AAP Lead Testing Webinar Series

This event is the first of a 4-part webinar series developed as part of the American Academy of Pediatrics (AAP) project, ***Increasing Capacity for Blood Lead Testing and Interpretive Guidance for Blood Lead Results.***

The webinar materials are developed and presented by pediatric lead experts from the AAP to educate primary care providers on various aspects of lead exposure prevention, testing, treatment, and follow up care.

Disclaimer

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Understanding CDC's Blood Lead Reference Value: Laboratory Best Practices & How To Interpret Results

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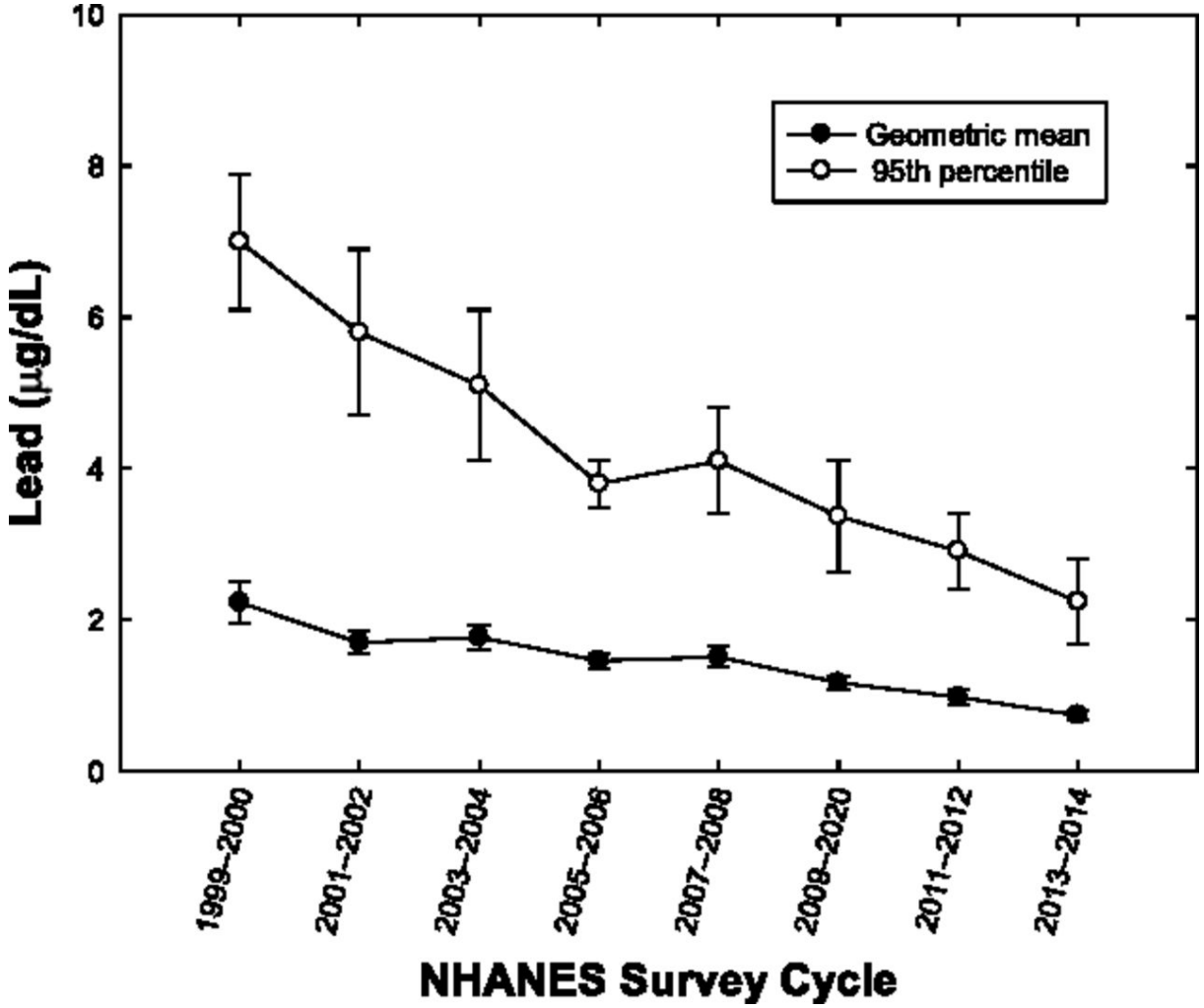
Objectives

