Lead:  Update on an old poison

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Objectives

At the end of the presentation, participants will be able to:

• Discuss the history of lead and understand how we ended up where we are
• Describe the sources of lead (common and new) for children, adolescents and pregnant women
• Provide education to patients regarding management of elevated blood lead
Lead (Pb)

![Periodic Table of the Elements](image-url)

Courtesy of sciencenotes.org
Epidemiology

Prevalence

- More than **500,000** children with blood lead levels (BLL) > 5 mcg/dL
  - 1976
    - 88% children with BLL >10 mcg/dL
    - Mean 15 mcg/dL
  - 2010
    - 0.8% children with BLL >10 mcg/dL
    - Mean 1.3 mcg/dL

CDC Website
## Blood lead levels considered toxic

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Toxic Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to 1971</td>
<td>≥60 mcg/dL (2.88 micromol/L)</td>
</tr>
<tr>
<td>1972-1975</td>
<td>≥40 mcg/dL (1.93 micromol/L)</td>
</tr>
<tr>
<td>1975-1985</td>
<td>≥30 mcg/dL (1.45 micromol/L)</td>
</tr>
<tr>
<td>1985-1991</td>
<td>≥25 mcg/dL (1.20 micromol/L)</td>
</tr>
<tr>
<td>1991-present</td>
<td>≥10 mcg/dL (0.48 micromol/L)</td>
</tr>
<tr>
<td>2010-present</td>
<td>≥5 mcg/dL (0.24 micromol/L)</td>
</tr>
</tbody>
</table>

mcg: micrograms; dL: deciliter; micromol: micromoles; L: liter.
The Loyal West in the Times of the Rebellion (1865)
Dr. John Lockhart Gibson

http://www.publichealthreports.org
History

http://www.nmic.org/nyccelp/documents/dutchboy

laugingsquid.com
Who is at risk?

- Age <6 years (12-36 months)
  - Poorly developed blood-brain barrier
- Urban > Rural
- Low-income > middle-income
- Older housing (before 1978)
- Refugees
- Foster children
- Adolescents with environmental exposure

Wright et al. (2003)
CDC website
Beaucham (2014)
Sources of Lead

- Ingestion or Inhalation
  - Dust containing lead
- Lead based paint (1978)
  - Windowsills
- Soil, food and water contamination
- Imported goods
  - Toys, crayons, cosmetics, cookware

Etzel (2012)
Agency for Toxic Substances & Disease Registry, CDC (2010)
## Occupational Exposures

<table>
<thead>
<tr>
<th>Plumbers, pipe fitters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead miners</td>
</tr>
<tr>
<td>Lead smelters and refiners</td>
</tr>
<tr>
<td>Auto repairers</td>
</tr>
<tr>
<td>Glass manufacturers</td>
</tr>
<tr>
<td>Shipbuilders</td>
</tr>
<tr>
<td>Printers</td>
</tr>
<tr>
<td>Plastic manufacturers</td>
</tr>
<tr>
<td>Police officers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steel welders or cutters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Construction workers (especially renovation and rehabilitation)</td>
</tr>
<tr>
<td>Rubber product manufacturers</td>
</tr>
<tr>
<td>Gas station attendants (past exposure)</td>
</tr>
<tr>
<td>Battery manufacturers</td>
</tr>
<tr>
<td>Battery recyclers</td>
</tr>
<tr>
<td>Bridge reconstruction workers</td>
</tr>
<tr>
<td>Firing range instructors</td>
</tr>
</tbody>
</table>
# Environmental Sources

<table>
<thead>
<tr>
<th>Homes/Buildings</th>
<th>Hobbies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead-containing paint/pigment</td>
<td>Glazed pottery making</td>
</tr>
<tr>
<td>Soil/dust near lead industries</td>
<td>Target shooting at firing ranges</td>
</tr>
<tr>
<td>Plumbing leachate</td>
<td>Lead soldering (e.g., electronics)</td>
</tr>
<tr>
<td>Ceramic ware (especially imported)</td>
<td>Painting</td>
</tr>
<tr>
<td>Leaded gasoline</td>
<td>Preparing lead shot</td>
</tr>
<tr>
<td>Vinyl miniblinds*</td>
<td>Stained-glass making</td>
</tr>
<tr>
<td>lead-painted homes</td>
<td>Car or boat repair</td>
</tr>
<tr>
<td></td>
<td>Home remodeling</td>
</tr>
</tbody>
</table>

