

Toxicology of Exposure to Lead in Humans

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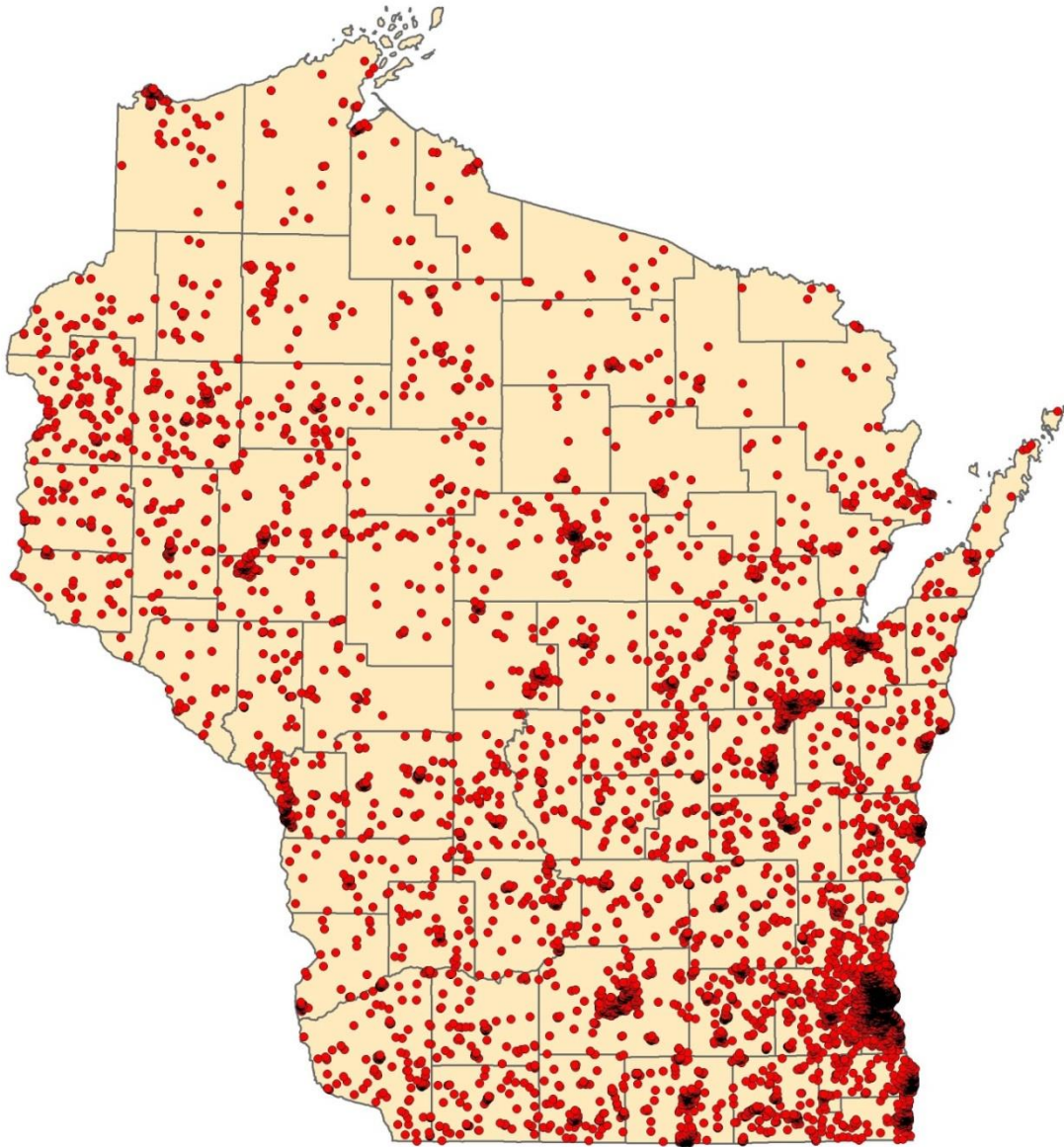
March 10, 2017



Lead is widely present in the environment

- Used since ancient times due to its workability, low melting point, and resistance to corrosion.
- Past and current uses include:
 - Paint pigments
 - Water pipes, solder, fixtures
 - Fuel additives
 - Electronics
 - Lead-acid batteries
 - Projectiles
- Naturally-occurring lead in Wisconsin geology.





Lead poisoning in Wisconsin is a statewide problem.

Each red dot represents an address associated with a lead-poisoned child, 1996 to 2006.

More than 44,000 children.

Old lead paint most important cause of exposure.

