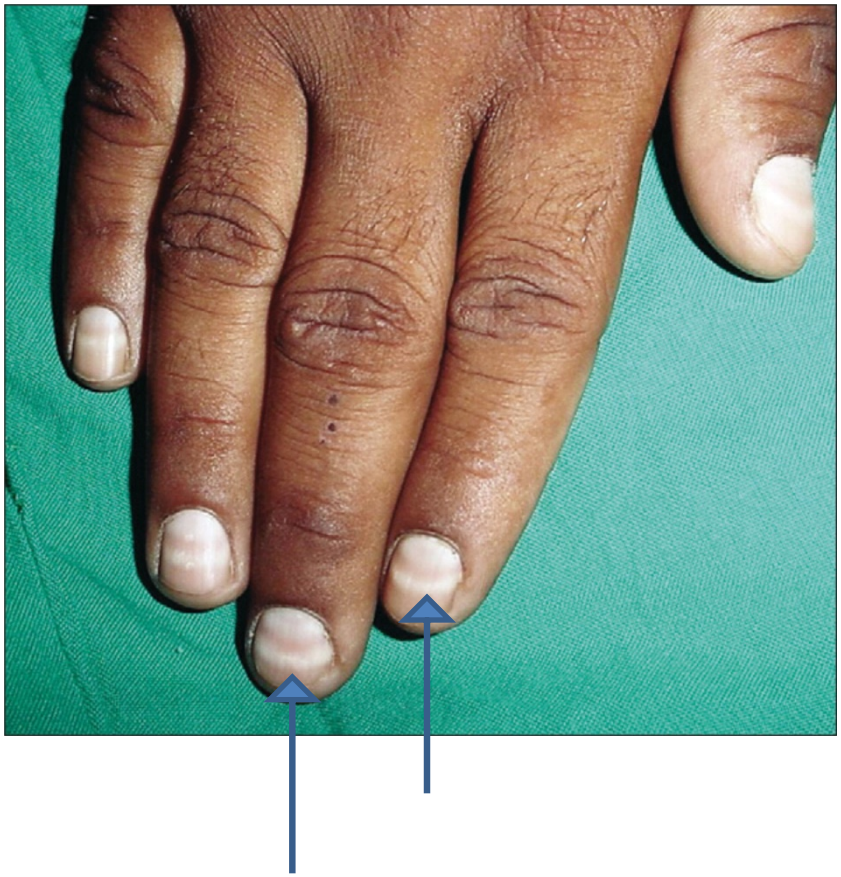


Figure 1. Mees' Lines

Figure 2. Hyperkeratosis—arsenic poisoning

Why arsenic accumulates in keratin rich tissues such as hair, skin & nails?

Arsenic forms covalent complex with sulfhydryl groups of cysteine & because keratin contains many cysteine residues, this makes it one of the major sites for accumulation of arsenic.

