Lead Exposure: Pregnancy & Beyond

Presented by:

Steve Lamm, MD, Georgetown University, MotherToBaby/Organization of Teratology Information Specialists member
Claire Coles, PhD, Emory University, MotherToBaby Georgia & PEHSU Region 4
Robert Geller, MD, Emory University, PEHSU Region 4
Richard K. Miller, PhD, University of Rochester Medical Center, MotherToBaby UR Medicine

Hosted by the National Society of Genetic Counselors

Overview

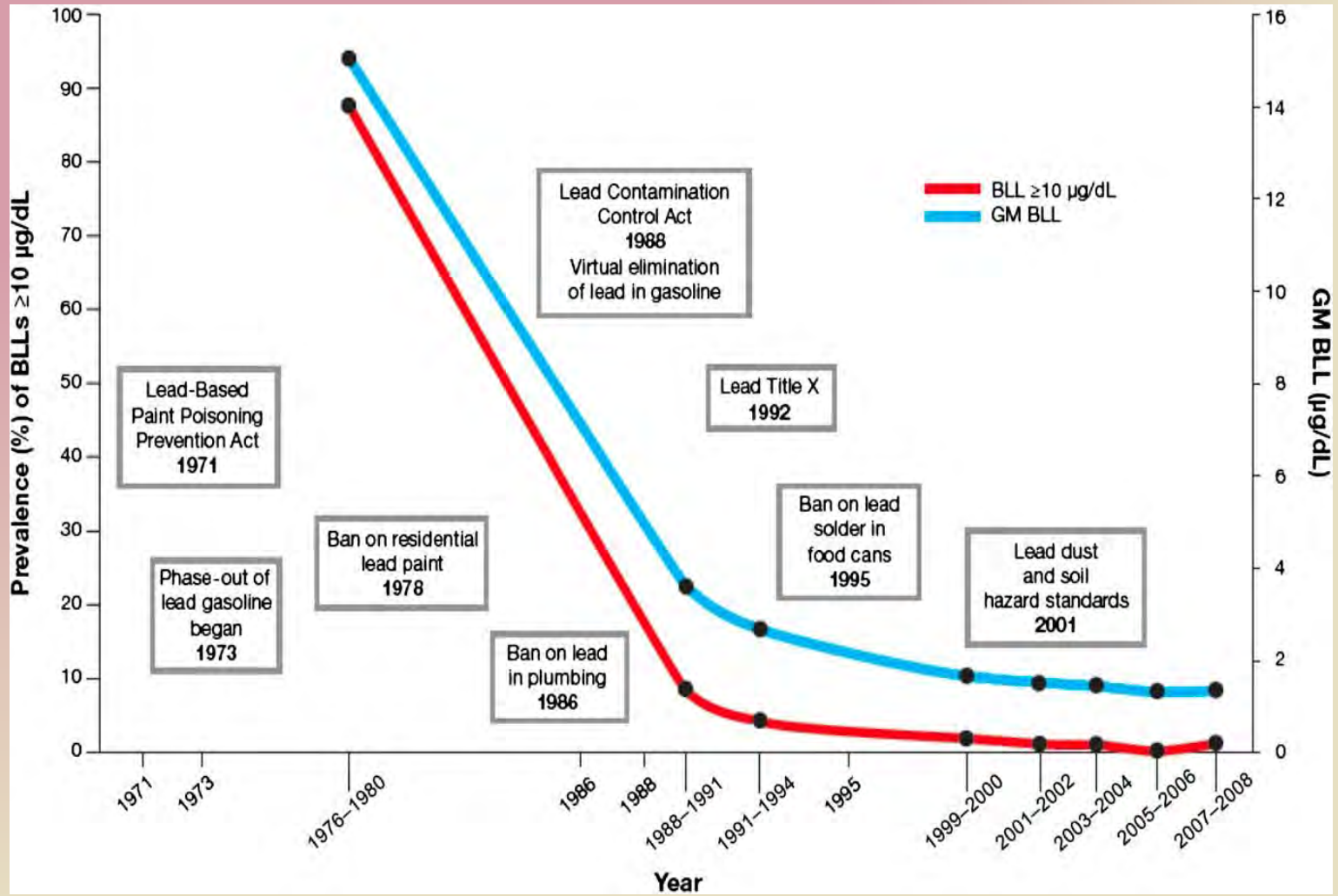
by Steven H. Lamm, MD, DTPH

Member of MotherToBaby, a service of the Organization of Teratology Information Specialists (OTIS) & The Teratology Society;
also, Department of Pediatrics (Epidemiology)
Georgetown University School of Medicine
(202) 333-2364

CDC Recommendations and Public Health Approach

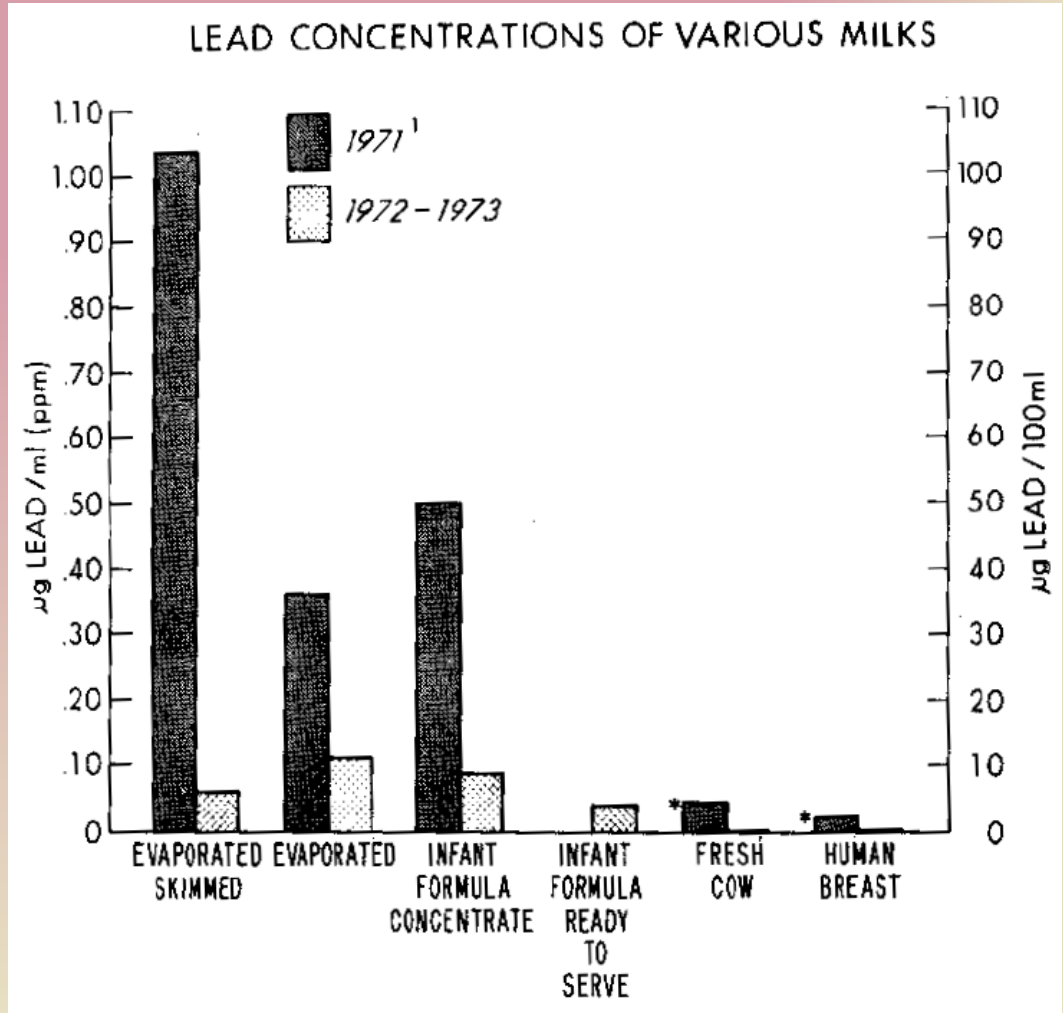
Lead has been recognized as a neurotoxin since the times of the Romans.

Its modern regulation in the United States goes back fifty years to the **early 1970's with** reduction of lead in Paint, Gasoline, and Infant Formula.