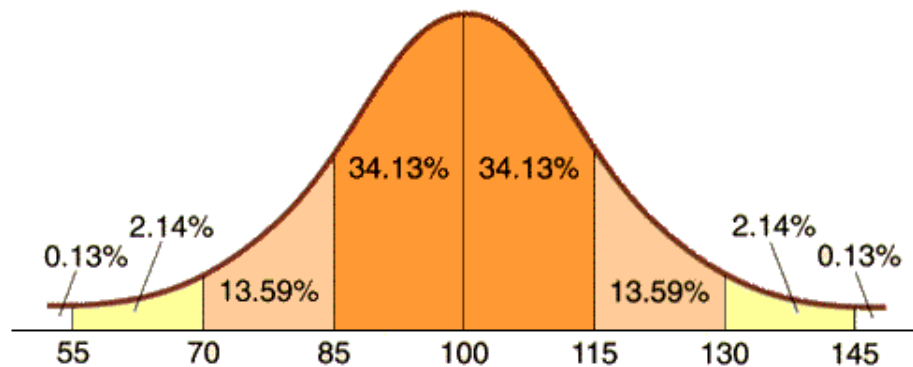


Lead has numerous effects on health

- Neurological effects
- Peripheral neuropathy
- Renal effects
- Blood effects
- Blood pressure
- Rate of uptake > rate of excretion, due to accumulation in bone



Lead poisoning is the most serious environmental health threat facing young children in the U.S.



“Normal” IQ distribution

- Lead poisoning interferes with the normal development of a child’s brain.
- 2-4 IQ point deficit for each microgram of lead per deciliter of blood ($\mu\text{g}/\text{dL}$) increase in blood lead above $5 \mu\text{g}/\text{dL}$

-WI Dept. Health Services. 2008. Report of Childhood Lead Poisoning in Wisconsin. PPH 45109 (5/08)

-N Engl J Med 348;16 www.nejm.org april 17, 2003



Blood Lead Concentrations Corresponding to Adverse Health Effects

From: Agency for Toxic Substances and Disease Registry/Division of Toxicology and Environmental Medicine. *Toxicological Profile for Lead. 2005*

| Blood Lead Concentrations Corresponding to Adverse Health Effects | | |
|---|----------------------------|--------------------|
| Life Stage | Effect | Blood lead (µg/dL) |
| Children | Depressed ALAD* activity | < 5 |
| | Neurodevelopmental effects | <10 |
| | Sexual maturation | <10 |
| | Depressed vitamin D | >15 |
| | Elevated EP** | >15 |
| | Depressed NCV*** | >30 |
| | Depressed hemoglobin | >40 |
| | Colic | >60 |
| Adult | Depressed ALAD* | < 5 |
| | Depressed GFR**** | <10 |
| | Elevated blood pressure | <10 |
| | Elevated EP (females) | >20 |
| | Enzymuria/proteinuria | >30 |
| | Peripheral neuropathy | >40 |
| | Neurobehavioral effects | >40 |
| | Altered thyroid hormone | >40 |
| | Reduced fertility | >40 |
| | Depressed hemoglobin | >50 |
| Elderly Adult | Neurobehavioral effects | > 4 |

*aminolevulinic acid dehydratase (ALAD)

