

Analytical Methods
for **Measuring Lead**
in **Blood**

**Toolkit for establishing
laws to eliminate
lead paint**

Second Edition

Module C-1



**Global Alliance to
Eliminate Lead Paint**

Outline

- Background
- Reasons for Measuring Lead in Blood
- Blood Sampling
- Brief Information on Different Analytical Methods
- Quality Control Considerations
- Summary

Background

- Lead exposure is primarily assessed through its measurement in whole blood (venous blood).
- The most common laboratory methods to measure blood lead concentrations are:
 - Atomic Absorption Spectrometry (AAS)
 - Inductively Coupled Plasma Mass Spectrometry (ICP-MS)
 - Anodic Stripping Voltammetry (ASV)

Analytical methods differ in their limit of detection, accuracy, costs and technical requirements (e.g. sample preparation, calibration, and skilled personnel)

Reasons for Measuring the Blood Lead Concentrations

- To determine the need for the active management and medical interventions to address lead exposure, such as identification of, and removal from, the source of exposure, or chelation therapy;
 - To determine the effectiveness of risk mitigation measures;
 - As part of a health screening or surveillance programme to identify lead-exposed children;
 - For exposure and risk assessment, for example a prevalence study of lead exposure related to lead paint or other sources;
 - For occupational monitoring

Measurement Units

- The commonly used units for reporting blood lead concentration are micrograms of lead per decilitre of blood ($\mu\text{g}/\text{dL}$), micrograms per litre ($\mu\text{g}/\text{L}$) and micromoles per litre ($\mu\text{mol}/\text{L}$).
- The conversion factor between mass and molar units is the atomic mass of lead: 207.19.
- For conversion from mass to molar units the value should be divided by the atomic mass.
- For conversion from molar to mass units the value should be multiplied by the atomic mass.

Blood Sampling

- Essential to avoid external contamination of the sample.
 - Personnel should be trained in good sampling and handling techniques to avoid contamination.
 - Collect, store and transport samples in a lead-free environment.
 - Thoroughly cleanse the skin around the puncture site.
 - Use lead-free sampling equipment and tubes. If not available send 'blanks' from same batch to the laboratory for testing of background lead content.
- Observe universal biosafety precautions.

Blood Sampling (Continued)

- Collect whole blood in a tube containing EDTA or heparin.
 - Invert the filled tube 8–10 times to ensure adequate mixing.
 - Clotted samples should be rejected – analytical results will be unreliable.
- Make sure to label the tube with the patient's identification details.
 - Refrigerate samples (<4°C) that are awaiting analysis – do not freeze.
 - Note: does not apply to samples measured using point-of-care device, which should be kept at room temperature.

Choice of Analytical Method is Determined by Resources and Needs

Resource issues include:

- Availability of trained laboratory staff;
- Cost of reagents and other materials e.g. special gases, compressed air;
- Typical number of analyses needed (cost per analysis)
 - Economy of scale possible with methods that allow multiple analyses;
- Special operating requirements e.g. reliable electricity supply, cooling water.

Choice of Analytical Method is Determined by Resources and Needs

Need for required limit of detection varies according to the reason for the analysis.
For example:

- Population studies –method accurate to $<1 \mu\text{g/dL}$ may be needed, e.g. geometric mean blood lead concentration in USA in 2011–12 was $0.973 \mu\text{g/dL}$.
- Confirmation of lead exposure and decisions on management – method accurate to $5 \mu\text{g/dL}$ acceptable.
- In severe cases of poisoning – method to accurately measure $>65 \mu\text{g/dL}$ may be needed

Analytical Methods Used to Measure Lead in Blood

Laboratory methods:

- Flame atomic absorption spectrometry (FAAS)
 - Electrothermal atomic absorption spectrometry (ETAAS) or graphite furnace atomic absorption spectrometry (GFAAS)
 - Inductively coupled plasma mass spectrometry (ICP-MS)
 - Anodic stripping voltammetry (ASV) - Point-of-care or field-testing methods
 - ASV technique
 - Portable ASV device

Flame Atomic Absorption Spectrometry (FAAS)

- Short analysis time (seconds)
- Relatively easy to use
- Relatively few interferences
- Relatively low capital and running costs
- Large sample size usually needed
- Relatively high detection limit (5 $\mu\text{g}/\text{dL}$)
- Cannot be left unattended (flammable gas)

Electrothermal Atomic Absorption Spectrometry (ETAAS) or Graphite Furnace Atomic Absorption Spectrometry (GFAAS)

- Low detection limit (<1µg/dL)
- Can analyse small samples (50–100 µL)
- Can be fitted with autosampler so multiple samples can be processed
- Well documented applications
- May be left unattended
- No need for sample preparation

Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

- Very low limit of detection (0.02 µg/dL)
 - Can analyse small samples (50–100 µL)
 - Very fast analysis time (<1min)
 - Wide analytical working range
 - Multi-element capabilities and can be economical if used for large sample runs
 - Potential to perform isotopic ratio analyses with some forms of ICP-MS, which may help to identify the source of the lead