Lead in Infant Formulas – Knowledge does bring Response

- Infant formula is a specific lead exposure that is unique to infants.
- 1971 levels indicated that the average newborn received its maximum permitted lead exposure from its formula alone.
- Note the rapid reduction of lead levels in infant formulas by 1972-73 after the industry was notified about lead problem.

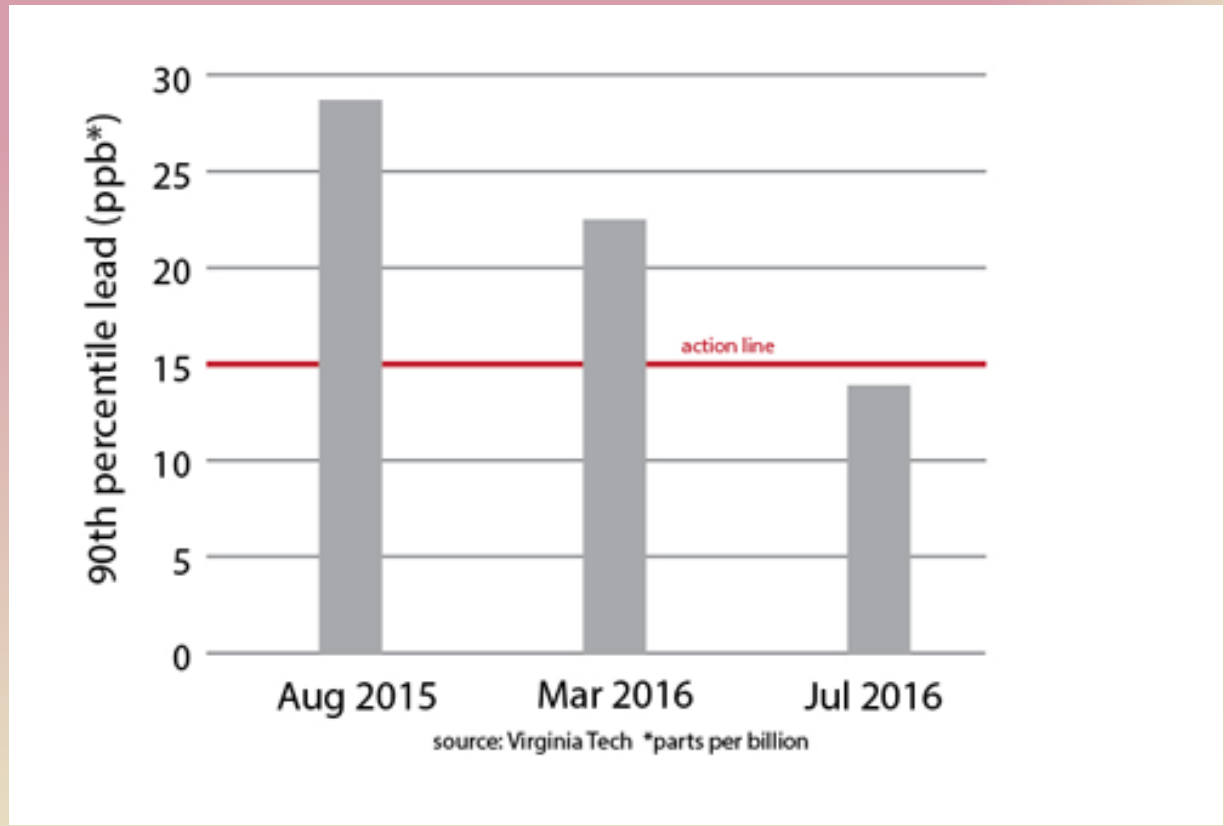


Common External Sources of Exposure

Common

- Indoor Dust and Paint
- Renovations
- Drinking Water
- Soil
- Occupational
- Hobbies
- Cosmetics
- Foreign medicines
- Glazed pottery

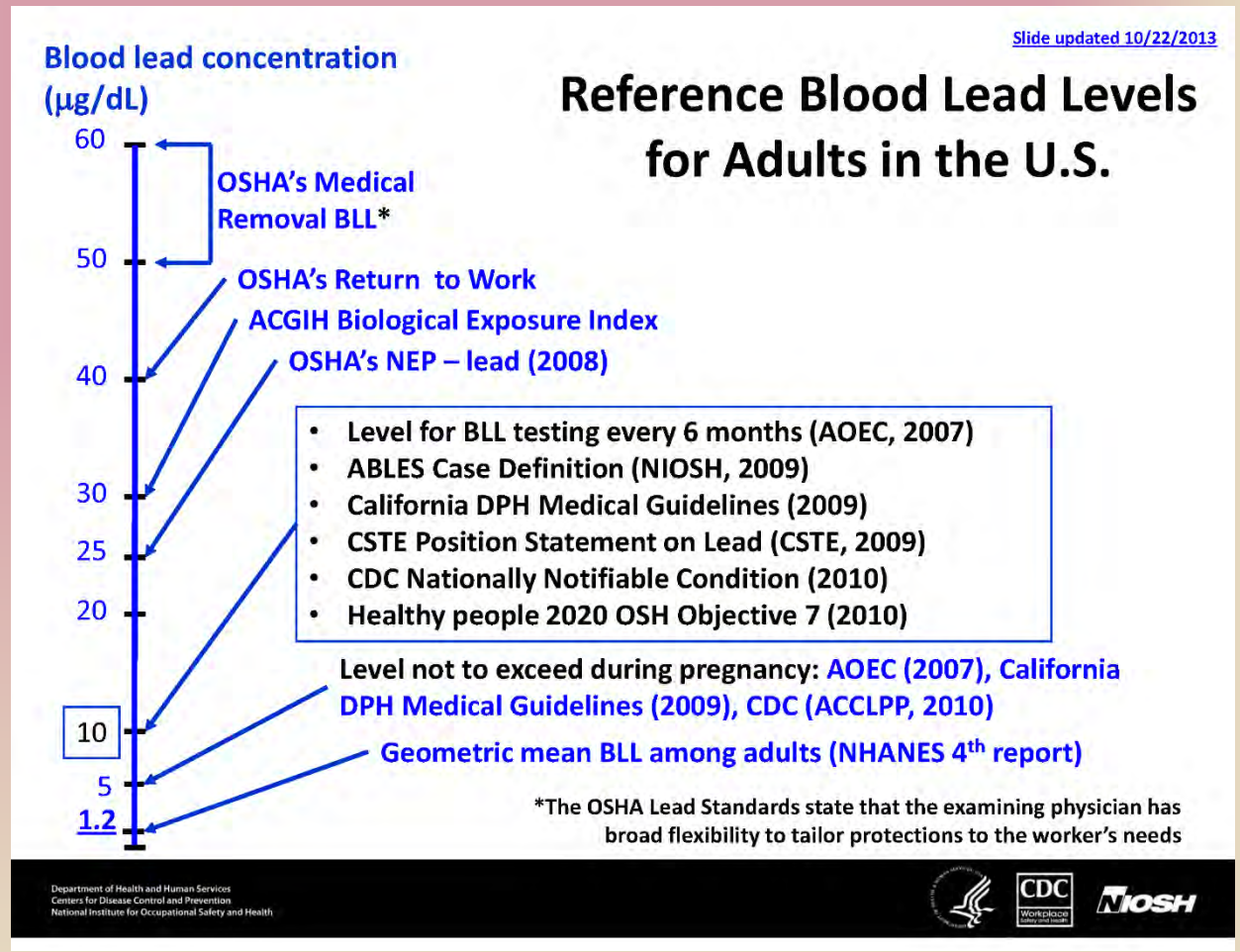
Drinking Water



Current Lead Regulations

Environmental

- Ambient air 0.15 ug/m^3
- Lead paint 90 ppm (mg/L)
- Painted surfaces 1 ug/cm^2 (XRF)
- Floor – Screen 25 ug/ft^2
- Risk assessment 40 ug/ft^2
- Playground soil 400 ppb (ug/gm)
- Drinking water 15 ppb in <10%