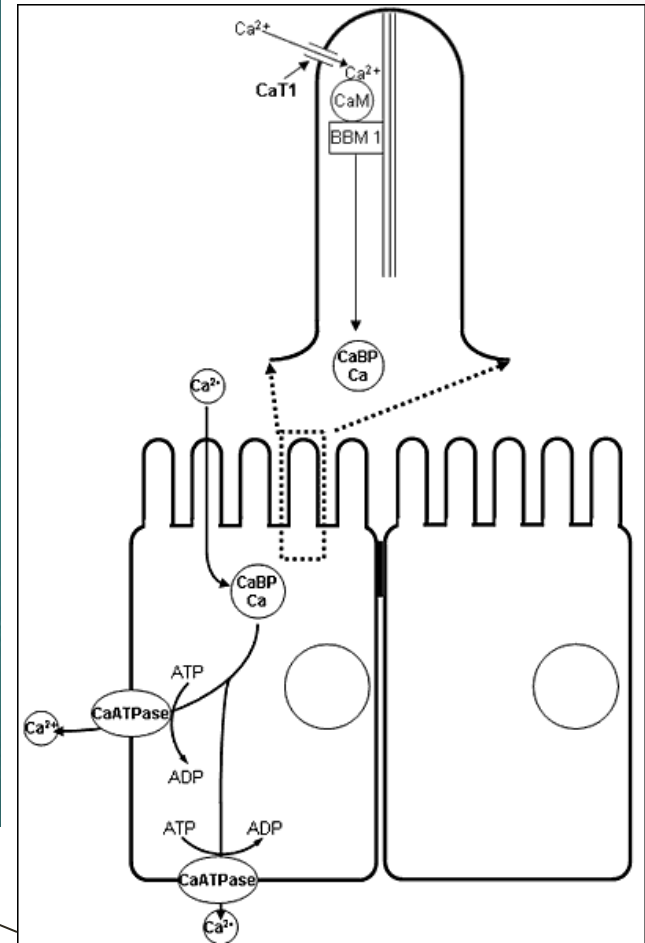
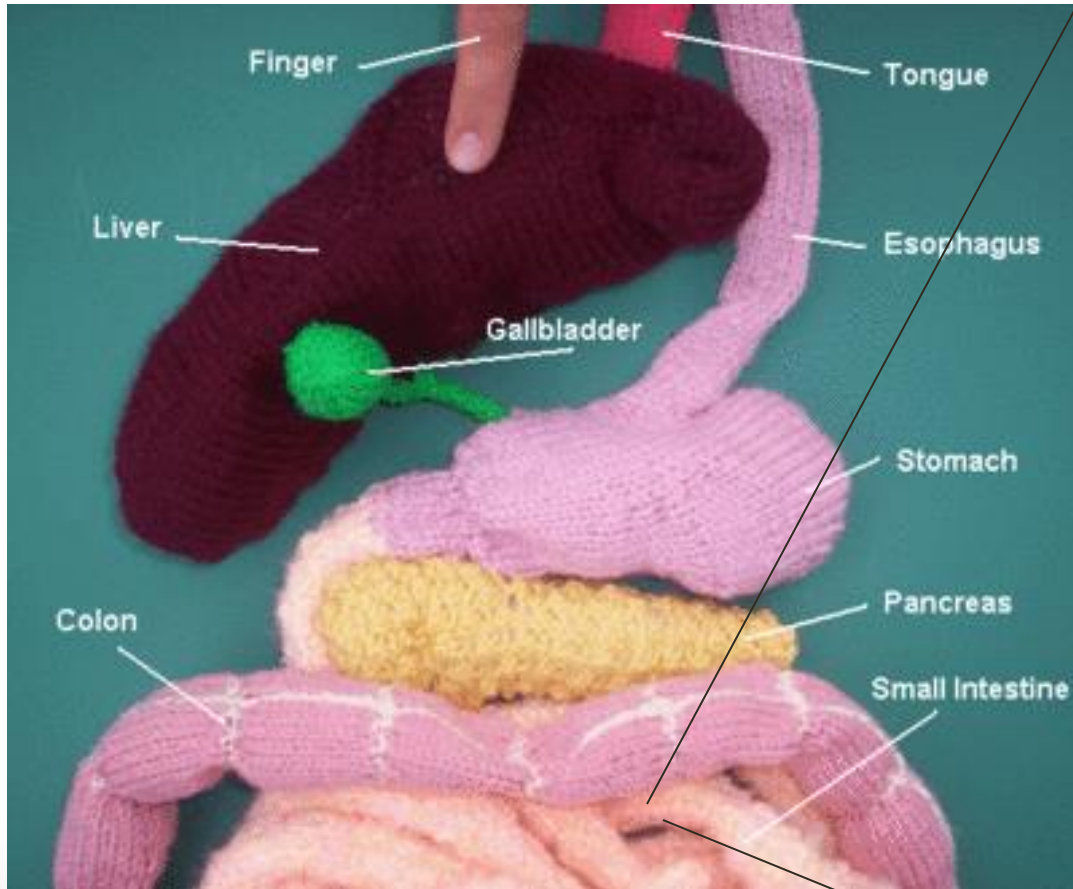
**erythrocyte porphyrin (EP)