1. Understand what the reference level means to the actions taken in children with elevated blood lead levels
2. Describe laboratory tests used to evaluate blood lead levels
3. Discuss limitations of various methods of blood lead testing and how it impacts decision making in pediatric practices

Reference Value

Reference Value



Source: National Health and Nutrition Examination Survey (NHANES)

CDC Reference Value: What Does it Mean??

- It is a number based on a nationally representative population of children between 1-5 years of age who had lead levels done and 97.5% of children were below that number.
- It does NOT indicate lead "poisoning" or "toxicity". It is just a reference point based on population data.
- It is NOT indicative of what the clinical laboratory can tell you about the individual child in your practice.

Recommended Actions Taken at Reference Value

Blood Lead Level (BLL)					
<5 µg/dL	5–9 µg/dL	10–19 µg/dL	20–44 µg/dL	45–69 µg/dL	≥70 µg/dL
Routine assessment of nutritional and developmental milestones Anticipatory guidance about common sources of lead exposure	Routine assessment of nutritional and developmental milestones Environmental assessment of detailed history to identify potential sources of lead exposure	Routine assessment of nutritional and developmental milestones Environmental assessment of detailed history and environmental investigation** including home visit to identify potential sources of lead exposure Nutritional counseling related to calcium and iron intake; consider	Complete history and physical exam Neurodevelopmental assessment Environmental investigation of the home and lead hazard reduction Lab work:	Complete history and physical exam Complete neurological exam including neuro-developmental assessment Environmental investigation of the home and	Hospitalize and commence chelation therapy in conjunction with consultation with a medical toxicologist or a pediatric environmental health specialty unit Proceed with additional actions according to interventions for BLLs between 45-69 µg/dL

Source: Centers for Disease Control and Prevention (CDC); National Center for Environmental Health (NCEH)/Lead

Recommended Actions Taken at Reference Value

PEHSU Pediatric Environmental Health Specialty Units

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Recommendations on Medical Management of Childhood Lead Exposure and Poisoning

No level of lead in the blood is safe. In 2012, the CDC established a new "reference value" for blood lead levels (5 mcg/dL), thereby lowering the level at which evaluation and intervention are recommended (CDC).

Lead level	Recommendation
< 5 mcg/dL	1. Review lab results with family. For reference, the geometric mean blood lead level for children 1-5 years old is less than 2 mcg/dL . 2. Repeat the blood lead level in 6-12 months if the child is at high risk or risk changes during the timeframe. Ensure levels are done at 1 and 2 years of age. 3. For children screened at age < 12 months, consider retesting in 3-6 months as lead exposure may increase as mobility increases. 4. Perform routine health maintenance including assessment of nutrition, physical and mental development, as well as iron deficiency risk factors. 5. Provide anticipatory guidance on common sources of environmental lead exposure: paint in homes built prior to 1978, soil near roadways or other sources of lead, take-home exposures related to adult occupations, imported spices, cosmetics, folk remedies, and cookware.
5-14 mcg/dL	1. Perform steps as described above for levels < 5 mcg/dL. 2. Re-test venous blood lead level within 1-3 months to ensure the lead level is not rising. If it is stable or decreasing, retest the blood lead level in 3 months. Refer patient to local health authorities if such resources are available. Most states require elevated blood lead levels be reported to the state health department. Contact the CDC at 800-CDC-INFO (800-232-4636) or the National Lead Information Center at 800-424-LEAD (5323) for resources regarding lead poisoning prevention and local childhood lead poisoning prevention programs. 3. Take a careful environmental history to identify potential sources of exposures (see #5 above) and provide preliminary advice about reducing/eliminating exposures. Take care to consider other children who may be exposed.

