



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

1 1IA 11A																	18 VIIIA 8A
1 H Hydrogen 1.0079	2 He Helium 4.00260																
3 Li Lithium 6.941	4 Be Beryllium 9.01218											5 B Boron 10.811	6 C Carbon 12.011	7 N Nitrogen 14.00674	8 O Oxygen 15.9994	9 F Fluorine 18.998403	10 Ne Neon 20.1797
11 Na Sodium 22.989768	12 Mg Magnesium 24.305	3 III B 3B	4 IV B 4B	5 V B 5B	6 VI B 6B	7 VII B 7B	8 VIII 8	9 VIII 8	10 VIII 8	11 IB 1B	12 IIB 2B	13 Al Aluminum 26.981539	14 Si Silicon 28.0855	15 P Phosphorus 30.973762	16 S Sulfur 32.066	17 Cl Chlorine 35.4527	18 Ar Argon 39.948
19 K Potassium 39.0983	20 Ca Calcium 40.078	21 Sc Scandium 44.95591	22 Ti Titanium 47.88	23 V Vanadium 50.9415	24 Cr Chromium 51.9961	25 Mn Manganese 54.938	26 Fe Iron 55.847	27 Co Cobalt 58.9332	28 Ni Nickel 58.6934	29 Cu Copper 63.546	30 Zn Zinc 65.39	31 Ga Gallium 69.732	32 Ge Germanium 72.64	33 As Arsenic 74.92159	34 Se Selenium 78.96	35 Br Bromine 79.904	36 Kr Krypton 83.80
37 Rb Rubidium 85.4678	38 Sr Strontium 87.62	39 Y Yttrium 88.90585	40 Zr Zirconium 91.224	41 Nb Niobium 92.90638	42 Mo Molybdenum 95.94	43 Tc Technetium 98.9072	44 Ru Ruthenium 101.07	45 Rh Rhodium 102.9055	46 Pd Palladium 106.42	47 Ag Silver 107.8682	48 Cd Cadmium 112.411	49 In Indium 114.818	50 Sn Tin 118.71	51 Sb Antimony 121.760	52 Te Tellurium 127.6	53 I Iodine 126.90447	54 Xe Xenon 131.29
55 Cs Cesium 132.90543	56 Ba Barium 137.327	57-71 Lanthanide Series	72 Hf Hafnium 178.49	73 Ta Tantalum 180.9479	74 W Tungsten 183.85	75 Re Rhenium 186.207	76 Os Osmium 190.23	77 Ir Iridium 192.22	78 Pt Platinum 195.08	79 Au Gold 196.9665	80 Hg Mercury 200.59	81 Tl Thallium 204.3833	82 Pb Lead 207.2	83 Bi Bismuth 208.98037	84 Po Polonium [209]	85 At Astatine [209]	86 Rn Radon [222]
87 Fr Francium 223	88 Ra Radium 226	89-103 Actinide Series	104 Rf Rutherfordium [261]	105 Db Dubnium [262]	106 Sg Seaborgium [266]	107 Bh Bohrium [264]	108 Hs Hassium [269]	109 Mt Meitnerium [268]	110 Ds Darmstadtium [269]	111 Rg Roentgenium [272]	112 Cn Copernicium [277]	113 Uut Ununtrium unknown	114 Uuq Ununquadium [289]	115 Uup Ununpentium unknown	116 Uuh Ununhexium [286]	117 Uus Ununseptium unknown	118 Uuo Ununoctium unknown
			57 La Lanthanum 138.9055	58 Ce Cerium 140.115	59 Pr Praseodymium 140.90765	60 Nd Neodymium 144.24	61 Pm Promethium 144.9127	62 Sm Samarium 150.36	63 Eu Europium 151.9655	64 Gd Gadolinium 157.25	65 Tb Terbium 158.92534	66 Dy Dysprosium 162.50	67 Ho Holmium 164.93032	68 Er Erbium 167.26	69 Tm Thulium 168.93421	70 Yb Ytterbium 173.04	71 Lu Lutetium 174.967
			89 Ac Actinium 227	90 Th Thorium 232	91 Pa Protactinium 231	92 U Uranium 238	93 Np Neptunium 237	94 Pu Plutonium 244	95 Am Americium 243	96 Cm Curium 247	97 Bk Berkelium 247	98 Cf Californium 251	99 Es Einsteinium [254]	100 Fm Fermium [257]	101 Md Mendelevium [258]	102 No Nobelium [259]	103 Lr Lawrencium [262]
			Alkali Metal	Alkaline Earth	Transition Metal	Basic Metal	Semimetals	Nonmetals	Halogens	Noble Gas	Lanthanides	Actinides					