Portable ASV

- Small sample size (50 μ L)
- Can be used at non-laboratory sites
- Uses finger prick (capillary sample), though venous samples can also be used
- Simple to use, does not require skilled laboratory personnel
- Low purchase and running costs
- Rapid results
- Has comparable accuracy with laboratory-based methods

Portable ASV - Limitations

- Limited analytical working range
- Levels above 5 $\mu\text{g}/\text{dL}$ should be confirmed by a high-complexity laboratory method
- High risk of sample contamination
- Risk of low-biased results on venous blood collected with certain types of evacuated blood tubes

Quality Control Considerations

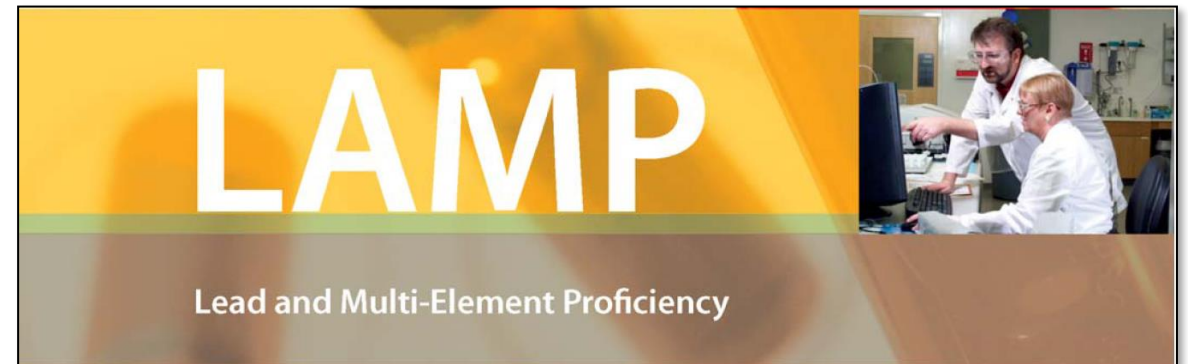
- Important that analytical results are reliable.
 - Laboratory should have in place an adequate quality management system e.g.:
 - Standard operating procedures;
 - Documented training and monitoring of staff performance;
 - Use of certified reference standards;
 - Internal quality control procedures – daily checks of analytical accuracy;
 - Participation in external quality assessment scheme e.g. US LAMP.

Laboratory Quality Assurance - LAMP

- A voluntary program that focuses on assuring the quality of blood lead, cadmium, and mercury analyses.
- Each quarter US CDC provides spiked blood samples, which are analyzed by participating laboratories who return the results to CDC.
- CDC provides detailed reports on the laboratories about how well they performed these analyses.
- No charge for participation.

LAMP program:

<https://www.cdc.gov/labstandards/lamp.html>



Summary

- Measurement of the blood lead concentration is the most widely accepted method for identifying lead exposure and having the possibility to carry out this analysis is important for public health, occupational health and the clinical management of lead poisoning.
- A range of analytical methods are available – the decision about which one to use is determined by the available resources and the limit of detection required.
- Point-of-care devices are available and have a role in screening for lead exposure. While they have been used to guide clinical management in extreme circumstances, this use should be validated by laboratory measurements.
- Quality assurance procedures are important to ensure the reliability of analytical results.

Available WHO Resources

- Brief guide to analytical methods for measuring lead in blood, second edition



<https://apps.who.int/iris/handle/10665/333914>

References

1. World Health Organization (2020). Brief guide to analytical methods for measuring lead in blood, 2nd ed. World Health Organization. <https://apps.who.int/iris/handle/10665/333914>. License: CC BY-NC-SA 3.0 IGO
2. Measurement procedures for the determination of lead concentrations in blood and urine: approved guideline, 2nd edition. CLSI document C40-A2. Wayne, PA, United States of America: Clinical and Laboratory Standards Institute; 2013.
3. Neri AJ et al. Analysis of a novel field dilution method for testing samples that exceed the analytic range of point-of-care blood lead analyzers. *Int J Environ Health Res.* 2014; 24(5):418-428)
4. Komárek M et al. Lead isotopes in environmental sciences: A review. *Environment International.* 2008; 34:562–577
5. Brown MJB, US Centers for Disease Control and Prevention, personal communication, 2015
6. Centres for Disease Control and Prevention (CDC). Lead and Multi-Element Proficiency website <https://www.cdc.gov/labstandards/lamp.html>

References – Sample Collection

1. Step-by-step guide for collecting capillary sample. US Centers for Disease Control and Prevention:

Poster: https://www.cdc.gov/nceh/dls/pdf/Poster_Capillary_Blood.pdf, accessed 15 February 2021

Video demonstration: Mission Unleaded: How to test children for lead with maximum accuracy

<https://www.youtube.com/watch?v=g2p2qREch9g>, accessed 15 February 2021

2. Guidelines on drawing blood: best practices in phlebotomy. Geneva: World Health Organization; 2010 (<https://apps.who.int/iris/handle/10665/44294>, accessed 15 February 2021)



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