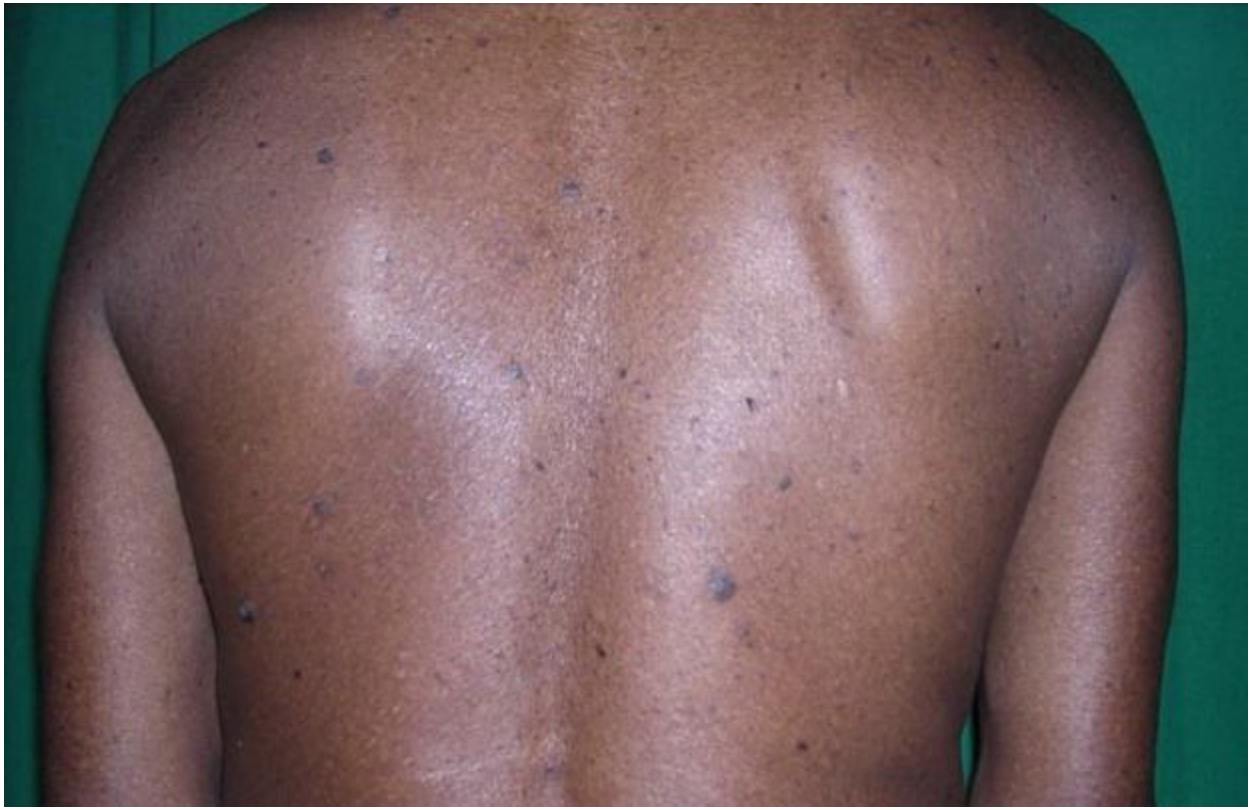


Figure 3. Raindrop pigmentation—arsenic poisoning

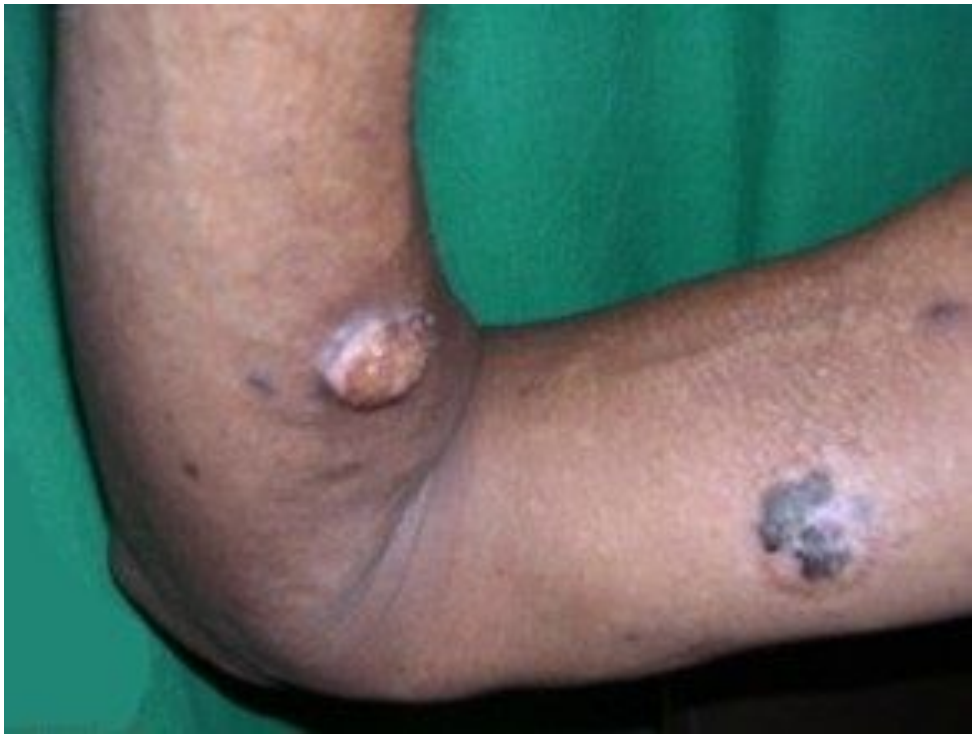


Figure 4. Skin cancers—arsenic poisoning

Cadmium :

Sources of exposure:

- Food due to the use of cadmium-containing water for irrigation of plants.
- Cigarette smoking.

Some toxic effects of cadmium:

- Kidney damage
- Skeletal damage, &
- Prostate & kidney cancer.

Skeletal damage:

- Long-term high cadmium exposure may cause skeletal damage, first reported from Japan, where the itai-itai (ouch-ouch) disease (Fig. 5) (a combination of complications of osteomalacia & osteoporosis) was discovered in the 1950s.

- The exposure was caused by cadmium-contaminated water used for irrigation of local rice fields.

Cadmium may affect bone directly through:

- direct interference with incorporation of calcium in bone cells, &
- direct stimulation of bone resorption, &
- impairment of bone formation.

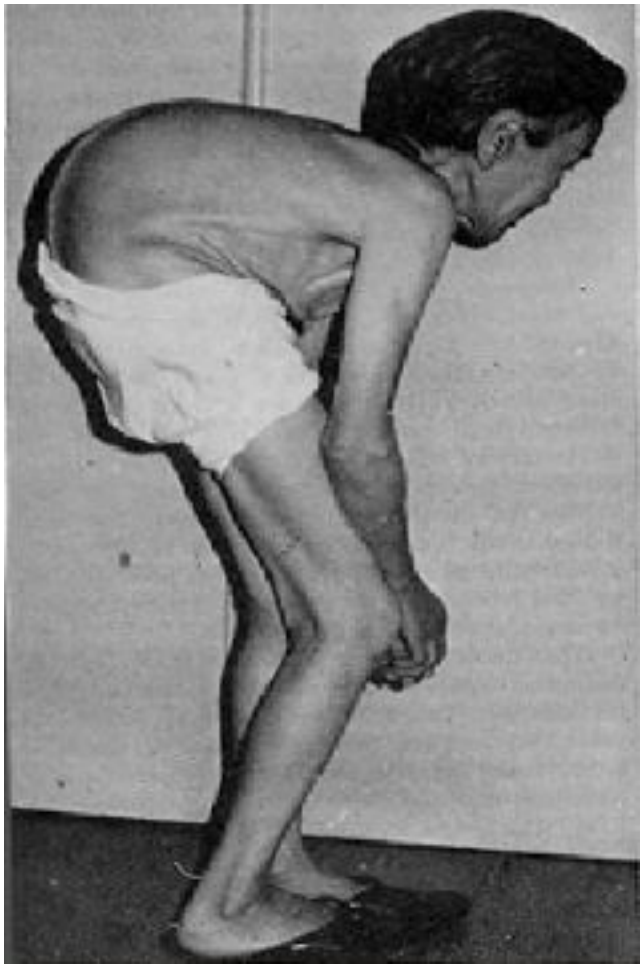


Figure 5. Itai-itai disease

Rice fields

Exposure:

- Young children are particularly vulnerable to the toxic effects of lead.