Source: www.pehsu.net

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Recommended Actions Taken at Reference Value

- Environmental investigations at BLLs 5 – 19 µg/dL vary according to local conditions based on jurisdictional requirements and available resources
- Providers must know available resources and how to respond to lead level results

Laboratory Test Available to Evaluate Blood Lead Levels

Commonly Used Available Methods

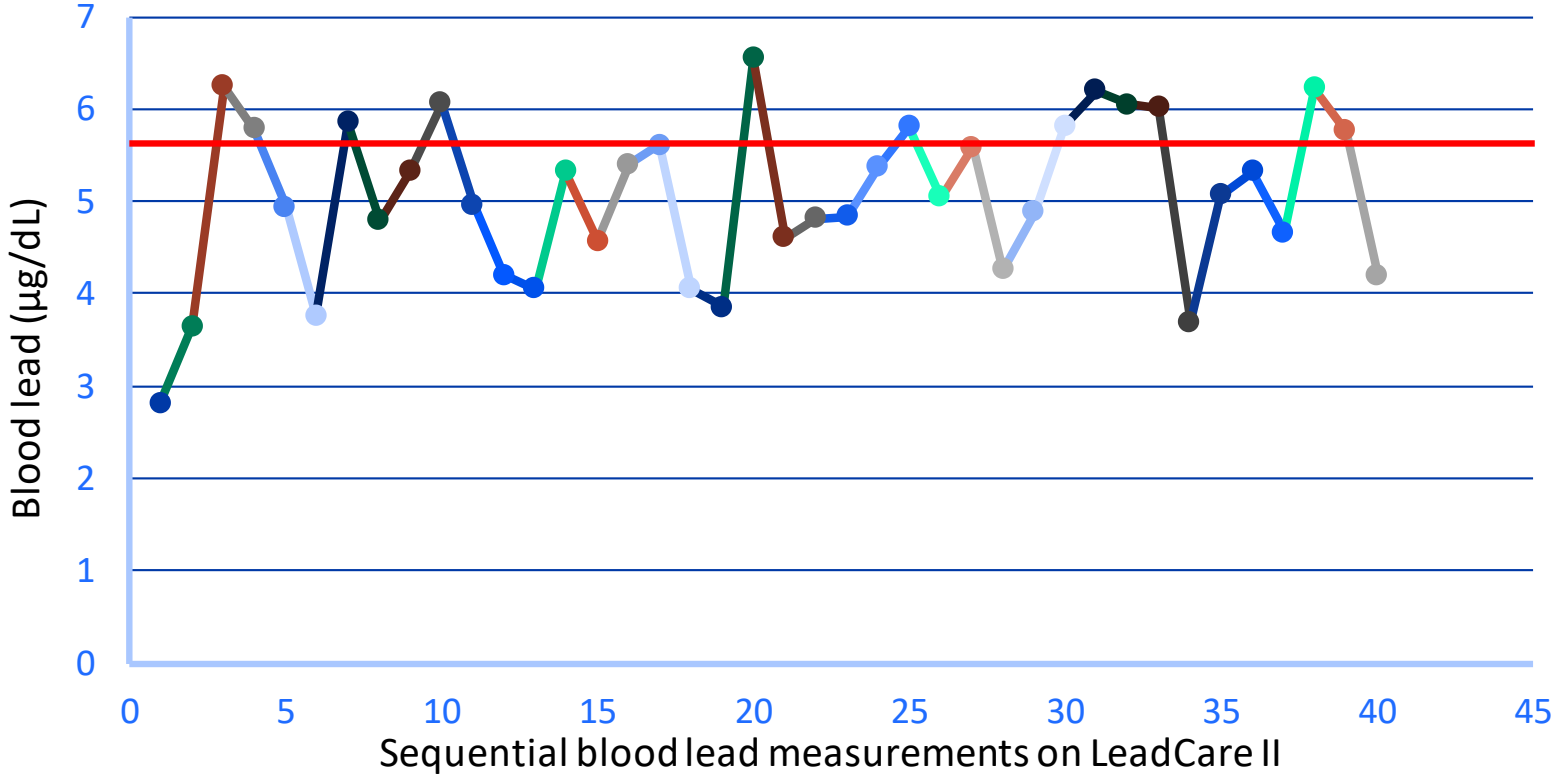
- Anodic Stripping Voltammetry (ASV)
  - Disposable screen printed electrode technologies
  - (LeadCare® II)
- Graphite furnace atomic absorption spectrometry (GFAAS)
  - Reference method
- Inductively coupled plasma mass spectrometry (ICP-MS)
  - Reference method

