

Pb intoxication

Also known as Plumbism, Colica Pictonum, Saturnism, Decon's colic or Painter's colic.

Sources of lead intoxication

- Workplaces: abandoned (industrial) lead sites (from mines to garages working with old car batteries), Industries (mining or lead smelting) often have high levels around => ingestion or inhalation, past use of lead in gasoline has contaminated soils (along roadways)
- Soil: Direct contamination (playing child) or by grown food there
- Drinking water: lead water pipes (repairs!)
- Food: Grown on contaminated soil or uptake through leaves, contaminated while handling (e.g. packaging), ceramic table ware, leaded-crystal glassware, cans...
- Paint: Old paint contaminates soil and houses, deteriorating paint becomes dust
- And traditions like melting lead over a flame to tell your fortune at New Years Eve (German-speaking countries)
- Organic and Inorganic lead
- Today: inorganic lead more spread, but...
- tetra-ethyl-lead (still used as additive in fuel) can be absorbed through the skin (highly lipophilic!)
- Lead in compact form non-toxic, forms protective layer of lead carbonate ($PbCO_3$) in air, but...
- ...consider old window panes and water pipes!

How lead enters the body

- Ingestion: children mainly because of lead paint - lead enters through normal hand-to-mouth activity. As well home remedies may contain lead.
- Inhalation (all inhaled, but "only" 20-70 % of ingested lead is absorbed!): in old times because of leaded gasoline, nowadays in workers in lead-using industries and in do-it-yourself home renovation
- Dermal: organic lead can be absorbed through skin (unusual for normal population)

And where it goes to...

Half time in blood are days, in soft tissues are weeks and in mineralizing tissue (teeth/bones) 20 - 30 years, which can lead to

- Endogenous exposure: Pb may be released into bloodstream (for calcium stress because of pregnancy, lactation, osteoporosis or calcium deficiency).
- toxic to many organs and tissues incl. heart, bones, intestines, kidneys, reproductive & nervous system
- Influences development of the nervous system (learning/behavior disorders)
- Symptoms: abdominal pain, confusion, head ache, anemia, irritability and in severe cases: seizures, coma, death

Toxicity Principle

Enzymes and Metal Replacement

- Enzymes are affected, since Pb binds to sulfhydryl groups (-SH)
- Ability to mimic other metals (cofactors) used in enzymatic reactions, displacing them (calcium, iron and zinc)
- Eliminates metals in compounds: $PbCO_3$ built into bone instead of $CaCO_3$
- Influence on heme synthesis (main cause for pathology) leading to anemia...
- interference with essential enzyme ALAD (delta-aminolevulinic acid dehydratase) needed for heme synthesis (cofactor in hemoglobin)
- inhibits enzyme ferrochelatase, which catalyzes the joining of protoporphyrin and Fe^{2+} to form heme.
- Lead's interference with heme synthesis results in production of zinc protoporphyrin.
- buildup of heme precursors, such as aminolevulinic acid, may directly or indirectly harm neurons.

Diagnosis

Lead concentration	leading to
150 $\mu\text{g/l}$	ALAD inhibition
400 $\mu\text{g/l}$	ALA will be found in urine. Coproporphyrin III as well in urine (in severe cases: dark brown coloring). Makes grey-yellowish skin color in chronic lead intoxication.
200-600 $\mu\text{g/l}$	protoporphyrin concentration in erythrocytes increases => basophilic stippling (you can see it in light microscopy!)
500 $\mu\text{g/l}$ (200 $\mu\text{g/l}$ for children)	anemia (inhibited heme production) and decrease of erythrocyte life span. Anulocytes (ring-shaped, monoconcave, hypochrome erythrocyte with central white area - less than 1/3 of surface is red) develop

Treatment

Treatment with chelating agent, that has greater affinity for lead than for calcium (lead chelate is formed by exchange).

- Acute oral uptake of toxic amount: irrigation of stomach, administer active carbon to bind organic Pb compounds, and sodium sulfate to change soluble Pb salts into hardly soluble lead sulfate.
- Chelating agents bind Pb (Pb displaces Ca in complex to be disposed by kidney)
- ethylenediamine-tetraacetic acid (EDTA) – effective mostly extracellular *1
- D-penicillamine – effective mostly intracellular *1
- Chronic intoxication: 2,3-Dimercapto-1-propanesulfonic acid (DMPS)
- 1 Administer both together, ensure drinking lots of water and working diuresis

Links

Sources

- Wikipedia. *Lead poisoning* [online]. [cit. 2014-03-06]. <http://en.wikipedia.org/wiki/Lead_poisoning#Pathophysiology>.
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- Wikipedia. *Lead* [online]. [cit. 2014-03-06]. <http://en.wikipedia.org/wiki/Lead#Biochemistry_of_poisoning>.
- THOMAS, Herdegen. *Kurzlehrbuch Pharmakologie und Toxikologie*. 2nd edition. 2010. ISBN 978-3131422927.