- Environmental sources of lead exposure in children are shown in (Fig. 6).

- A major route of exposure for the general population is from food & water.

- Other potential sources of lead exposure are battery making, soldering, jewelry making, & pottery making.

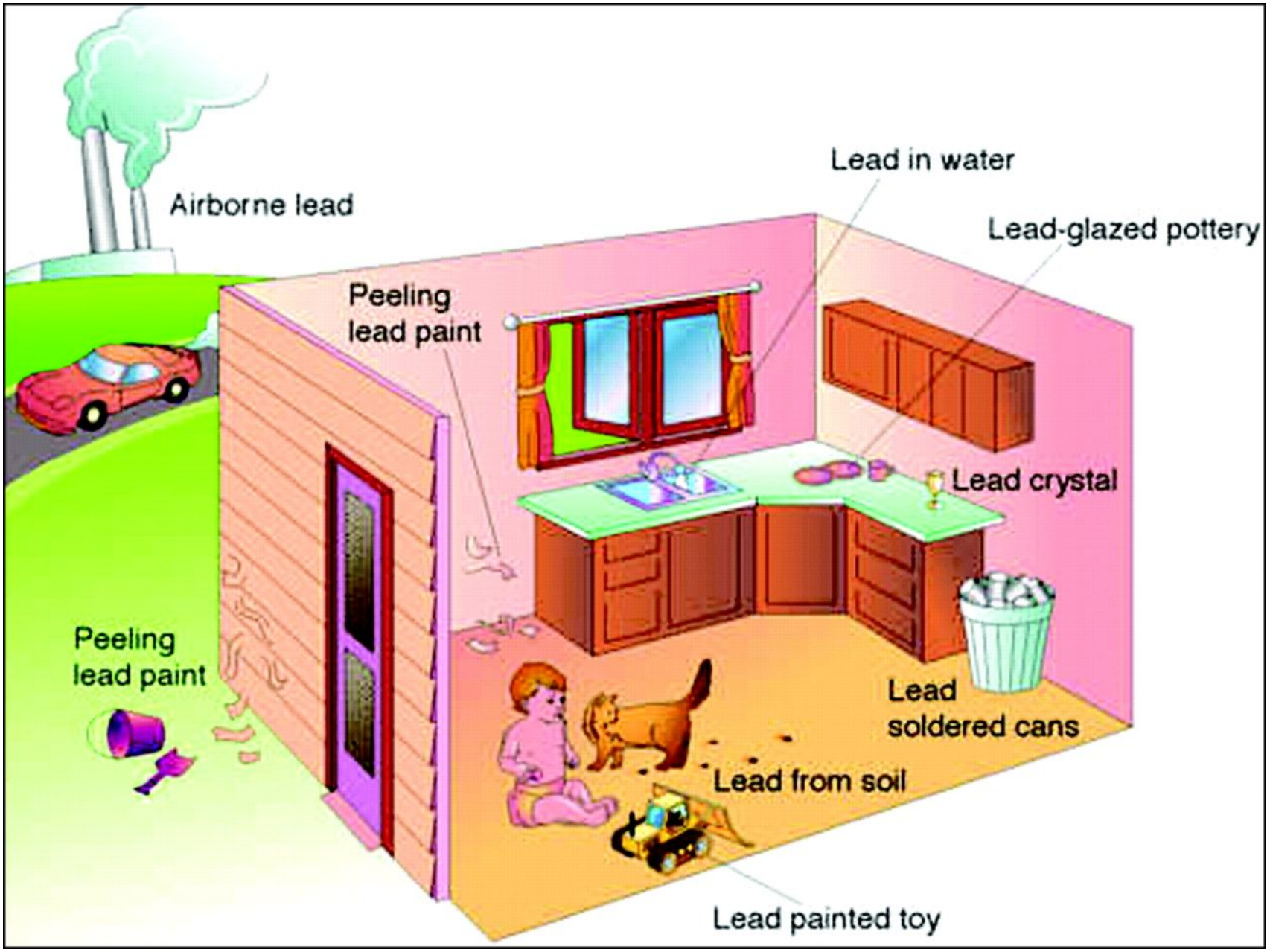


Figure 6. Environmental sources of childhood lead exposure

Some effects of lead:

- The majority of lead which is absorbed is stored in the bones & teeth. In children, about 70% of lead is distributed in this way; in adults up to 95%.

- The hypermineralisation is reflected in the form of densities which are the classic “lead lines” observed on x-ray (Fig. 7).

- Hypermineralisation occurs because lead is an osteoclast poison, so bone density is increased due to unopposed action of osteoblasts.