LeadCare® II

- Point of Care testing
  - Physician's offices
  - Local health departments
  - Hospitals
- CLIA waived
- Capillary blood samples only
  - Confirmation testing should be venous blood by a different method
- Reportable range is 3.3 – 65 µg/dL
- State health department reporting is the same as for lab-based tests

Sequential Blood Lead Measurement on LeadCare II

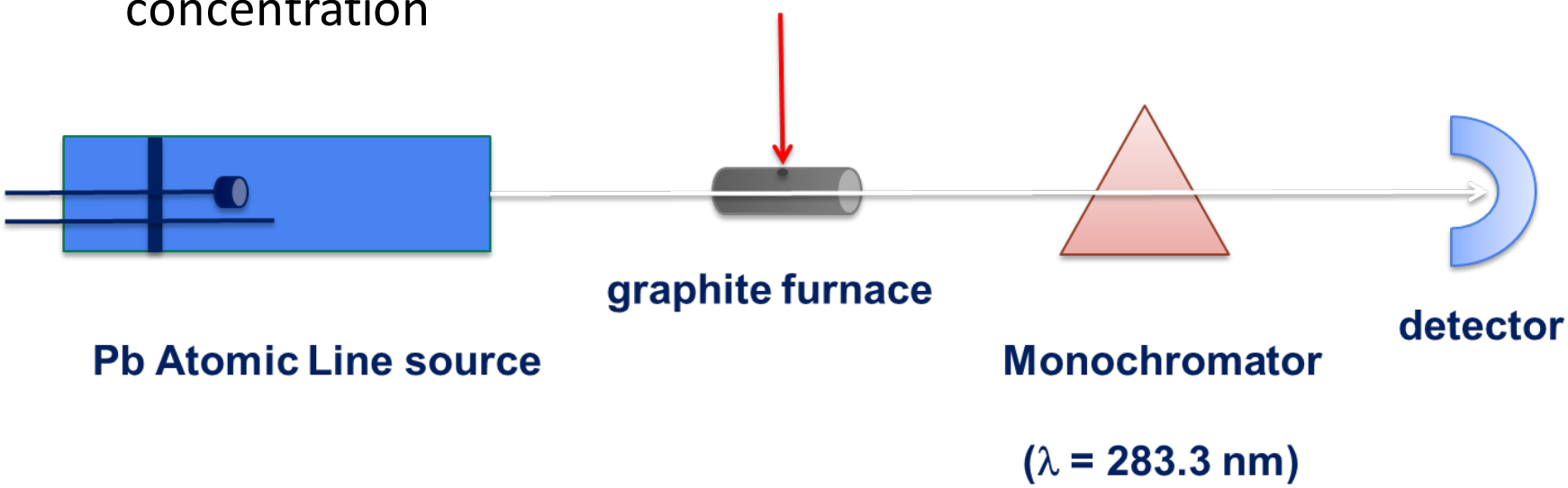
- Simulation of sequential blood lead level measurements for person with constant, true blood lead of 5.0 µg/dL



Source: National Center for Environmental Health (NCEH)/ATSDR Board of Scientific Counselors, Semi-Annual Meeting, January 2017