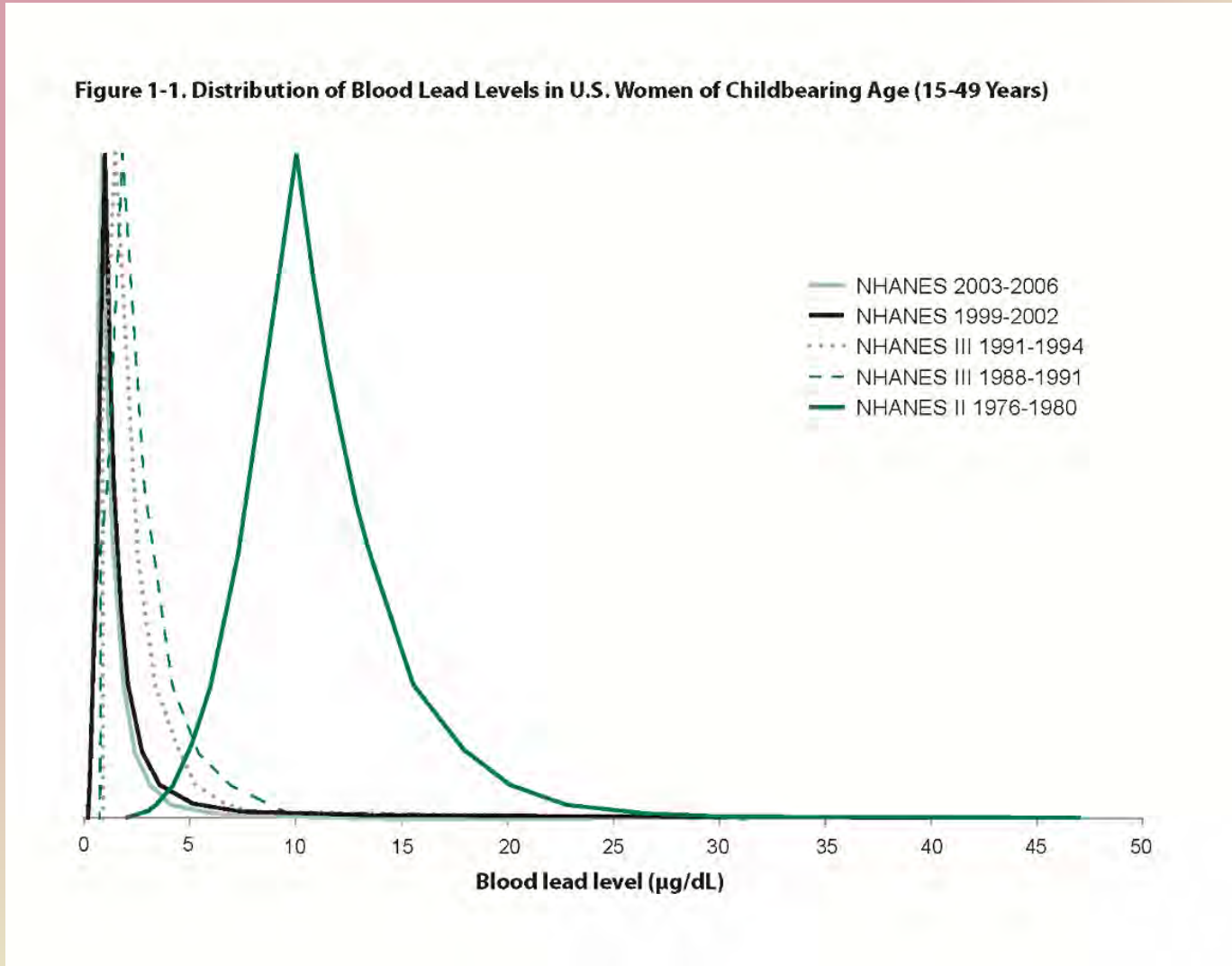


Internal Source of Exposure

- Over 90% of lead in the adult is stored in bone.
- Pregnancy and Lactation are both associated with increased bone turnover, and that means release of bone lead to increase blood lead.
- Thus, lead sources can be either endogenous (internal) or exogenous (external) or both.

Lead levels in Women (15-49 years)

- Blood lead levels for WCBA have dropped remarkably in the past 35 years.
- It appears that what was the LCB in 1976-80 was the UCB in 2003-06.
- 5 µg/dL is today about the 99% level for WCBA.



Current Reference level is BLL < 5 µg/dL

- CDC - "**A BLL >= 5 µ**g/dL in a pregnant woman indicates that she has, or has recently had, exposure to lead well above that for most women of child-**bearing age in the US population." [CDC, 2010,** page 52]

- CDC is considering lowering the reference level to 3.5 µg/dl.

Algorithms for Response

Pregnancy

- Test All,
- If BLL < 5 µg/dL, Explain.
- If BLL ≥ 5 µg/dL, Explain.

Then – Retest in 1 month, find source and isolate from it.

- If BLL > 45 µg/dL, retest in 24 hrs.

Newborn

- If mother BLL > 5 µg/dL, test at birth (umbilical or venous).
- If neonate BLL > 45 µg/dL, retest and get immediate consult.
- If neonate BLL 25-44 µg/dL, retest in 2 weeks and get consult if not reduced.
- If neonate BLL 5-24 µg/dL, retest in 1 month.

Breast feeding

- Current recommendation – Continue if maternal BLL < 40 µg/dL (Subject to change) and infant BLL ≤ 5 ug/dL.

  Benefit exceeds Risk.

- Discontinue if maternal BLL > 20 µg/dL, infant BLL > 5 µg/dL and not falling.

- Consider endogenous lead source from mobilization of bone lead.

References

- Ettinger 2010. CDC Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women. US DHHS Atlanta, Nov 2010. (302 pp)
- CDC 2012. ACCLPP Report – Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. Jan 4, 2012. (65 pp).
- AAP 2016. Prevention of Childhood Lead Toxicity. Pediatrics July 20, 138(1), e20161493 (17 pp).
- MtB 2016. Questions and Answer on Lead during Pregnancy or Lactation. [Website]
- MTB 2016. Fact Sheet on Lead @ mothertobaby.org

Neurobehavioral Effects of Lead

by Claire D. Coles, PHD
Emory University
MotherToBaby Georgia
PEHSU Region 4

Lead

- Heavy Metal.
- Found in soil, air, included in gasoline, paint
- Problems first noted historically
- ug/dL (micrograms of lead per deciliter of blood)- reference level= 5ug/dL (CDC, 2016)
- Substantial reduction in environmental lead levels in last 40 years.
- Studied comprehensively

Effects of High Lead Exposure on Development

Historically, lead toxicity associated with fatigue, irritability, mental illness, decreased fertility, death.

Chronic exposure could produce neurotoxicity with intellectual disability ("IQ"), learning deficits, and behavioral problems.

Needleman (1974) found an inverse relationship between lead in children's teeth and IQ as well as increased "nonadaptive classroom behavior" in such children.

"ADHD"-like behaviors are greater in individuals with lead exposure-that is, impulsive behavior, lack of cognitive behavioral control. (Winneke, 2011)

The Lead and Development Controversies

- Everyone agrees that high lead levels are bad, but is there an effect on Cognition of lead levels at less than 5 to 10 ug/dL?
- Is it enough to test global IQ, or should other measures be used?
- Is prenatal or postnatal lead exposure more damaging to subsequent child development?
- Is behavior (that is to say, externalizing behavior and delinquency) affected by lead exposure?

Prenatal vs Postnatal Lead Exposure and Development?

- Questions about the relative risk of prenatal and postnatal exposure.
- In general, the risk appears to be higher when exposure is postnatal. Children can ingest more lead directly.
- There appear to be some risks associated with prenatal exposure at various levels and with breast feeding when maternal levels are greater than 20 ug/dl.
  - Neonates with elevated umbilical cord blood (>10 ug/dL) showed disturbance in arousal and sleep.(Mamtani, et al, 2008)
  - Later in infancy, the same infants had lower scores on the Bayley Mental Development Index at six months (MDI) (Al-Saleh, et al, 2009)
  - Lead can in breast milk (Ettinger, et al, 2004) but breast feeding is recommended unless maternal levels are high.