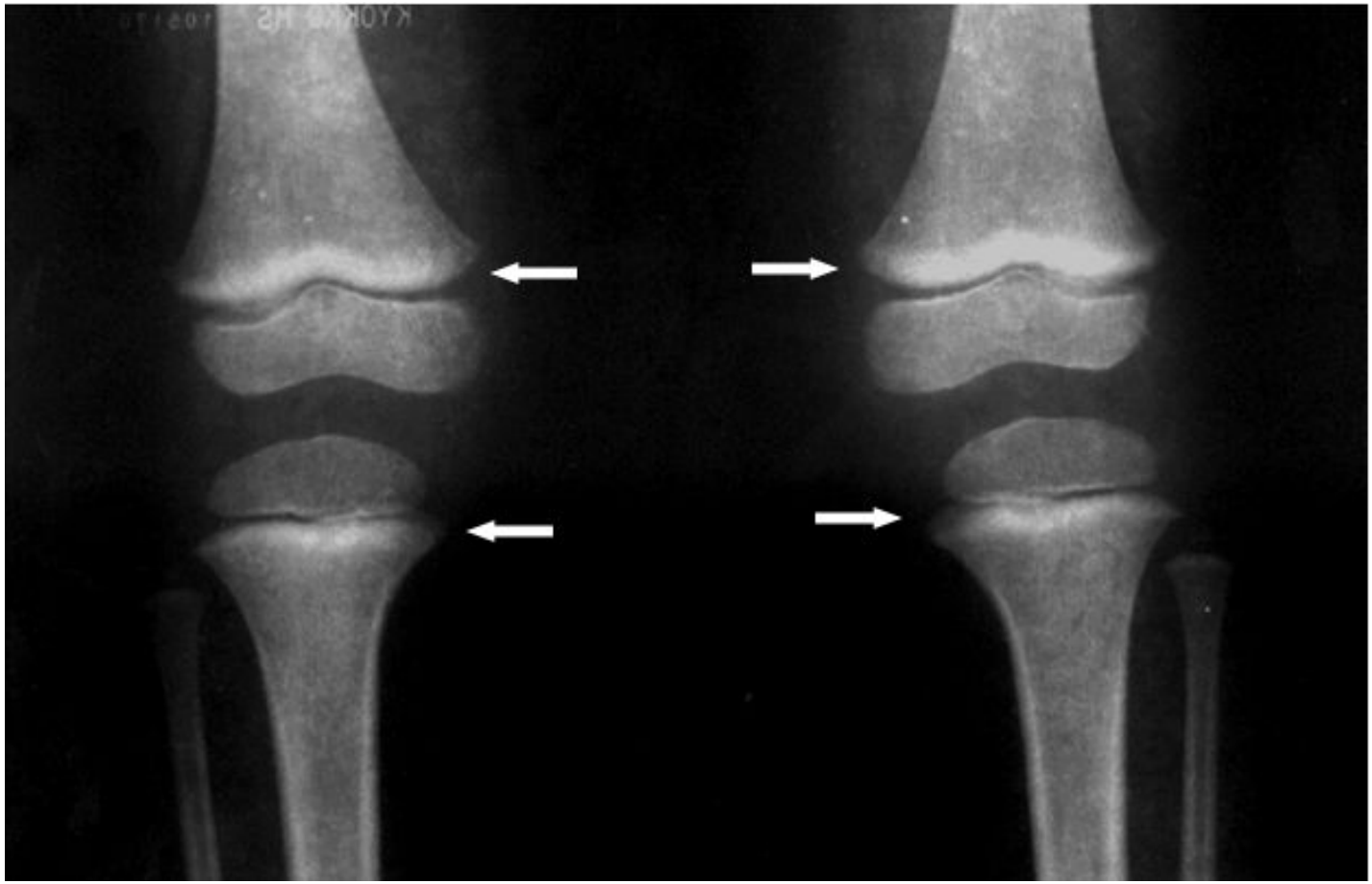
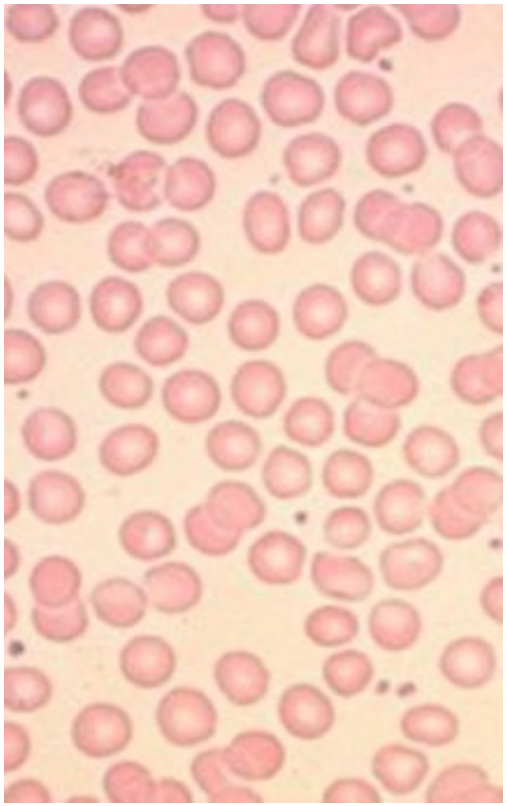
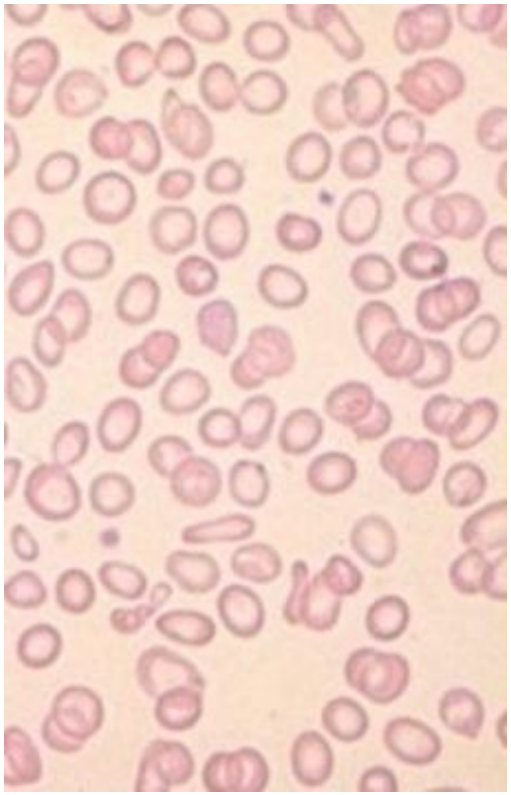


Figure 7. Longbone radiograph of knees - metaphyseal “lead bands".