***nerve conduction velocity (NCV)

****glomerular filtration rate (GFR)

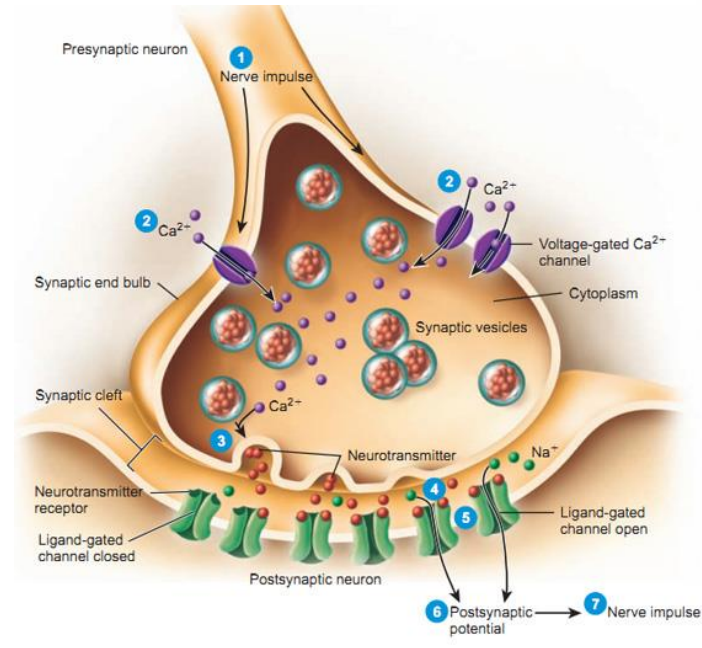
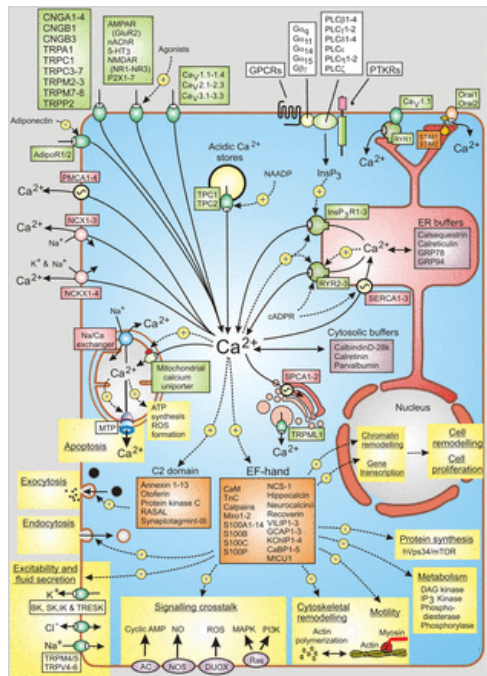


Lead (Pb) uptake primarily through calcium channels in small intestine



How does lead affect us at the cell and molecular level?

- Recurring theme of competition with, or inhibition of, calcium-dependent processes
 - Ca^{++} vs Pb^{++}
- *Many* molecular targets in cells and tissues



Public health definitions of lead poisoning

- 5 $\mu\text{g}/\text{dL}$: 5 micrograms lead per deciliter of blood: CDC policy reference value.
- No known biological role
- No “no-effect” level
- *Tolerable dose* does not equal to *no-effect dose*
- Children particularly vulnerable
 - Development
 - Uptake



The CDC blood lead Reference Value (formerly: Level of Concern) has decreased over time

| | Blood lead LOC |
|------------------------------|--|
| 1960s | 60 $\mu\text{g}/\text{dL}$ (micrograms Pb/deciliter blood) |
| 1970s | 40 $\mu\text{g}/\text{dL}$ |
| 1980 | 30 $\mu\text{g}/\text{dL}$ |
| 1985 | 25 $\mu\text{g}/\text{dL}$ |
| 1994 | 10 $\mu\text{g}/\text{dL}$ |
| 2012 reference value | 5 $\mu\text{g}/\text{dL}$ |
| Future reference value goals | < 5 $\mu\text{g}/\text{dL}$ (to be updated every 4 years) |

The LOC is a reference blood lead level based on the 97.5th percentile of the BLL distribution among children 1 –5 years old in the United States.

Ref. CDC Response to Advisory Committee on Childhood Lead Poisoning Prevention Recommendations in “*Low Level Lead Exposure Harms Children: A Renewed Call of Primary Prevention*” . CDC. 2012.

