The Association of Calcium Whole Blood Levels with Child Blood Lead Levels

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Diversity Program Consortium — Supported by the National Institutes of Health

Introduction

Lead Exposure: An ongoing public health problem

- Since the 1970s, measures have been taken to eliminate sources of lead exposure nationwide, decreasing child blood lead levels.

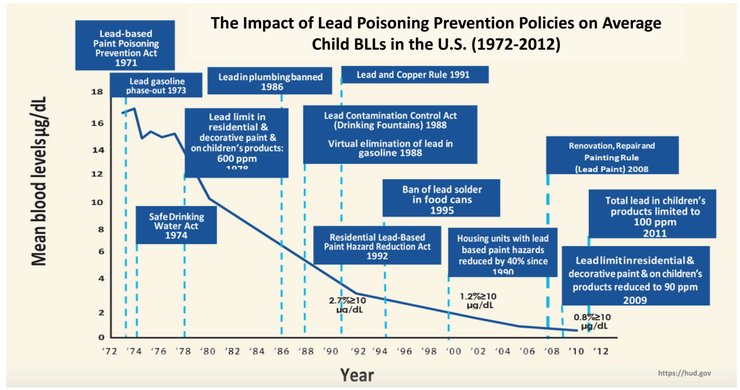


Figure 1. National regulations aimed to reduce blood exposure have decreased average child blood lead levels from ~17µg/dL in 1972, to 0.08%≥ 10µg/dL in 2012.

- Despite these successes, lead exposure remains the most important pediatric environmental health problem, with costs associated with lead-related health effects estimated in the billions of dollars.[6]

No level of lead exposure is safe for children

- Lead exposure is especially dangerous for children even at lower blood lead levels (<10 µg/dL), causing impairment of neurological development, neuropsychiatric disorders, and altering kidney function, among many other disruptions in development.[1]
- Hundreds of thousands of children nationwide are currently affected by lower-level lead exposure (<10µg/dL).

Adequate dietary calcium intake may decrease lead absorption

- An inverse relationship has been historically observed between calcium intake and blood lead concentration at the higher levels >10µg/dL.[3]
- More studies are needed to investigate the relationship between calcium whole blood levels and lower level lead exposure in children.

Mechanisms of Lead Absorption in the Body

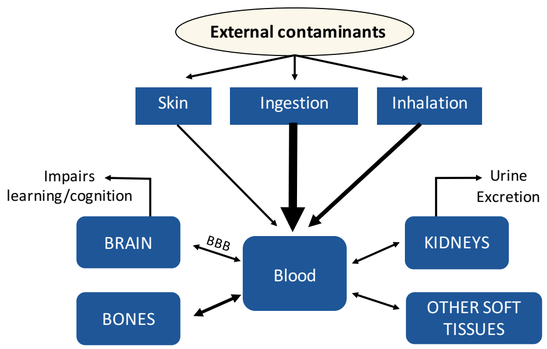


Figure 2. Lead enters the body through the skin, and mostly by ingestion and inhalation. Once in the blood, lead circulates and gets absorbed by soft and mineralized tissues.

Age-dependent effects:

- Behavioral patterns in children result in higher ingestion and inhalation rates.
- Children absorb a larger fraction of ingested lead.[6]
- Children have a lower glomerular filtration rate than adults, causing lower excretion.[6]
- Children have an immature blood brain barrier (BBB) allowing lead to reach the brain.

Calcium and Lead Compete for Transport into Blood

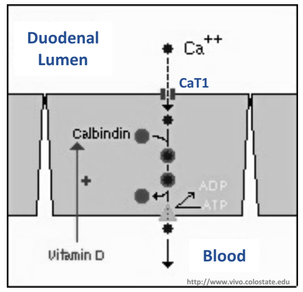


Figure 3. Active transport of calcium via luminal calcium transport protein 1 (CaT1) from the duodenal lumen into the blood.