- Microcytic & hypochromic anemia, as in iron deficiency. (Fig. 8)



Normal



Hypochromic microcytic anemia

Figure 8. Normal blood smear and a smear from a patient with hypochromic microcytic anemia.

- Blood film examination may reveal basophilic stippling of red blood cells (dots in red blood cells visible through a microscope) (Fig. 9).

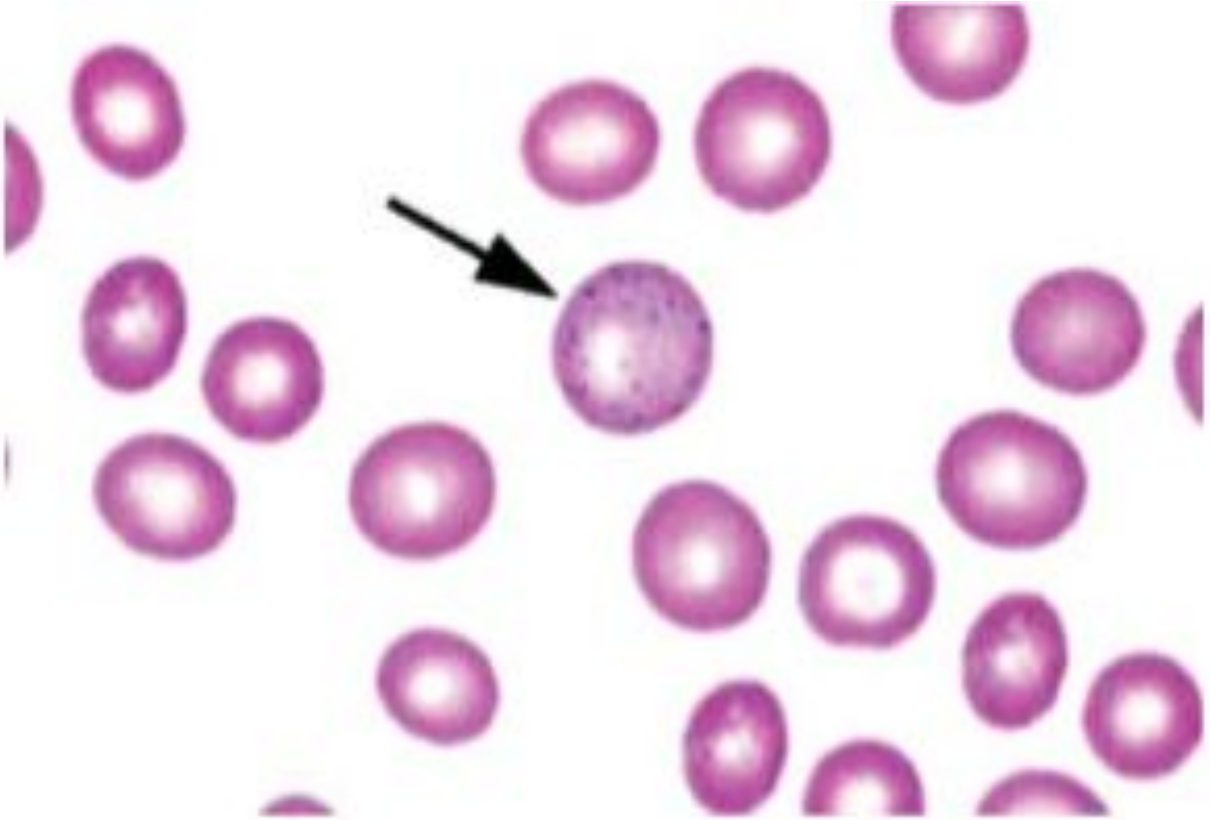


Figure 9. Basophilic stippled cell (arrowed)

Why lead causes basophilic stippling of red blood cells?

Pyrimidine 5' nucleotidase is an enzyme needed for the degradation of ribosomal RNA during reticulocytes maturation.

Lead inhibits that enzyme & that results in aggregation of residual ribosomes which are manifested by basophilic stippling.

- Chronic lead nephrotoxicity: consists of interstitial fibrosis & progressive nephron loss, azotemia & renal failure.

- A remarkable pathogenic feature of lead poisoning is the presence of inclusion bodies composed of lead-protein complex (Fig. 10).
  Lead-induced inclusion bodies are frequently nuclear, & are common in kidney.

