Review of acceptability criteria for the determination of lead in blood.

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Blood lead levels defined as lead poisoning (μg/dL)

Changing Methodologies for Blood Lead Screening

- Colorimetric methods
- Flame AAS methods

Venous blood (7 mL)

<table>
<thead>
<tr>
<th>Year</th>
<th>Blood Lead Level (μg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>&lt;10 labs</td>
</tr>
<tr>
<td>1970</td>
<td>60 μg/dL</td>
</tr>
<tr>
<td>1975</td>
<td>40 μg/dL</td>
</tr>
<tr>
<td>1980</td>
<td>30 μg/dL</td>
</tr>
<tr>
<td>1985</td>
<td>25 μg/dL</td>
</tr>
<tr>
<td>1990</td>
<td>10 μg/dL</td>
</tr>
<tr>
<td>1995</td>
<td>?</td>
</tr>
<tr>
<td>2000</td>
<td>?</td>
</tr>
</tbody>
</table>
Blood lead levels defined as lead poisoning (μg/dL)

Changing Methodologies for Blood Lead Screening

Venous blood (7 mL)

1976-1980 geo. mean = 15 μg/dL (children)

Colorimetric methods
60 μg/dL

Delves cup flame atomic absorption spectrometry

40 μg/dL

Capillary blood (200 μL)

30 μg/dL

10 μg/dL

25 μg/dL


<10 labs
Blood lead levels defined as lead poisoning (μg/dL)

- Colorimetric methods: 60 μg/dL
- Delves cup flame atomic absorption spectrometry: 40 μg/dL
- Graphite furnace atomic absorption spectrometry: 30 μg/dL
- Venous blood (7 mL): 25 μg/dL
- Capillary blood (200 µL): 10 μg/dL

Changing Methodologies for Blood Lead Screening

1965-1980 geo. mean = 15 μg/dL (children)
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- Colorimetric methods
  - Venous blood (7 mL)
  - 60 μg/dL

- Delves cup flame atomic absorption spectrometry
  - 40 μg/dL

- Graphite furnace atomic absorption spectrometry
  - 30 μg/dL

- Inductively coupled plasma mass spectrometry
  - 25 μg/dL

- Capillary blood (200 μL)
  - 10 μg/dL

1965-1980 geo. mean = 15 μg/dL (children)

2002 geo. mean = 2.2 μg/dL (children)

- Colorimetric methods
  - 7 mL

- Delves cup flame atomic absorption spectrometry
  - 40 μg/dL

- Graphite furnace atomic absorption spectrometry
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Federal Certification Issues

- In the US, all clinical labs must be certified under the Federal Law known as CLIA ‘88.
- PT program providers must also be approved under CLIA if the program is used for CLIA certification.
  - NY State’s PT program is CLIA approved.
  - Blood Pb is a regulated PT analyte. This means that PT performance is defined as ±4 µg/dL or ±10% around the target.
Occupational testing comes under OSHA regulations.

- Labs and PT programs require certification. Under OSHA, Blood Pb performance is less stringent, ±6 µg/dL or ±15%.
New York State certification issues

- Under NYS Public Health Laws, any lab that tests clinical specimens originating from within New York State must have a NYS lab permit.
  - Numerous specialties are listed on the permit:
    - Toxicology – Blood Lead
    - Trace Elements
  - The permit requires successful participation in NYS PT program and a satisfactory on-site inspection every two years.
  - Labs must follow NYS published standards for blood lead and/or trace elements.
Blood Lead Proficiency Testing
Programs

- Currently 4 programs operate in the US
  - CAP, NYS, PA and WI (all CLIA approved)

- Several programs outside the US include those operated by Québec, University of Surrey (UK), Birmingham EQAS, several other EC countries (IT, ES, FR, DE) and Australia.

- Varying standards for acceptable performance
### Blood Pb Performance Criteria: 10 µg/dL

<table>
<thead>
<tr>
<th>EQAS</th>
<th>Limits (µg/dL)</th>
<th>Between-lab SD</th>
<th>%RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLIA 88</td>
<td>±4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSHA</td>
<td>±6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>±2.9</td>
<td>1.7</td>
<td>17</td>
</tr>
<tr>
<td>France</td>
<td>±2.9</td>
<td>1.6</td>
<td>16</td>
</tr>
<tr>
<td>Germany</td>
<td>±2.2</td>
<td>1.7</td>
<td>17</td>
</tr>
<tr>
<td>Italy</td>
<td>±2.0</td>
<td>2.1</td>
<td>21</td>
</tr>
<tr>
<td>UK</td>
<td>±2.9</td>
<td>1.3</td>
<td>13</td>
</tr>
<tr>
<td>EC net</td>
<td>±3.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blood Pb Performance Standards in the US

- CLIA requires 3 test events a year, 5 challenges per event.

- A fixed target range is set at ±4 µg/dL, for values <40 µg/dL (i.e., ±40%) and ±10% ≥40µg/dL.