Lead: Effects on Child Development

- Meta-analysis of 26 epidemiological studies* found:
  - Moderate to high blood-lead levels (30-40 ug/dL) affect cognitive functioning (IQ) and ADHD
  - Lower level lead associated with small IQ (global) deficits (1-2 pts)
  - Unclear if levels as low as 5ug/dl cause risk for behavior or cognition in given individuals
  - Many confounders and effect modifiers must be considered
    - Socioeconomic Status (SES) (e.g., Poverty)
    - Reverse causality (e.g., Impulsivity)
    - Caregiving styles and factors (e.g., breast feeding)
    - Other toxins and teratogens (e.g., substance abuse)
    - Nutrition (e.g., iron deficiency)

*Pocock, et al (1994) Brit Med J, 1189-1196

Winneke, G (2011) Developmental aspects of environmental neurotoxicology: Lessons from lead and polychlorinated biphenyls. J. Neurological Sciences 308, 9-15

Experimental Studies of Lead Exposure and Child Development

- Motor Skills impaired during infancy/preschool
- BPb associated with ↓ fine motor functions when confounders controlled. Gross motor skills unaffected.

↓

- IQ in school aged children (4 to 8 years)-Several IQ points with low lead levels.

- Perceptual/Motor skills ↓ ; affected more than Language.

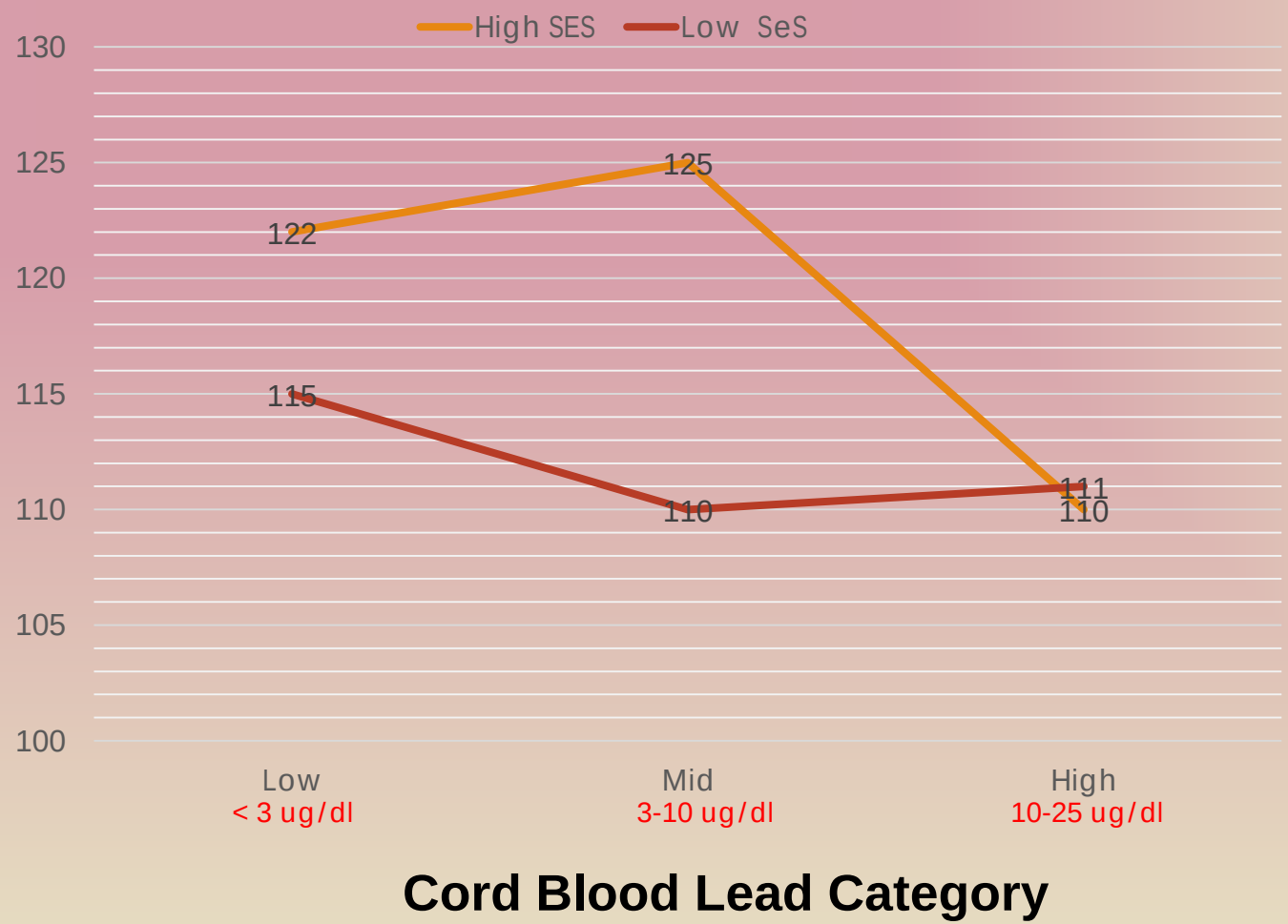
Effect Modification (Boston Prospective Study)

Bayley

Mental

Development

Index at 24 months



Bellinger et al. (1988) < 3, 3-<10, 10-<25 ug/dl. Conclusion: Early postnatal BLL 10-25 ug/dl assoc c lower MDI but only for low SES.

IQ at 5 years and Blood Lead: The Low Lead Controversy

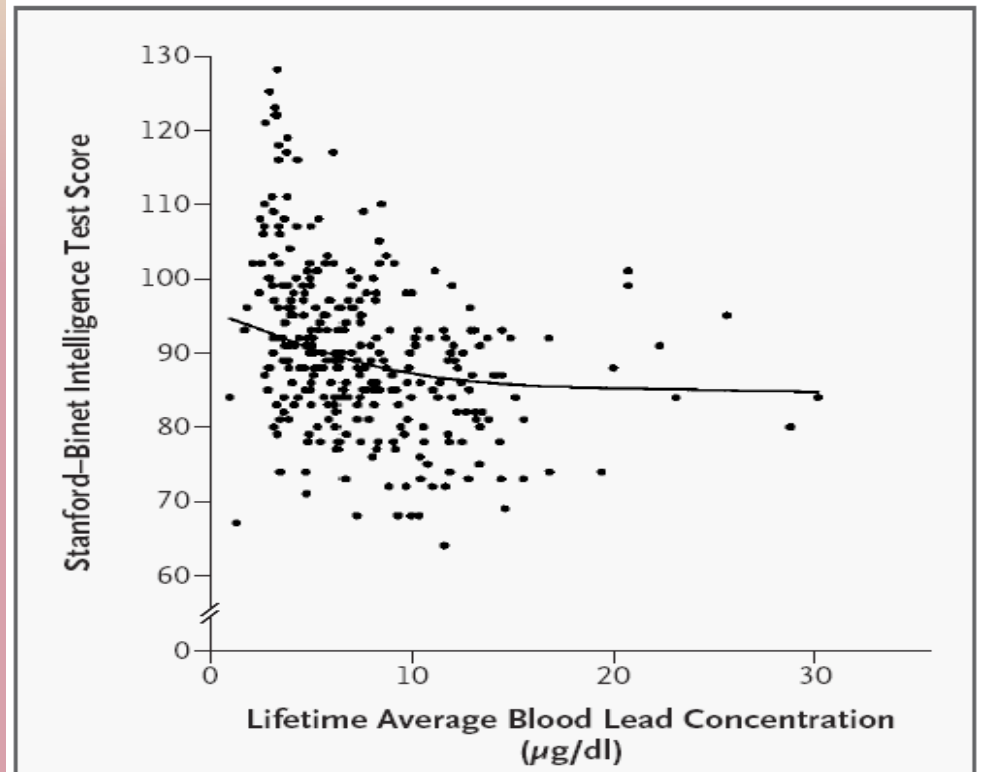


Figure 2. IQ as a Function of Lifetime Average Blood Lead Concentration.

IQ was assessed with use of the Stanford–Binet Intelligence Scale, fourth edition. The line represents the relation between IQ and lifetime average blood lead concentration estimated by the covariate-adjusted penalized-spline mixed model. Individual points are the unadjusted lifetime average blood lead and IQ values. To convert values for lead to micromoles per liter, multiply by 0.0483.