### Other sources

- Folk remedies
- Tobacco smoking
- Cosmetics
- Moonshine whiskey
- Gasoline "huffing"
Foreign Body Ingestion

Over 100,000 calls to PCCs each year

- Folk remedies
- Fishing sinkers
- Curtain weights
- Buckshot
- Toys (jewelry, plastic, paint)

VanArsdale et al. (2004)
Case Report

Lead Toxicity From a Toy Necklace

123 mcg/dL

VanArsdale et al. (2004)
Toxicokinetics

- Directly absorbed
- Absorption
  - Age (70% in children vs. 20% in adults)
  - Nutritional status (fasting, iron and calcium deficiency)
  - Route of exposure (GI or respiratory tract)

Agency for Toxic Substances & Disease Registry, CDC (2010)
Toxicokinetics

Distribution
- Blood, soft tissues, mineralized tissues (bone and teeth)
- Half Life
  - Blood 28-36 days
  - Soft tissue 40 days
  - Mineralized tissue >25 years

Excretion
- Retained amounts (33% children, 1% adults)

Agency for Toxic Substances & Disease Registry, CDC (2010)
Toxicokinetics

Molecular Level

- Interferes with divalent cations and sulfhydryl groups
  - Inhibits or mimics actions of calcium
- Reversible in vitro
- In vivo leads to cell death
  - CNS (uncouples mitochondrial oxidative phosphorylation)
- Disrupts signal transduction cascades
Clinical Manifestations

Lead poisoning
Lead buildup in the body causes serious health problems

Symptoms
- Headaches
- Irritability
- Reduced sensations
- Aggressive behavior
- Difficulty sleeping

- Abdominal pain
- Poor appetite
- Constipation
- Anemia

Additional complications for children:
Lead is more harmful to children as it can affect developing nerves and brains

- Loss of developmental skills
- Behavior, attention problems
- Hearing loss
- Kidney damage
- Reduced IQ
- Slowed body growth

Source: MedlinePlus/Mayo Clinic

Etzel (2012)
Lowest exposure

- Asymptomatic
- Decreased learning and memory
- Decreased verbal ability
- Early signs of hyperactivity
- Lowered IQ
- Impaired speech and hearing
Low Exposure

- Myalgias
- Mild fatigue
- Irritability
- Lethargy
- Occasional abdominal discomfort
Moderate Exposure

- Arthralgia
- Fatigue
- Difficulty concentrating
- Muscle weakness
- Tremor

- Headache
- Abdominal pain
- Vomiting
- Weight loss
- Constipation
High Exposure

- Muscle weakness or paralysis
- Encephalopathy
  - Seizures, coma, death
- Abdominal colic
- Lead lines on gingival tissue

Courtesy of UpToDate
Skeletal Lead Lines

Courtesy of UpToDate
Neurologic

Intelligence/Cognition
Academic Achievement
Behavioral Issues
  • Emotional lability
  • Anxiety
  • Hyperactivity
Loss of milestones

Liu et al. (2014)
Bellinger et al. (1991)
Cognition

- National Health and Nutrition Examination Survey (NHANES)
- 4853 children (6-16 years of age)
- Cognitive deficits even with blood lead level (BLL) <5 mcg/dL
- For every 1 mcg/dL increase in BLL
  - 1 and 0.7 point decrease in reading and arithmetic scores, respectively

Lanphear et al. (2000)
Reading Readiness in Kindergarten

- N=3406
- Average blood lead level 4.3 mcg/dL
- PALS-K test to assess reading readiness

Mclaine et al. (2013)
Hematologic

- Hypochromic, normocytic or microcytic, reticulocytosis
- Decreased hemoglobin synthesis
  - >40 mcg/dL
- Hemolysis
  - >70 mcg/dL
Other Systems

Reproductive
- Fertility

Renal
- Hypertension

Endocrine
- Vitamin D and growth

Etzel (2012)
Agency for Toxic Substances & Disease Registry, CDC (2010)
The presence of symptoms:

- Lethargy
- Decreased appetite
- Intermittent abdominal pain
- Vomiting
- Pica
- Nutritional status (particularly iron and calcium)
- Family history of lead poisoning
- History of lead poisoning in playmates
- Foreign birthplace or recent foreign residence

Etzel (2012)
Environmental History

- Age of housing
- Home renovations
- Work history of parents
- Hobbies of all family members
- Water source
- Play areas
- Daycare
Physical Exam

- Growth parameters
- Blood pressure
- Neurologic assessment
- Neurobehavioral assessment
- Language development
- Abdominal tenderness

Etzel (2012)
Screening

- Universal Screening/Testing (12 and 24 months)
  - Inadequate data
  - Insured through Medicaid
  - >27% housing built before 1950
  - >12% of children 12-36 months with blood lead level >5 mcg/dL
  - Recently entering United States (6 months - 6 years)
    - Immigrant, adoptee, foster, refugee
  - <72 months and missed previous screening

Etzel (2012)
Reference Value

Blood lead level (BLL) >5 mcg/dL
Who else should be tested?