- Scoring at least 4 out of 5 correct (80%) is considered satisfactory performance.

- Maintaining satisfactory performance in at least 2 out of 3 consecutive test events is considered successful PT.
How should PT acceptability criteria be determined?
Performance criteria for PT

- Systematic hierarchical approach that takes account of analytical and clinical considerations.
  - Current state-of-the-art of analytical capability;
  - Performance goals set by regulatory bodies, PT/EQA schemes; and
  - Criteria based on clinical parameters, e.g., biologic variation, clinical outcomes

Kenny et al. Consensus agreement. Scan Clin Lab Invest 1999;59:585
Performance criteria

- Performance criteria that take account of realities...


...recommended ±3 µg/dL
Analytical Procedures for the Determination of Lead in Blood and Urine; Approved Guideline

Volume 21 Number 9

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This document provides guidelines for the measurement of lead in blood and urine, including specimen collection, measurement by graphite furnace atomic absorption spectrometry (GFAAS) and anodic stripping voltammetry (ASV), quality assurance, and quality control. A guideline for global application developed through the NCCLS consensus process.
NCCLS C40-A
Recommended that the acceptable criterion for blood lead laboratory performance at 10 µg/dL be tightened to ±2 µg/dL (i.e., ±20%) 2001
Performance Standards: terms

- **Accuracy**
  - Closeness to true value, bias, systematic errors.
- **Precision**
  - random errors (SD)
- **Repeatability**
  - notion of agreement between-runs, day-to-day.
- **Reproducibility**
  - Agreement between-labs using the same method
New York State PT Program

- Blood is obtained from lead-dosed goats.
- Animals are dosed with lead acetate to produce physiologically-bound Pb in blood.
- Whole blood is preserved with EDTA.
- Around 105 laboratories participate of which 10-12 are independent reference labs.
- Program provides certification for NY State, CLIA ‘88, OSHA and other states.
- Program expanded in 2001 to include Hg, As, and Cd as well as Pb in blood. Urine and serum trace elements added too.
Lead-dosed goats

Wadsworth Center, Griffin Laboratory, Guilderland, NY
NY State Trace Elements PT

- Trace Elements in Whole Blood (Caprine)
- As, Hg, Cd and Pb.

www.wadsworth.org/testing/lead/ptprogram.htm
### NYS PT: Between-Lab SD at 11 µg/dL and 6 µg/dL

<table>
<thead>
<tr>
<th></th>
<th>11 µg/dL</th>
<th>6 µg/dL</th>
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</thead>
<tbody>
<tr>
<td>GFAAS</td>
<td>1.1</td>
<td>0.7</td>
</tr>
<tr>
<td>ASV bench</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>ICP-MS</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>ASV Leadcare</td>
<td>2.3</td>
<td>1.4</td>
</tr>
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</table>

Source: NYS DOH PT reports for blood lead 2006
Changing the current limits for blood Pb

Questions:
- Is there a need for better performance?
- Can labs do a better job?
- If yes, how much better?
- Is there any previous experience to guide us?
NYS Blood Lead PT Performance 1979 – 1992

PT records missing: 1981 - 1982
1982 - 1983

Acceptable limits tightened to ±4 µg, ±10%

% results reported satisfactorily per survey

Annual test cycle (July 1 to June 30)

P. J. Parsons *Environmental Research* (1992) 57 149
NYS BLOOD Pb LABORATORY PERFORMANCE: 1979 – 2006

Source: New York State Department of Health Proficiency Testing Program for Blood Lead

% results satisfactory

Test Event Annual Cycle

Source: New York State Department of Health Proficiency Testing Program for Blood Lead
<table>
<thead>
<tr>
<th>PT Test Event</th>
<th>2005 #2</th>
<th>2005 #3</th>
<th>2006 #1</th>
<th>2006 #2</th>
</tr>
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<tr>
<td>±4</td>
<td>2</td>
<td>10</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>±3</td>
<td>3</td>
<td>12</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>±2</td>
<td>9</td>
<td>22</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>±1</td>
<td>19</td>
<td>26</td>
<td>13</td>
<td>16</td>
</tr>
</tbody>
</table>

Blood Lead Limits and Laboratory Performance
Conclusions

- A phased approach is recommended in which the limit is tightened one step at a time.
- Implementing a tighter standard of ±3 μg/dL (±10%) now, is both desirable and feasible, and is consistent with current European standards.
- We re-visit the impact of this change in 12-24 months to see if improvements in lab performance have occurred, and then consider implementing ±2 μg/dL.
Potential Issues

- Older LeadCare systems may not be able to meet new standards.
- New Leadcare system is waived and so is not subject to PT oversight; will be subject to NYS PT if used by a certified lab.
- Need to educate users in the limitations of the various technologies.
Acknowledgements

- Staff of the Lead Poisoning/Trace Elements Laboratory, New York State Dept of Health