Source:

Canfield, Henderson, et al. (2003) New Engl J Med, 1517-1526

Lead Exposure and Behavior Problems

- ADHD symptoms appear to be common in a number of studies and include:
  - hyperactivity, impulse disinhibition, distractibility, and conduct problems. (Braun, et al. 2006; Nigg, et al, 2010; Wang, et al., 2008).
  - Evidence includes both behavioral surveys and experimental paradigms. (Minder et al., 1994; Chido, et al, 2007)

- Behavior problems were noted by Cincinnati Lead Study (1979-1985) (Dietrich, et al, 2001)
  - Longitudinal Sample Reassessed at X=15.6 years
  - 92% African-American, low SES
  - Higher levels of self-reported delinquent behavior in adolescence associated with BPb levels > 15 ug/dl at 6.5 yrs.
  - Not all environmental factors controlled.
  - Both prenatal and postnatal lead exposure affected outcomes

Treatment for Elevated Body Lead Levels

by Robert J. Geller, MD
Emory University
PEHSU Region 4

Lead Poisoning – What to Do?

- Terminate exposure to further lead
- Abate housing
  - Lead paint
  - Lead plumbing
  - Renovate safely
- Avoid leaded pottery for cooking / eating
- Avoid ethnic remedies that contain lead

Interventions for the Individual

- Early detection
  - Screening questions and blood levels
- Supportive care
  - Early intervention programs have been proven to mitigate lead-driven disabilities
- Symptom- based monitoring and treatment
  - Hypertension, for example
- Chelation

Natural History of Human Lead Body Burden

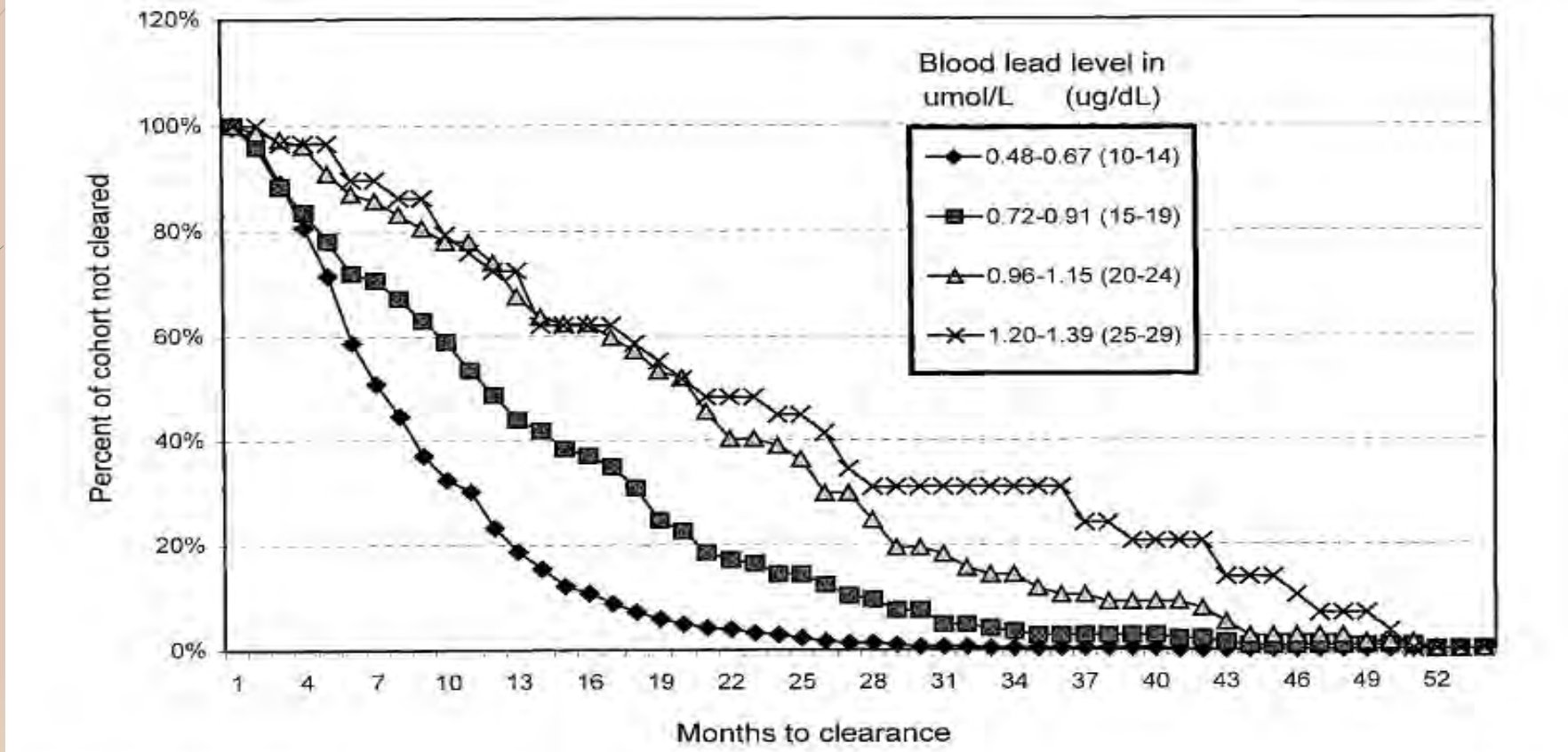


Figure 2. Kaplan-Meier survival analysis showing the percentage of cohort categorized by lead level cleared over time in months.

Roberts JR et al. Clin Toxicol 2001; 39: 153-160.

Lead Poisoning – What to Do?

- The real question should be, “What can we do that makes a difference?”

Elevated Lead Levels

- Optimal = 0
- Current US Population average ≈ 2 µg/dL
- CDC Intervention Level = 5 µg/dL
- Chelation Level ?
  - One chelator's FDA labeling uses level > 45 µg/dL