Graphite Furnace Atomic Absorption Spectrometry

- Electrical heated graphite coded tubes or rods that vaporize sample
- Amount of light energy absorbed at frequency characteristic to element
- Amount of light absorption can be linearly correlated to concentration



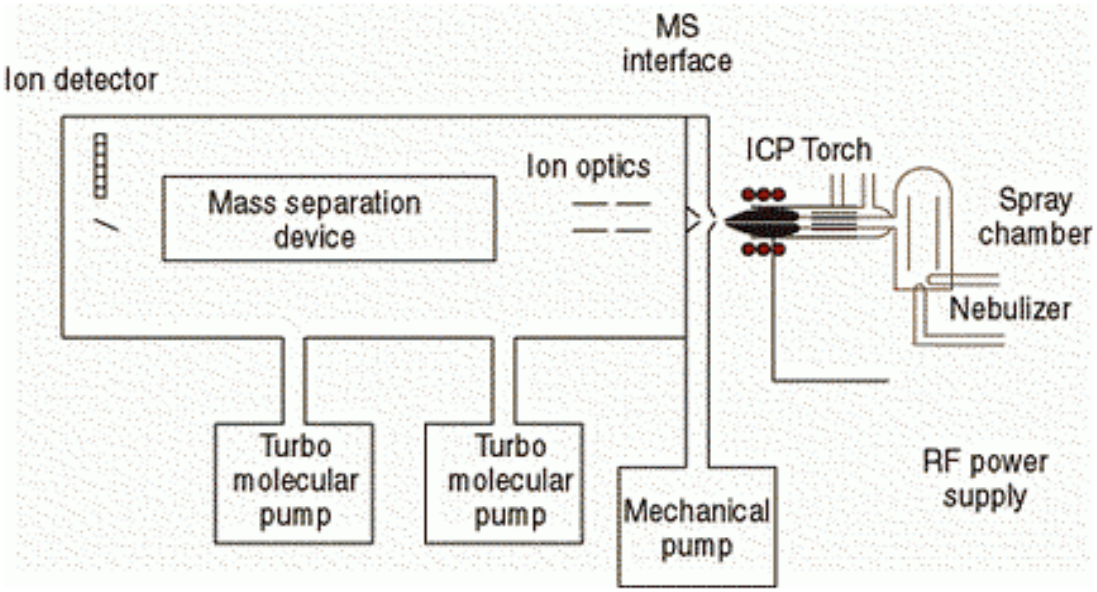
Source: Courtesy of Patrick Parsons, PhD

Graphite Furnace Atomic Absorption Spectrometry

- Hospital or reference lab settings
- CLIA: High complexity
- Capillary or venous samples
  - Can be used for venous confirmation on different blood sample
- Reportable range: capable of accurately measuring to 1 µg/dL

Inductively Coupled Plasma – Mass Spectrometry

- Provides high temperature ion source resulting in all bonds broken irrespective of their chemical bonding
- Accounts for total content of an element



Inductively Coupled Plasma – Mass Spectrometry

- Hospital or reference lab settings
- CLIA: High complexity
- Capillary or venous samples
  - Can be used for venous confirmation on different blood sample
- Reportable range: capable of accurately measuring below 1 µg/dL with better precision compared to GFAAS

Best Estimates of Precision of Blood Lead Measurements at 5 ug/dL

	95% confidence interval (µg/dL)	N
LeadCare II	± 1.8	1469
GFAAS	± 1.5	908
ICP-MS	± 0.97	769

Source: National Center on Environmental Health (NCEH)/ATSDR Board of Scientific Counselors, Semi-Annual Meeting, January 2017

Limitations of Laboratory Instruments in Blood Lead Results Based on Reference Value

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Procedures for Collecting Samples for Lead Determination

- Capillary blood samples
  - Acceptable only for screening purposes
  - False positives can be frequent but inform the provider on environment