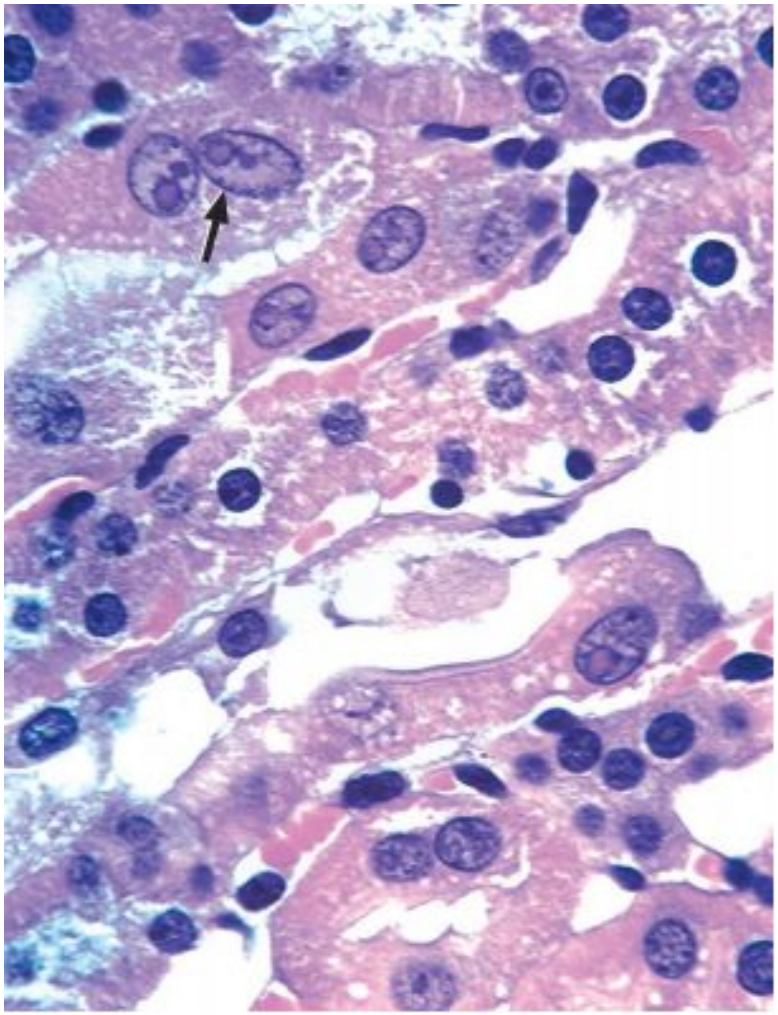


Figure 10. Lead-induced inclusion body formation in kidneys from wild-type (WT) mouse. Arrow indicates typical karyomegaly of P3 proximal tubular cell.

- In severe toxicity [Blood lead (BL) more than 100 mcg/100 ml], lead results in:
  - lead palsy: wrist drop (Fig. 11) or foot drop.
  - a bluish black lead line on gums (Burton's line) (Fig. 12).
  - lead encephalopathy: It is more common in children.