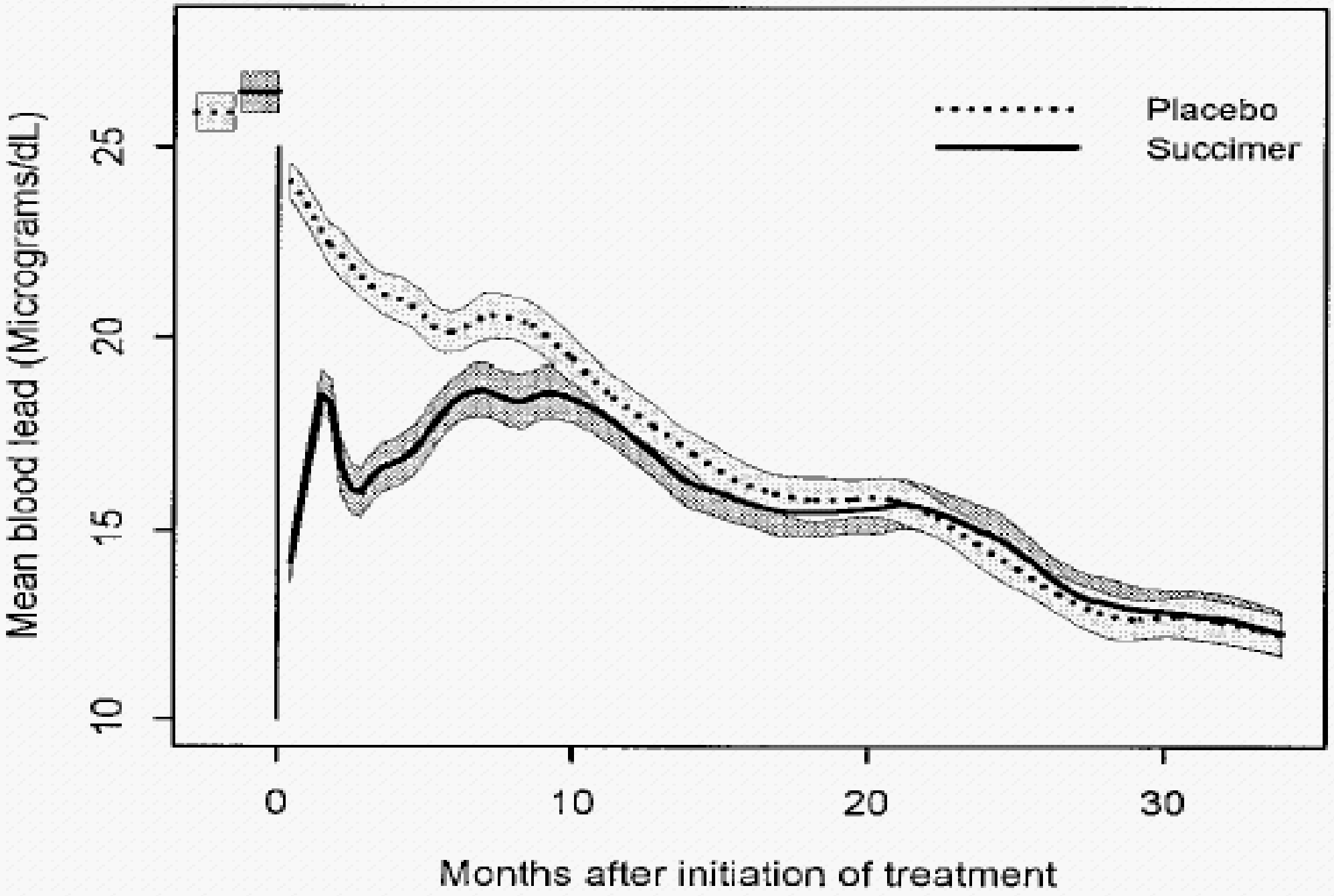
Initial Management

- Eliminate further exposure
- Confirm level as appropriate
- Supplement dietary calcium and iron
- Recheck level in an appropriate time frame

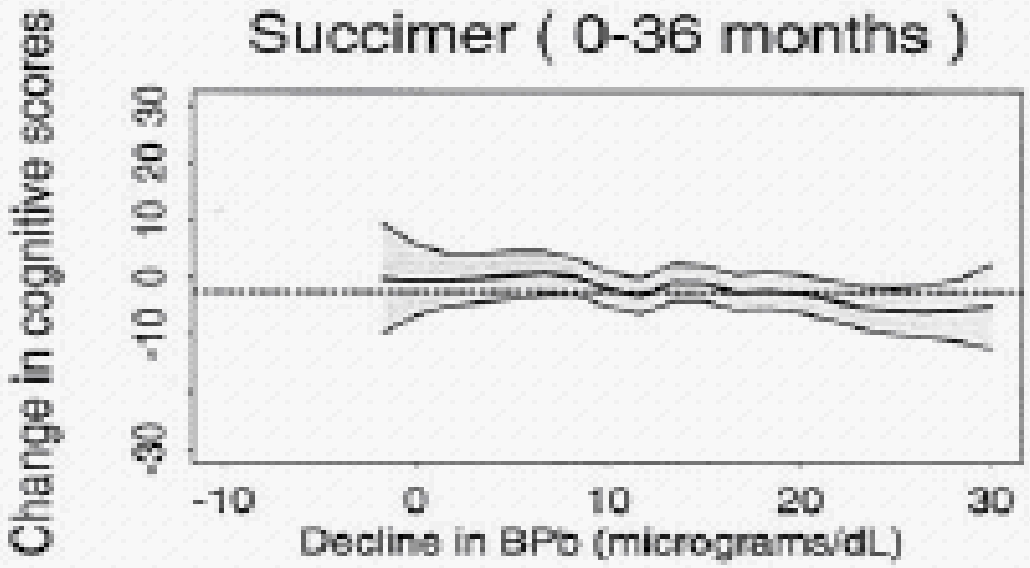
Lead Poisoning – What to Do Next?

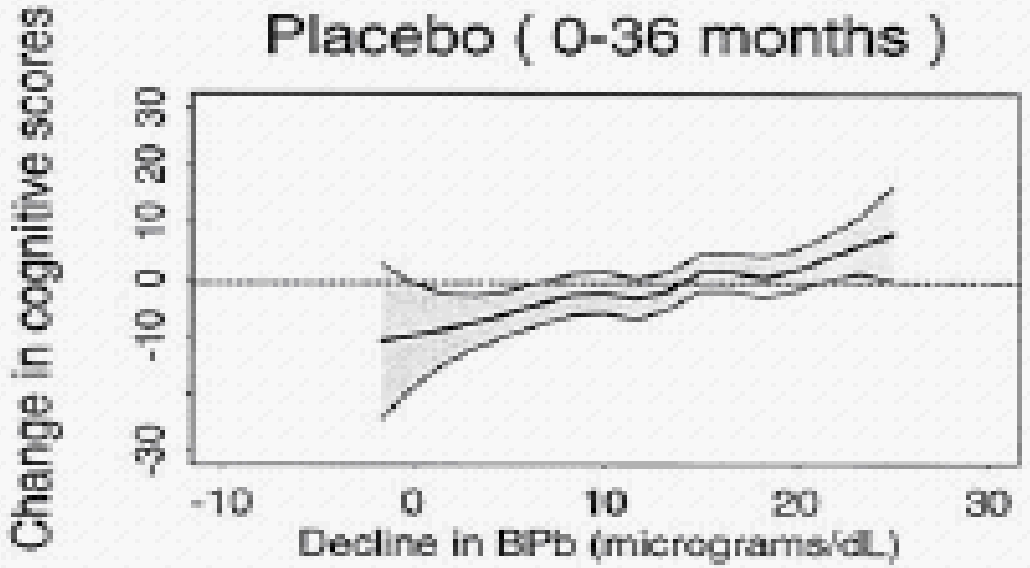
- Who should we chelate?
  - Data is limited
  - TLC trial – Newark, NY, Baltimore, 1993-2000
  - Double blind controlled study
  - Attempted to address the environment and provide nutritional supplements
  - Didn't abate new residences after patients moved

TLC


Placebo
Succimer
Mean blood lead (Micrograms/dL)
10
15
20
25
0
10
20
30
Months after initiation of treatment

TLC Outcomes





Increase in cognitive test score by decline in blood lead level using a moving average smooth, with estimated 95% confidence band. Based on 741 total children from the TLC Trial, 1994–2000.

TLC Outcomes - 2

- Study not intended to address subgroup analyses
- No difference generated in *post-hoc* analyses between children chelated below age 2 and after age 2, but power insufficient to decisively conclude this
  - Personal communication, Walter Rogan, 2/29/12

What about other chelators?

- IV = Calcium disodium EDTA
- IM = BAL (dimercaprol)
- Oral
  - DMPS
    - FDA approved in US for compounding use only
  - Penicillamine
    - Not FDA approved for lead chelation