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

Epidemiology

Blood lead levels considered toxic

Prior to 1971	≥ 60 mcg/dL (2.88 micromol/L)
1972-1975	≥ 40 mcg/dL (1.93 micromol/L)
1975-1985	≥ 30 mcg/dL (1.45 micromol/L)
1985-1991	≥ 25 mcg/dL (1.20 micromol/L)
1991-present	≥ 10 mcg/dL (0.48 micromol/L)
2010-present	≥ 5 mcg/dL (0.24 micromol/L)

mcg: micrograms; dL: deciliter; micromol: micromoles; L: liter.



*The Loyal West in the Times of the
Rebellion (1865)*

Dr. John Lockhart Gibson



History



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



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

Plumbers, pipe fitters

Lead miners

Lead smelters and refiners

Auto repairers

Glass manufacturers

Shipbuilders

Printers

Plastic manufacturers

Police officers



Steel welders or cutters

Construction workers (especially renovation and rehabilitation)

Rubber product manufacturers

Gas station attendants (past exposure)

Battery manufacturers

Battery recyclers

Bridge reconstruction workers

Firing range instructors



Environmental Sources

Homes/Buildings

Lead-containing paint/pigment

Soil/dust near lead industries

Plumbing leachate

Ceramic ware (especially imported)

Leaded gasoline

Vinyl miniblinds*

lead-painted homes



Hobbies

Glazed pottery making

Target shooting at firing ranges

Lead soldering (eg, electronics)

Painting

Preparing lead shot

Stained-glass making

Car or boat repair

Home remodeling

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)



Case Report

Lead Toxicity From a Toy Necklace **123 mcg/dL**



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)

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)