Procedures for Collecting Samples for Lead Determination

- Filter paper collection
  - Varied opinions on reliability and technique
  - Potential for contamination and variable volume
  - Guidelines for methods of measuring lead from filter paper

Procedures for Collecting Samples for Lead Determination

- Instrument precision
  - ICP-MS and GFAAS can be reproducible to ± 0.2 µg/dL at low levels
  - Reporting at low levels as clinical value is open to interpretation
  - Quantitation limits
  - Current CLIA regulations within the United States require that the acceptability limits be no larger than ± 4 µg/dL (0.19 µmol/L) below 40 µg/dL (1.93 µmol/L), or ± 10% of the target value above that concentration
  - Repeat testing

Laboratory Reporting

- Prior to reporting patient test results, the laboratory must provide performance specifications
  - Accuracy
  - Precision
  - Reportable Range
  - Reference Intervals

Laboratory Reporting

- Accuracy
  - Degree of closeness of measurements of a quantity to that quantity's actual value
- Precision
  - Also called reproducibility or repeatability
  - Same results:
    - Day-to-day
    - Run-to-run
    - Within run
    - Operator variance

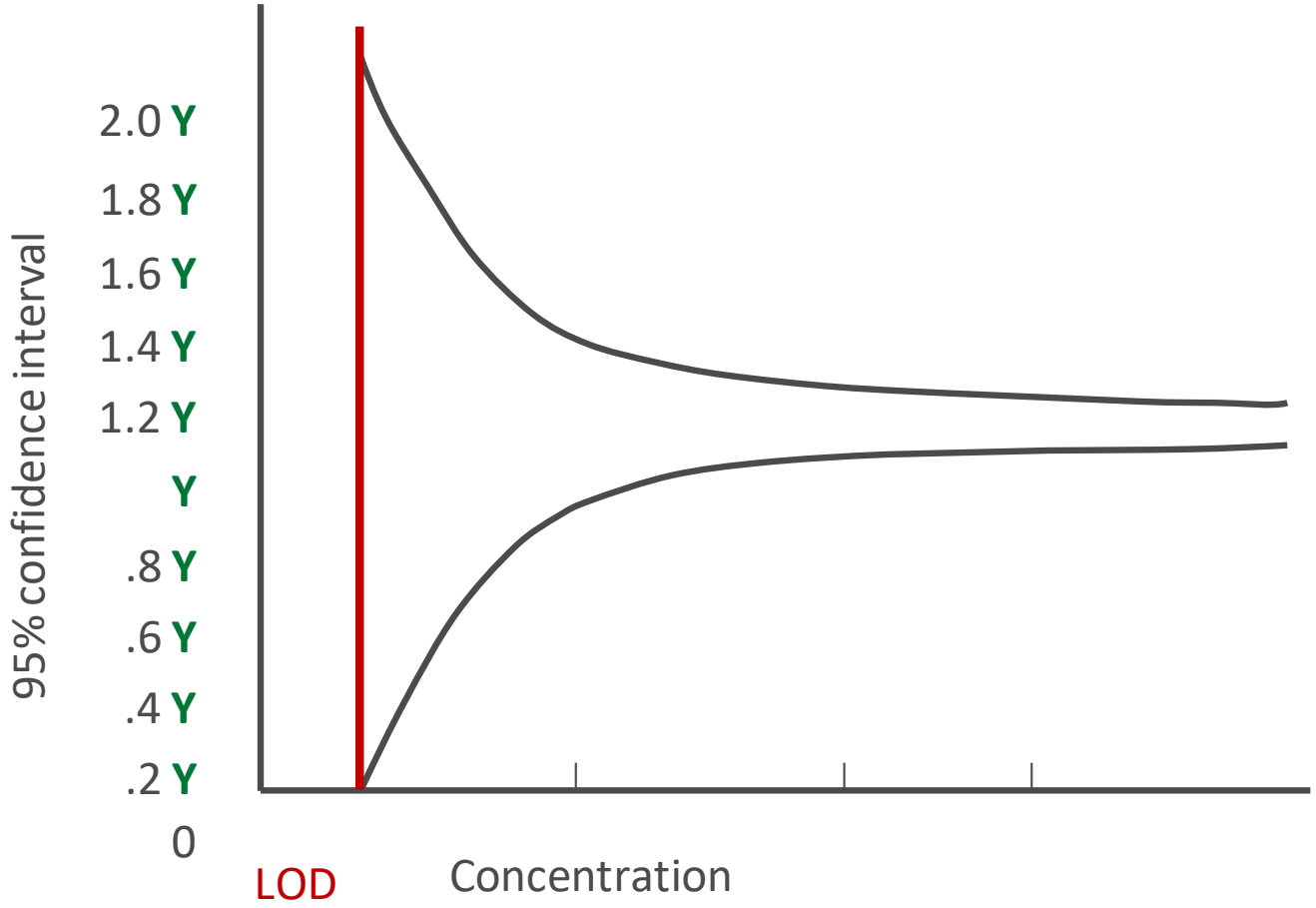
Laboratory Reporting

- Reportable range
  - Laboratory is responsible for establishing how high and low the results can be reported
  - Based on LOD and LOQ
- Reference intervals or "normal values"
  - Must be appropriate for laboratory's patient population
  - May establish own reference range or use published ranges

Laboratory Reporting

- Limit of Detection
  - Lowest concentration of analyte that the test can detect or distinguish from a blank
- Limit of Quantification
  - Lowest quantity that can be accurately measured

Imprecision Increases Non-Linearly Near the Limit of Detection



Adapted from JK Taylor, Quality Assurance of Chemical Measurements, 1987.

Laboratory Reference Interval for Lead

- Different than CDC Reference Value (different meaning)
- Based on LOD and LOQ of instrumentation and what can most accurately be reported
- Current agreement is that precision for measurements made at 3.5 µg/dL will not be better than the current estimates at 5 µg/dL
- CDC changes in reference value will not change laboratory reference levels until better precision can be made