Lead Exposures During Pregnancy: Exposure and Remediation

Richard K. Miller, PhD, ATS

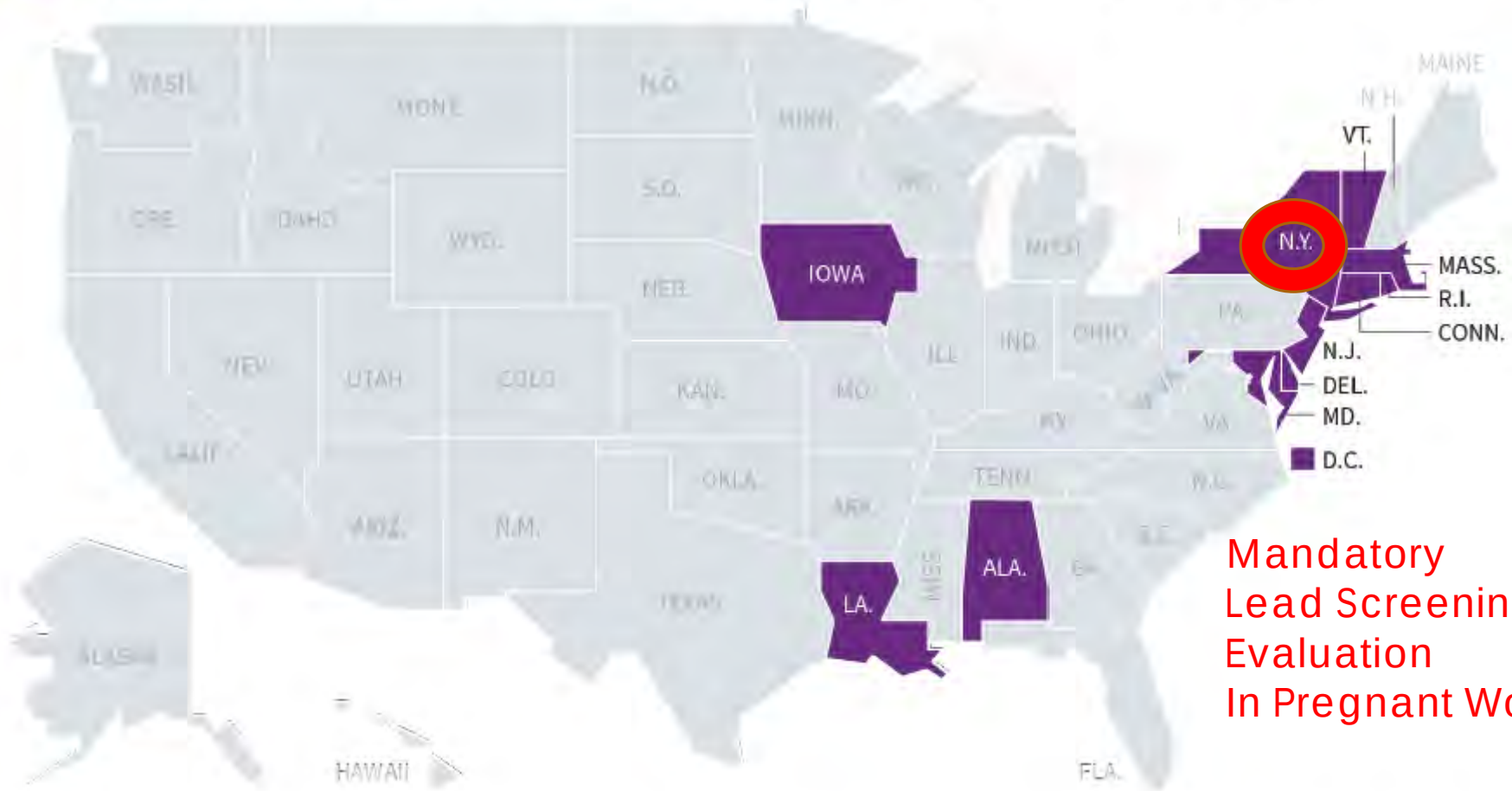
Director, MotherToBaby UR Medicine
Finger Lakes Children's Environmental Health Center
Professor of Obstetrics/Gynecology, of Environmental Medicine,
of Pathology and Clinical Laboratory Medicine
University of Rochester School of Medicine and Dentistry,
and Teratology Society member
mothertobaby@urmc.rochester.edu

States requiring testing

Blood lead tests are mandated for all children in 11 U.S. states and Washington, D.C. Some other states mandate tests for all children in areas with exposure risks, such as housing with lead paint or lead-tainted soil.

Requires blood poisoning testing for all children

Does not require blood poisoning testing for all children



Mandatory
Lead Screening
Evaluation
In Pregnant Women

Note: Minimum testing requirements in the 11 states and Washington D.C. are as follows: Alabama, Louisiana, New Jersey, New York and Vermont require testing at age one and again at age two; Connecticut requires testing once per year for children between 9-36 months of age; Delaware requires testing at age one and testing again at two if the child has exposure risk; Iowa requires at least one test by age 6; Maryland requires children born in 2015 or later to be tested at age one and again at age two; Massachusetts requires testing by age one, and again at ages two and three; Rhode Island requires two tests by age three; and Washington D.C. requires two tests by 26 months of age.

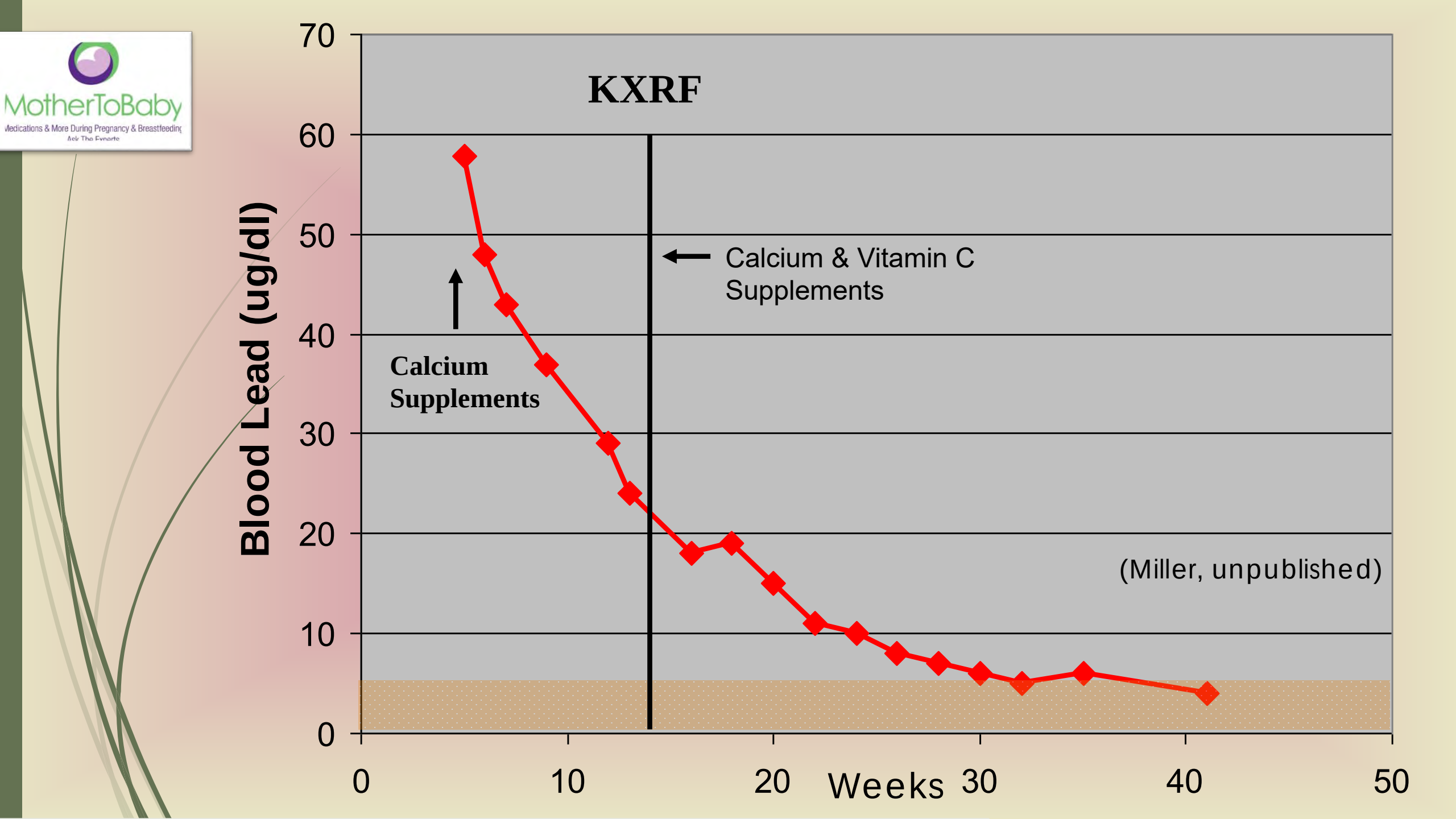
Sources: States

J Schneyer, MB Bell, Reuters, June 9, 2016

Lead Screening and Blood Testing Experience in New York State Since 1995 - Actions and Interventions

- Mandatory Lead Screening at 1st Prenatal Visit
- Follow up with Blood Lead Level Testing (BLL)
- Refer to Teratogen Information Services; County Dept of Health
- Follow-up with monthly BLL
- Interventions – Calcium, Iron, Vitamin C - Last resort -Chelation
- EXPERIENCE - Test all women in first trimester for Lead exposure
- Inspect all rental properties and require *Certificate of Occupancy* (Coalition to Prevent Lead Poisoning, Rochester, New York)

http://www.letsmakeleadhistory.org/
https://www.health.ny.gov/environmental/lead/exposure/childhood/finalplantoc.htm
http://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf

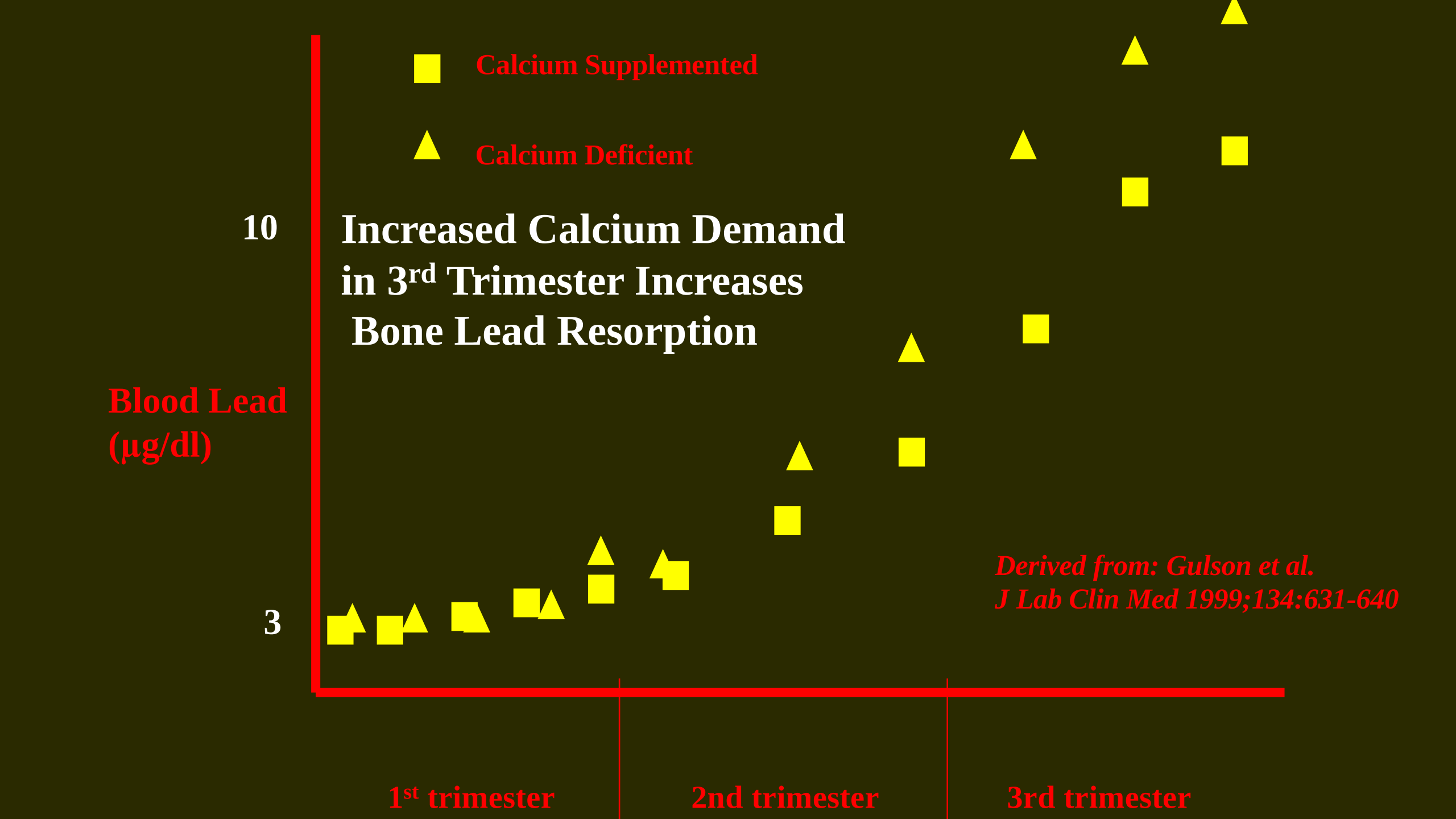

KXRF
Blood Lead (ug/dl)
70
60
50
40
30
20
10
0
Calcium & Vitamin C Supplements
Calcium Supplements
(Miller, unpublished)
0
10
20
Weeks
30
40
50

Lead in Bone

> 95% of the body burden of lead is in the skeleton.

Half-life of Lead in bone is 20-30 years.

Lead is released from bone during pregnancy at increased rate.


Calcium Supplemented
Calcium Deficient
Increased Calcium Demand in 3rd Trimester Increases Bone Lead Resorption
10
3
Blood Lead (µg/dl)
Derived from: Gulson et al. J Lab Clin Med 1999;134:631-640
1st trimester
2nd trimester
3rd trimester

TOP TEN Elevated Blood Lead in Pregnant Women –

1. Medicines – Ayurvedic Medicines (imported)
2. Remodeling/Repair Home - Apartment
3. Workplace – Electronics/Auto Repair/ Ceramic Industry
4. Cosmetics – Eye Shadow (imported)
5. Ethnic Imported Foods – Salsa – Candies/Clay Pots
6. Hair Dyes - (imported)
7. Gun Shot Fragments –
8. Hobbies – Metal Work; Jewelry Making
9. Water Consumption – Drinking Coolers
10. Urine Drinking

Experience for MotherToBaby UR Medicine, 2016

TOP TEN - Elevated Blood Lead in Pregnant Women –
*(MOST DIFFICULT TO **IDENTIFY**)*

1. Urine Drinking
2. Water Consumption – Drinking Coolers
3. Hair Dyes - (imported)
4. Ethnic Foods – Salsa (imported), Candies
5. Medicines – Ayurvedic Medicines (imported)
6. Hobbies – metal work, jewelry making
7. Workplace – Electronics/Auto Repair
   Ceramics Industry/ Bridge Repair
8. Cosmetics – Eye Shadow (imported)
9. Remodeling/Repair Home - Apartment
10. Gun Shot Fragments

Experience for MotherToBaby UR Medicine, 2016

TOP TEN - Elevated Blood Lead in Pregnant Women –
*(MOST DIFFICULT To **REMEDIATE**)*

1. Gun Shots Fragments
2. Medicines – Ayurvedic Medicines (imported)
3. Workplace – Electronics/Auto Repair
4. Workplace - Ceramics Industry/ Bridge Repair
5. Cosmetics – Eye Shadow (imported)
6. Ethnic Imported Foods – Salsa – Candies/Clay pots
7. Remodeling/Repair Home/ Apartment
8. Hair Dyes - (imported)
9. Water Consumption – Drinking Coolers
10. Urine Drinking

Experience for MotherToBaby UR Medicine, 2016

Lead Exposures in Pregnant Women –
KEYS TO SUCCESS

1. PREVENTION - Certificate of Occupancy for every rental property which must include a lead inspection certification.
2. LEAD TESTING of pregnant women in FIRST Trimester (Not just Screening)
3. Engage Patient and her Physician – detailed history and repeat follow up (including family members if at risk)
4. REPEAT BLOOD LEAD TESTING MONTHLY WHEN ELEVATED
5. INTERVENTIONS – Removal; Therapy (Calcium, Iron, Vitamin C); ~~Chelation~~
6. Work closely with Local and State Departments of Health
7. Workplace – Work with employer and patient – for testing and actions to remove patient from workplace exposures (verify new area is lead free). Assist Workplace with recommendations for remediation.
8. Eliminating residential source of Lead - Remodeling/Repair Home/ Apartment; Home inspections by Certified Lead Inspectors
9. Water Consumption; Behavior modification for Ethnic Imported Foods – Salsa – Candies in clay pots; Urine Drinking; Hair Dyes (Imported)

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5. INTERVENTIONS – Removal; Therapy (Calcium, Iron, Vitamin C); ~~Chelation~~
6. Work closely with Local and State Departments of Health
7. Workplace – Work with employer and patient – for testing and actions to remove patient from workplace exposures (verify new area is lead free). Assist Workplace with recommendations for remediation.
8. Eliminating residential source of Lead - Remodeling/Repair Home/ Apartment; Home inspections by Certified Lead Inspectors
9. Water Consumption; Behavior modification for Ethnic Imported Foods – Salsa – Candies in clay pots; Urine Drinking; Hair Dyes (Imported)

Lead Exposures in Pregnant Women –
KEYS TO SUCCESS

1. PREVENTION - Certificate of Occupancy for every rental property which must include a lead inspection certification.
2. LEAD TESTING of pregnant women in FIRST Trimester (Not just Screening)
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