http://www.cdc.gov/nceh/lead/acclpp/cdc_response_lead_exposure_recs.pdf

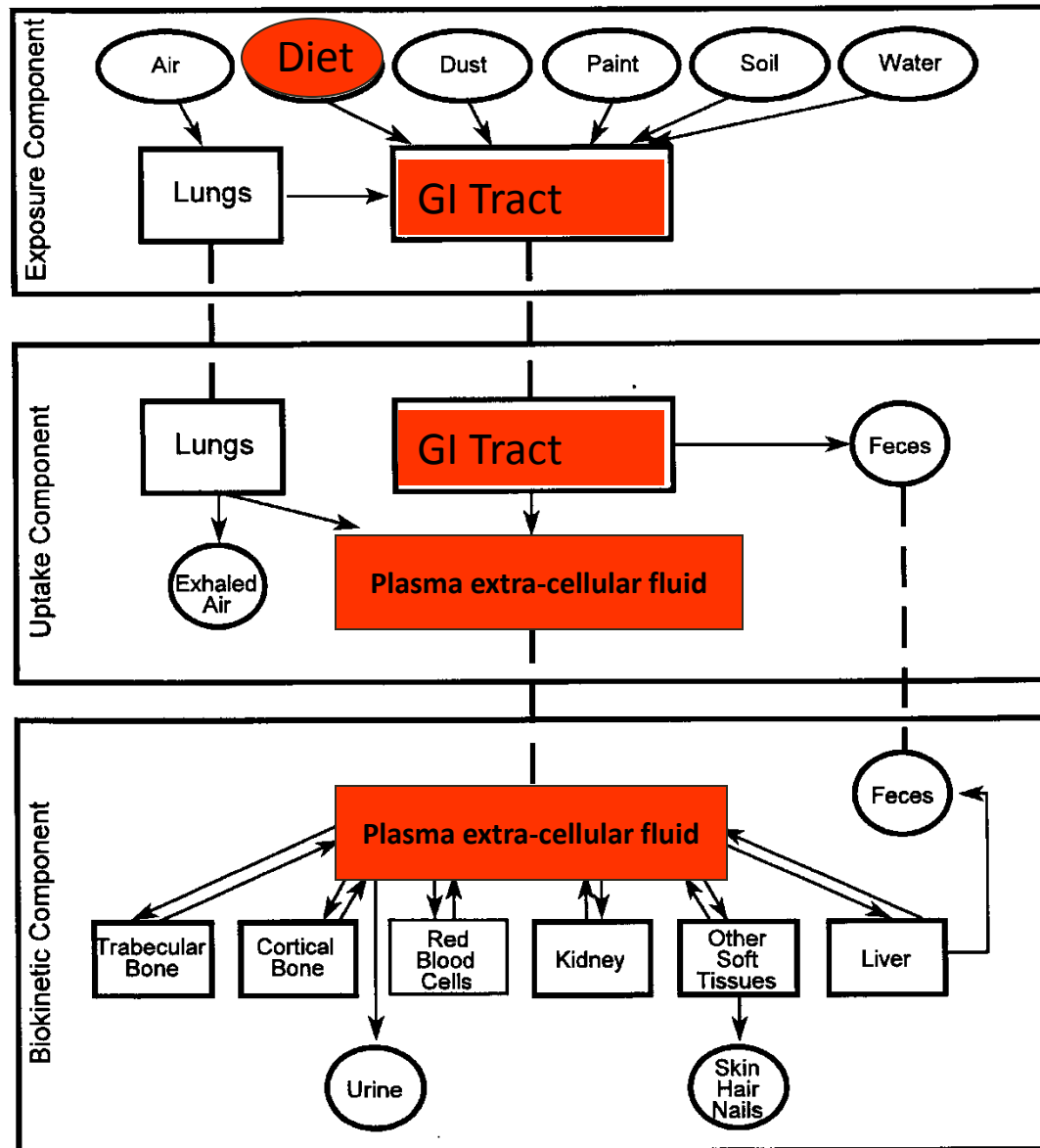


How are decisions made about acceptable environmental concentrations of lead?

- The EPA *Integrated Exposure Uptake and BioKinetic* (IEUBK) model is used to predict blood lead resulting from environmental exposure.
- Key policy-making tool for the EPA.



IEUBK “Uptake” conceptual model



What happens when a medical test reveals a child with elevated blood lead level (BLL)?

- In Milwaukee, a tiered response from the Childhood Lead Poisoning Prevention Program:
 - BLLs 5-9 ug/dL: receive a letter and educational materials.
 - Venous BLLs 10-19: Pub Health Serv. Assoc. visits the home.
 - Venous BLLs 20+: Pub Health Nurse home visit and care coordination; risk assessor inspects the home.
 - Venous BLL 45+: Immediate poisoning response

- For more information : **Childhood Lead Poisoning Case Management Services**

<http://city.milwaukee.gov/health/lead-Case-Management#.WKyrdv7rurS>



What about lead in water?

- Lead in residential and municipal water systems historically managed as a *secondary* source of exposure.
- Many communities are now paying extra attention to this source of exposure.
 - DHS is working with Milwaukee and other Wisconsin communities on this issue.
- There are several options to manage lead in water; removal is the only permanent solution.



Summary

- There are many sources of environmental lead exposure, both major and minor.
- Lead has numerous targets in the body, and affects both children and adults.
- Acceptable environmental Pb concentrations have decreased over time.
- Lead poisoning is preventable! There has been much progress in eliminating environmental lead, but still much to be done.



For more information on this topic from the Wisconsin Bureau of Environmental and Occupational Health:

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