Fig 11. Wrist drop

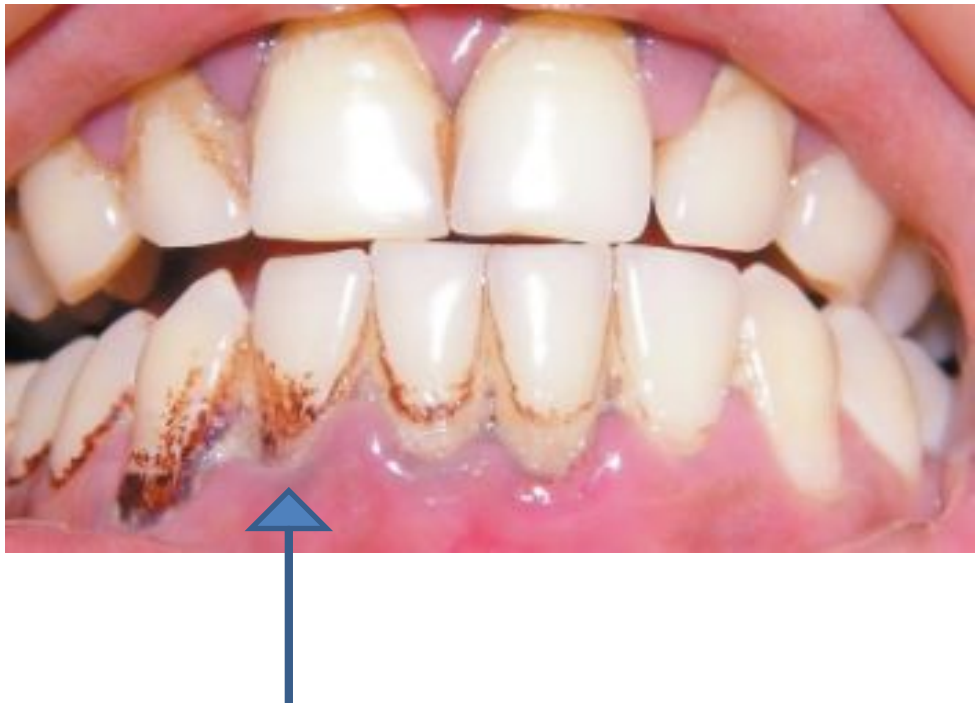


Figure 12 . Burton’s Line

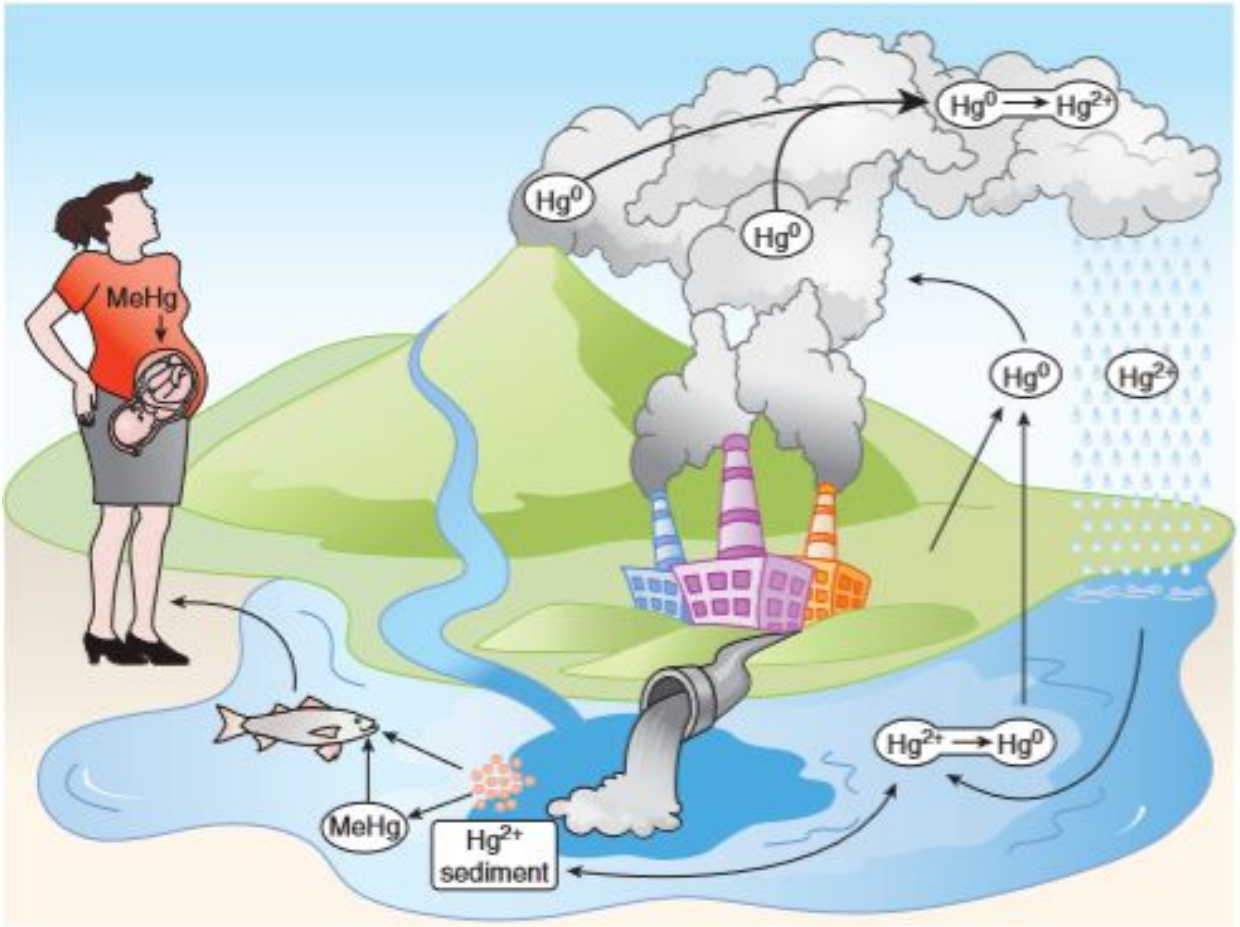
Why lead causes Burton's line?

This line is caused by a reaction between circulating lead with sulphur ions released by oral bacterial activity which deposits lead sulphide at the junction of the teeth & gum.

Mercury:

Sources of exposure:

- Breaking of mercury fluorescent light bulbs.
- Liquid mercury following breakage of thermometers.
- Dental amalgam.
- Methyl mercury from consumption of fish.



The movement of mercury in the environment

Don't put them in the trash.

Fluorescent lamps contain mercury.
It is illegal to put them in the trash.
For disposal options, go to www.GreenGuardian.com or call 877-630-0668.

A brief human history of mercury poisoning

Qin Shi Huang,
1st emperor of China

200 BC

Mad hatters

19th-20th century

Minimata disaster

1950s

Iraq grain disaster

1971

Karen Wetterhahn,
Dartmouth professor

1997

Minimata disease:

- Between 1953 & 1970, around Minamata Bay in Japan, more than 2000 people were diagnosed to be suffering from a curious cluster of neurological symptoms comprising paraesthesiae, narrowing of vision, dysarthria, diminution of hearing, amnesia, ataxia, staggering gait, weakness, & emotional instability.

- Some developed paralysis & became stuporous, & out of all the people afflicted nearly a hundred died. The condition has been known as the Minimata disease (Fig. 13).

- It was caused by consumption of fish contaminated with methyl mercury. The most severely affected victims were actually infants who had been exposed in utero.

Figure 13 . Minamata disease

Iraq grain disaster:

The shocking tragedy occurs in Iraq in 1971–72, when 500 people died out of a total of 6530 victims due to consumption of imported wheat and barley meant for sowing, treated with methyl mercury fungicide.