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

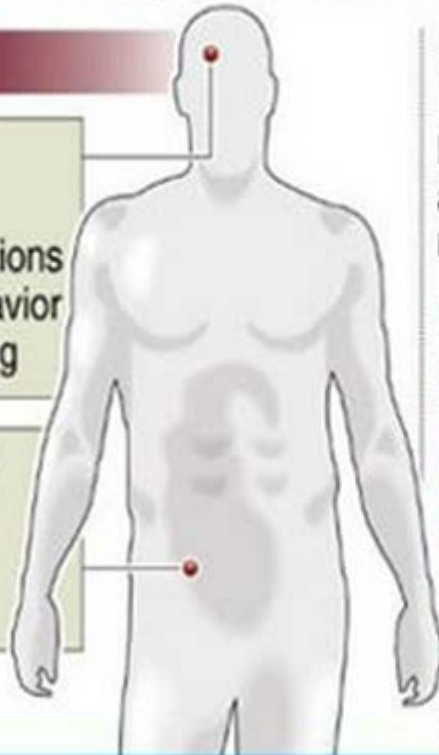
Lead poisoning

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

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

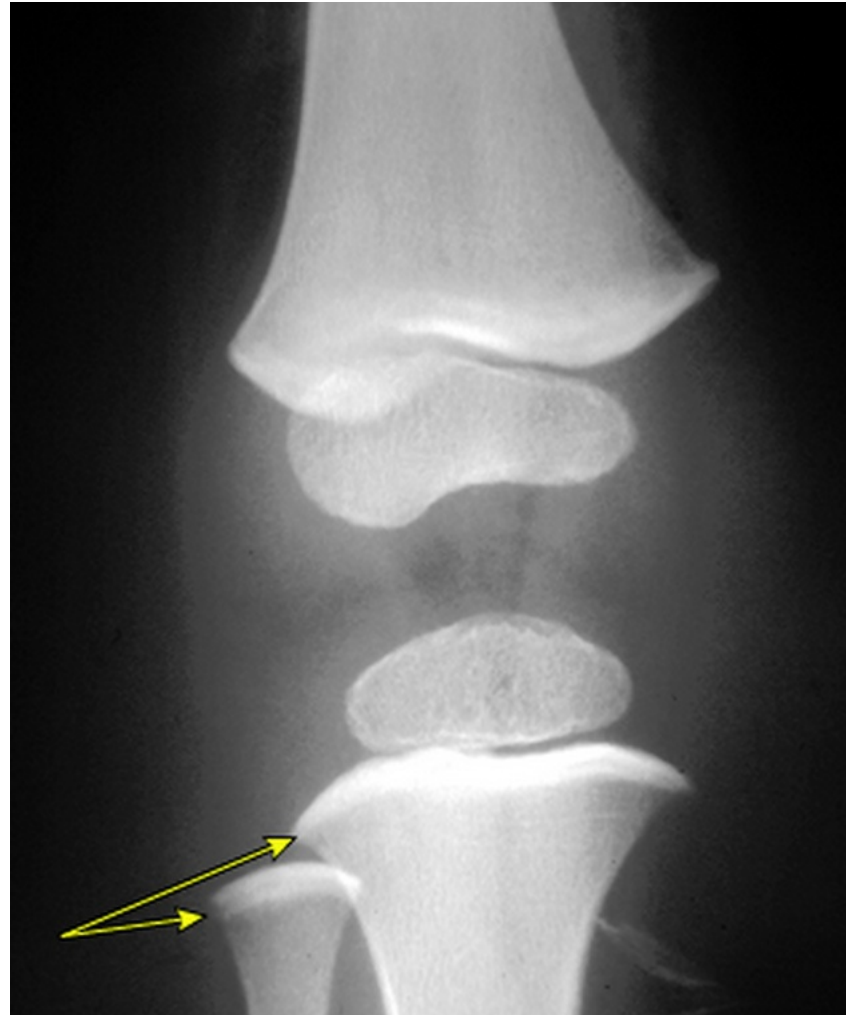
Abdominal colic

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

Cognition

R E S E A R C H A R T I C L E

BRUCE P. LANPHEAR, MD MPH ■ KIM DIETRICH, PHD

PEGGY AUINGER, MS ■ CHRISTOPHER COX, PHD

Cognitive Deficits Associated with Blood Lead Concentrations $<10 \mu\text{g}/\text{dL}$ in US Children and Adolescents

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

Reading Readiness in Kindergarten

PEDIATRICS®

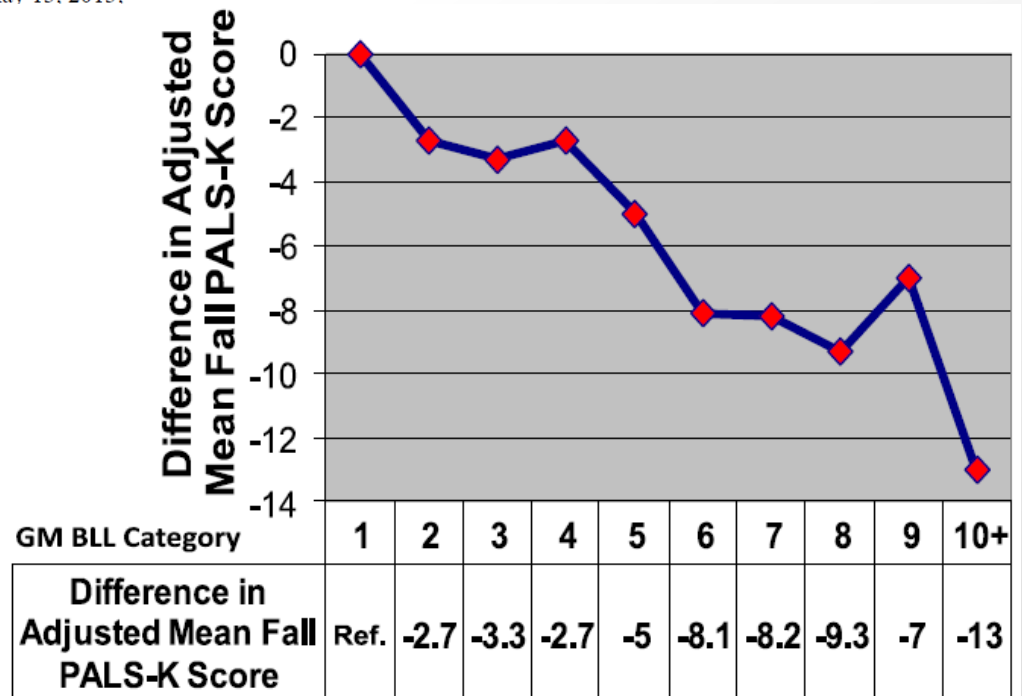
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Elevated Blood Lead Levels and Reading Readiness at the Start of Kindergarten