- Other reasons to obtain blood lead level
  - Growth delay
  - Speech or language delay
  - Anemia
  - Inattentiveness
  - Behavioral problems
  - Adolescents with exposure

Beaucham (2014)
Laboratory Evaluation

Repeat (confirm) venous lead level

Venous lead level in siblings

CBC, reticulocyte count, serum iron, iron binding capacity, and ferritin

Pre-treatment evaluation
  
  Serum electrolytes

  BUN, creatinine

  Calcium, magnesium

  AST/ALT, alkaline phosphatase,

  Urinalysis

Etzel (2012)
CDC Website
Management (<5 mcg/dL)

- Review results with family
- Repeat blood lead level (BLL) in 6-12 months
- If <12 months of age
  - Repeat BLL in 3-6 months
- Environmental history
- Assess nutrition, development and risk factors for iron deficiency
- Anticipatory guidance

Management (5-14 mcg/dL)

- Report to health department
- Perform the previous steps
- Repeat blood lead level in 1-3 months
  - If stable, repeat in another 3 months
- Nutritional counseling
  - CBC, Ferritin
  - Multivitamin with iron
- Developmental Assessment
Management (15-44 mcg/dL)

- Perform previous steps
- Repeat level within 1-4 weeks
- Further evaluation
  - Abdominal plain films
  - Gut decontamination

Management (>44 mcg/dL)

- Repeat level within **48 hours**
- Consider hospitalization
  - Management
    - Safety of the home (lead hazards)
    - Isolation of lead source
    - Social situation
    - Chronicity of exposure
  - Chelation therapy
Chelation therapy

- Moderate intoxication (45-69 mcg/dL)
  - DMSA (meso-2,3-dimercaptosuccinic acid [Succimer])
    - Oral
    - 10 mg/kg (350 mg/m²) TID for 5 days, followed by same dose BID for 14 days
    - Typically used until blood lead level is <45 mcg/dL
  - D-penicillamine
    - 2nd line agent (unless you live in Boston….)
• Severe intoxication (>70 mcg/dL)

• Consult a toxicologist/expert

• Dimercaprol (BAL)
  • 3-5 mg/kg (75 mg/m²) IM q4hr for 3-5 days

• Calcium disodium EDTA
  • Administered after BAL
  • 35-50 mg/kg/day (1000-1500 mg/m²) IV for 5 days

Agency for Toxic Substances & Disease Registry, CDC (2010)
Prevention and Health Care Role

- Primary prevention is key
  - Pediatricians play an important role
- Determine the need for lead testing
  - No safe lead level
- Provide education and anticipatory guidance
- Notify local health agencies
  - Abatement of lead source
  - Remediation steps

Agency for Toxic Substances and Disease Registry (2010)
Long Term Impact

Early Dentine Lead Levels and Educational Outcomes at 18 Years

David M. Fergusson, L. John Horwood, and Michael T. Lynskey
Christchurch Health and Development Study, Christchurch School of Medicine, New Zealand

• Poorer reading abilities
• More often left school early
• More often left school without qualifications
• Lower levels of success on examinations

Fergusson et al. (2014)
Long Term Impact

- Higher absenteeism in high school
- Lower class rank
- Poorer vocabulary and grammar scores
- Longer reaction time
- Poorer hand eye coordination
- Hypertension
- Reproductive problems

Needleman et al. (1990)
Take Home Points

- Lead exposure is still a major concern for children
- No known threshold for lead exposure and no safe lead level
- Current reference value is >5 mcg/dL (mean 1.3 mcg/dL)
- Neurocognitive effects cannot be reversed even with chelation
- Primary prevention is key
- Most children are asymptomatic
- Screening and parental education are important
- Chelation should be considered for blood lead level >44 mcg/dL in coordination with a toxicologist
- Health effects of lead exposure can persist into adulthood
References

References