Some effects of mercury poisoning:

Acute poisoning from inhalation:

- Dyspnea, cough, fever, stomatitis
- Deep red oral mucosa with “strawberry tongue” (Fig. 14)
- Skin rash (Fig. 15)

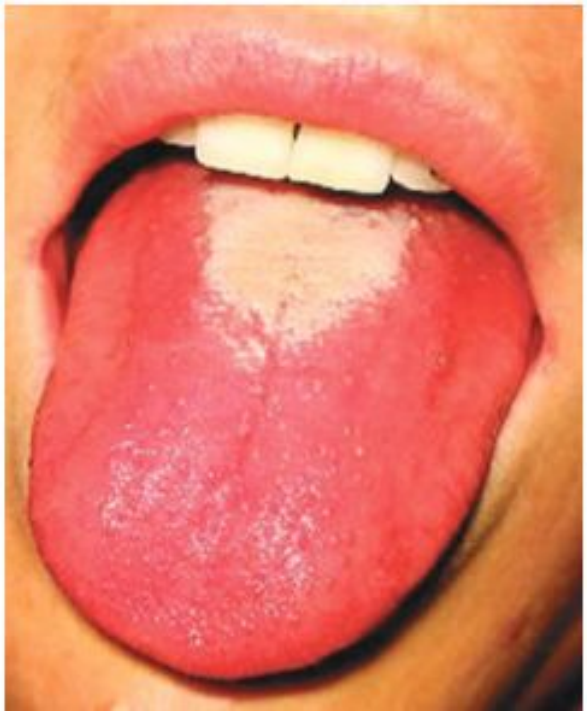


Figure 14 . Strawberry tongue

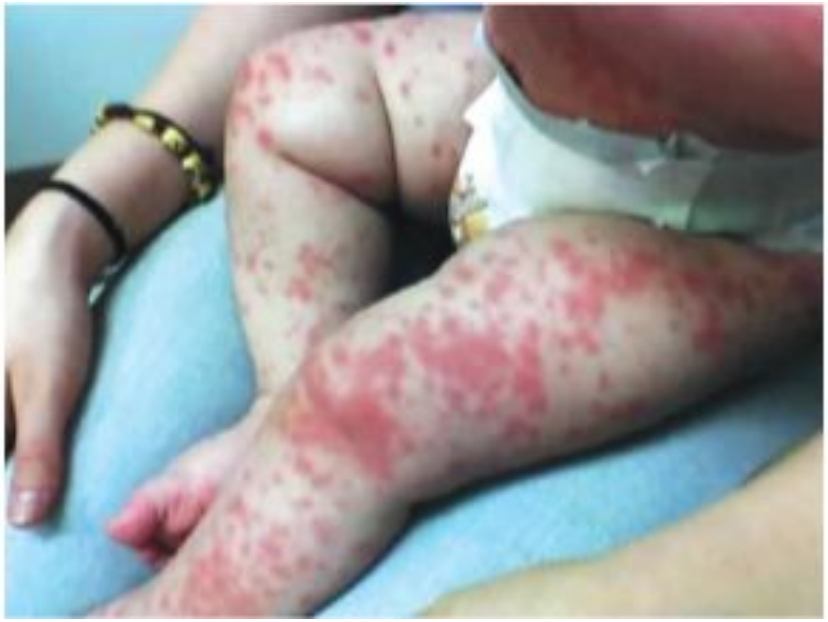


Figure 15 . Skin rash

Chronic poisoning by ingestion:

- Colitis
- Dementia
- Tremor
- Renal failure
- Acrodynia (Pink disease) (Fig. 16). This is seen mainly in children. The hands & feet become puffy, pinkish, painful, paraesthetic, perspiring & peeling.

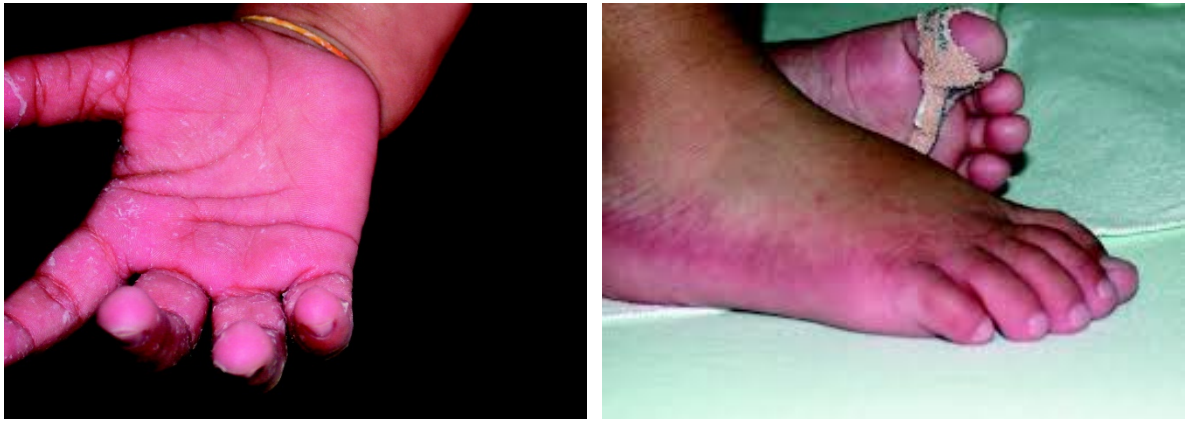


Figure 16 . Pink disease (Acrodynia)

Assessment of metal exposure:

- The biological half-life varies according to the metal as well as the organ or tissue. For example, the biological half-lives of cadmium in kidney & lead in bone are 20 to 30 years, whereas for some metals, such as arsenic or lithium, they are only a few hours to days.

- Blood, urine, & hair are the most accessible tissues for measuring metal exposure.

- Blood and urine concentrations usually, but not always, are reflective of more recent exposures.

- Hair can be useful in assessing variations in exposure to metals over the period of its growth. Analyses can be performed on segments of the hair, so that metal content of the newest growth can be compared with past exposures.
  Note: average hair growth is around 0.4 mm/day.


Thank
you