Pat McLaine, Ana Navas-Acien, Rebecca Lee, Peter Simon, Marie Diener-West and Jacqueline Agnew

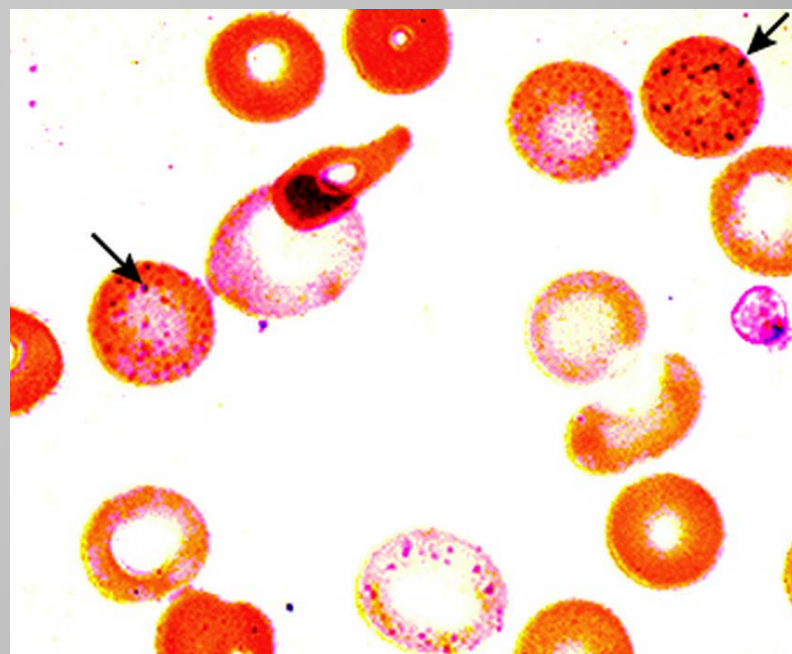
Pediatrics 2013;131:1081; originally published online May 13, 2013;
DOI: 10.1542/peds.2012-2277