Impact on Patient Care

Interpretation of Results

- There is no known safe level of blood lead for children
- Depending on method used, the actual result should be within ±2 SD knowing the precision is poorer at lower concentrations.
  - For example, a blood lead level of 4.9 µg/dL from LeadCare II could be in a range of 2.9 – 6.9 µg/dL (roughly)

Recommendations for "Action"

- There is no known safe blood lead level
- Local and state regulations guide involvement of health department for case management and home assessments (e.g., blood lead level of 4.9 µg/dL)
- Health care providers must supply education and be involved when the health departments cannot (e.g., blood lead level of 4.9 µg/dL)
  - CDC and Pediatric Environmental Health Specialty Unit (PEHSU) guidance
  - Virtual home assessments
  - Lead questionnaire to help determine source

Additional Testing

- Confirmatory testing
  - Capillary "screening" would be considered the first test to determine if the child has an elevated blood lead level.
  - If above 5 µg/dL, this should be repeated with a venous sample by a different method.
  - If venous is below LOR, consider lead may still be in environment and education on sources is still needed for primary prevention
- Repeat testing
  - If child has had EBLL confirmed by venous testing, all further testing should be by venous sampling.
- Follow testing schedule recommended by CDC and/or PEHSU

Summary

- CDC Lead Reference Value (5 µg/dL)
  - Based on data obtained from a representative population of children in the U.S.
  - This number will change based on the work we do to prevent lead poisoning
- Laboratory Lead Reference Value (5 µg/dL)
  - Based on precision testing of methods by laboratories to determine accurate results from LOD and LOQ
  - This number may change as precision in methods improves

Summary

- CDC and Laboratory Reference Values may not always be the same.
- Public health management is based on local and state jurisdictions and availability of resources. They may not be able to provide services at CDC Reference Value.
- Health care providers should understand limitations of methods for lead quantitation and provide appropriate education to families.

Questions?

Thank you!

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