Lead absorption via the gastrointestinal tract is inversely related to calcium intake

- Dietary calcium is absorbed into the blood by two mechanisms: passive, paracellular absorption in the jejunum and ileum, or active transport via CaT1 in the duodenum.[2]
  - Lead also uses these mechanisms to cross intestinal cells.
  - CaT1 has a high affinity for calcium and lead, making lead absorption more likely in individuals with insufficient calcium intake.

Adequate dietary calcium Intake in children

- Age specific: 0-6 months, 210 mg/day; 7-12 months, 270 mg/day; 1-3 years, 500 mg/day; and 4-8 years, 800 mg/day.[1]
- Blood is clinically tested to measure calcium levels in the body. Clinical reference values for adequate whole blood calcium levels in children are <2 years: 9-10.6 mg/dL, 1-17 years: 8.8-10.8 mg/dL .[4]

Lead Affects bone, Renal and Brain Function by Mimicking Calcium

Calcium is a co-factor in many cellular processes. Since lead competes with calcium on cross-membrane transporters, many cell-signaling pathways are affected by lead.

Lead replaces calcium in bone:

- Lead forms stable complexes with phosphate, allowing it to replace the calcium-phosphate that makes up the primary matrix of bone.[6]

Lead decreases renal function and excretion:

- Accumulation of lead in the kidneys has been shown to cause glomerular sclerosis and interstitial fibrosis due to scarring, and proximal tubular damage. [4]

Lead blocks Calcium binding needed for brain signaling

- Lead reduces presynaptic glutamate release (only at lower lead doses), blocks release of acetylcholine, and prevents maximal activation of protein kinase C (PKC) which is involved in processes such as neurotransmitter syntheses, and development of the blood brain barrier.[6]

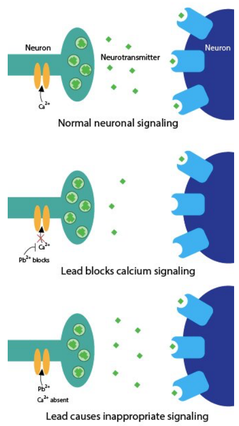


Figure 3. Schematic of lead interfering with neuron signaling.

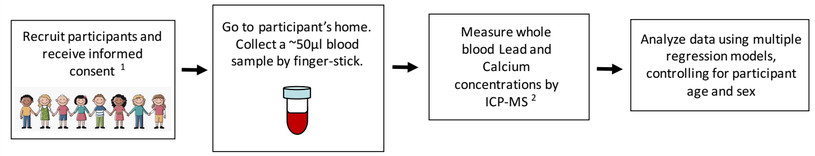
Hypothesis

Children with adequate whole blood calcium levels (<2 years: 9-10.6 mg/dL, 1-17 years: 8.8-10.8 mg/dL) will have lower blood lead levels compared to children with deficient blood calcium levels.

Project Aim

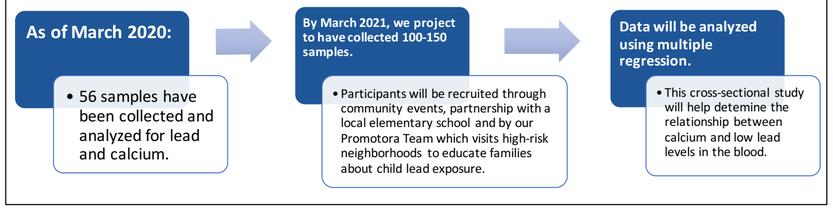
Measure child whole blood lead and calcium levels by inductively coupled plasma mass spectrometry (ICP-MS) to test the relationship between low-level lead exposure (<10µg/dL) and calcium absorption.

Methods



[1] Participants must be between 6mo-15 years old
[2] Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is performed by our partnering laboratory at KSU.

Progress to Date and Future Directions



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Acknowledgments

Research reported in this poster was supported by the National Institute of General Medical Sciences of the National Institutes of Health under linked Award Numbers RL5GM118969, TL4GM118971, and UL1GM118970, and by the U.S. Department of Housing and Urban Development, Lead Technical Studies Funding Program, SF424 (CS, PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health and HUD.