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



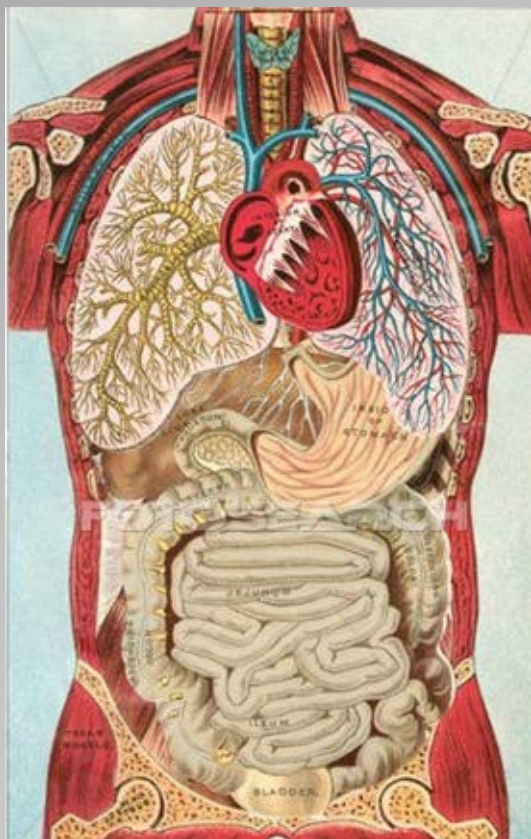
Hematologic

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



Courtesy of UpToDate

Other Systems



Reproductive

- Fertility

Renal

- Hypertension

Endocrine

- Vitamin D and growth

History

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

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

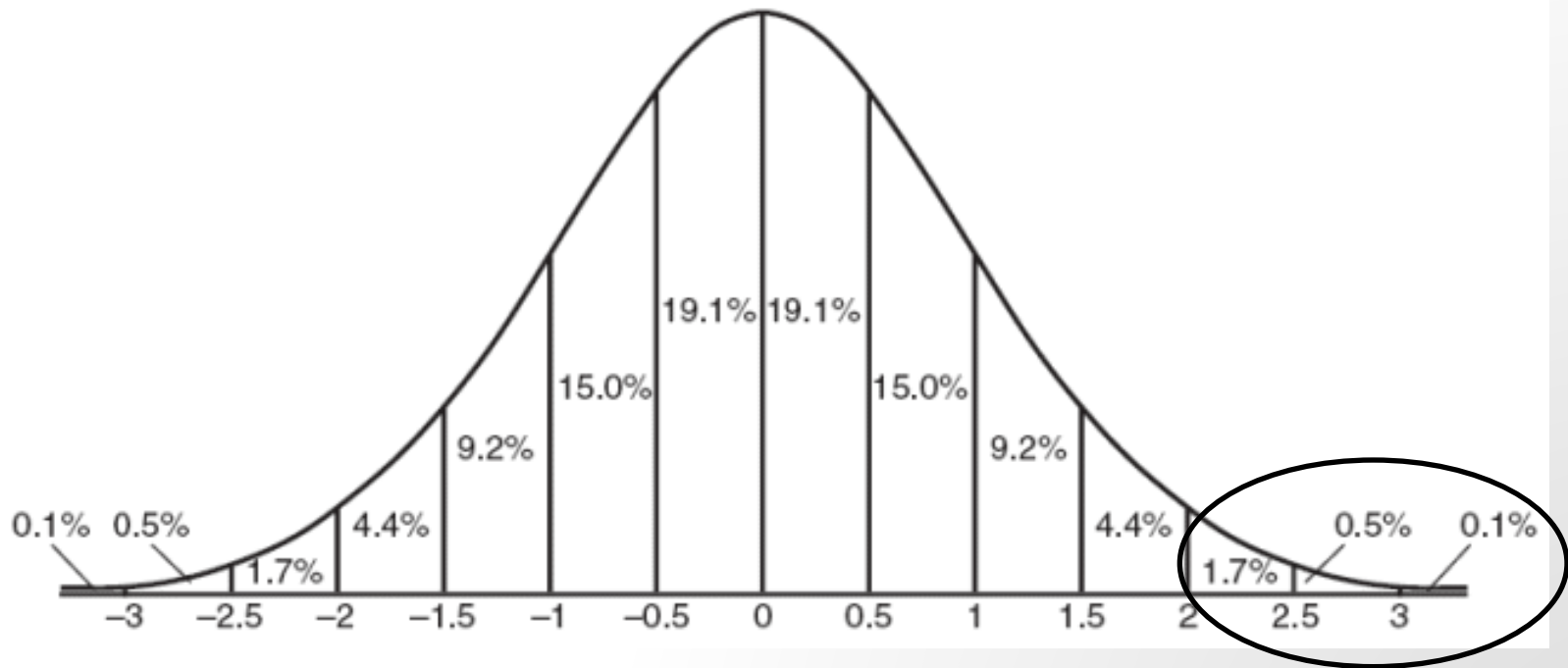
Abdominal tenderness

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

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



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

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

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

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

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



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

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