Western Occupational and Environmental Medical Association
Webinar – April 15, 2010

Occupational Lead Poisoning:
New Guidelines for Clinical Management

Speaker: Paul J. Papanek, MD, MPH
Occupational Health Service, Los Angeles Medical Center, Kaiser on the Job

PLEASE STAND BY
WEBINAR WILL BEGIN AT 12:00pm (PDT)
For Audio:
Call: 866-740-1260
Access Code: 7644915#

Faculty Disclosure:
Paul Papanek, MD, MPH has no conflict of interest to disclose.

Occupational Lead Poisoning:
New Guidelines for Clinical Management
WOEMA WEBINAR - April 15, 2010

Speaker: Paul J. Papanek, MD MPH
Special acknowledgment to the members of the
WOEMA Scientific Advisory Panel, 2009

James P. Seward, MD MPP MMM (Chair)
Robert C. Blink MD MPH
Robert Harrison, MD MPH
Warner Hudson, MD MPH
Ray Meister, MD MPH
Paul Papanek MD MPH
Hong Zhang, MD MPH MS
OSHA Lead Standard

- General Industry Lead Standard issued in 1979
- Scientific research over 30 years has demonstrated health effects at lower levels than previously understood.
- EPA has lowered acceptable blood lead for children
- OSHA Standard no longer offers sufficient protection to workers.

Overview of Lead Toxicity, by Blood Lead Level (PbB)

- **Current OSHA - Medical Removal**
  - 60: Peripheral Neuropathy
  - 50: Colic, arthalgia, gout
  - 40: Neurasthenic sx
  - 30: BP, stroke, CNS
  - 20: Peds development

- **Current OSHA - More Surveillance**
  - 70: Encephalopathy
  - 60: Peripheral Neuropathy
  - 50: Colic, arthalgia, gout
  - 40: Neurasthenic sx
  - 30: BP, stroke, CNS
  - 20: Peds development

- **Proposed Medical Removal**
  - 80: Anemia, stippling
  - 70: Encephalopathy
  - 60: Peripheral Neuropathy
  - 50: Colic, arthalgia, gout
  - 40: Neurasthenic sx
  - 30: BP, stroke, CNS
  - 20: Peds development
  - 10: Peds development
  - 0: Peds development
Routes of Exposure

- Respiratory - for fine particle including fume, absorption is as high as 50%.
- GI - swallowed lead - For adults, absorption is about 10%; for pre-school age children, absorption is as high as 30% to 50%.

The OHSA Standard contemplates that the respiratory route is overwhelmingly dominant. This is not true when PbA is under 50 mcg/cu meter.

Some Occupational Sources of Lead Exposure

- Pottery making
- Auto repair
- Manufacturing
- Construction
More Lead Exposures

OccLead Project 1993
Los Angeles County Surveillance

- 121 companies visited
- 1,384 new Blood Lead levels drawn
- 78 workers with PbB > 40 discovered
- 1,700 workers trained
- 36 facilities referred to Cal-OSHA or DA
Problems identified:

- Misleading interpretive information on BLL reports
- Lead standards based on medical information from 1970s
- Newer research shows adverse health effects at lower blood lead levels
- No adult equivalent to the CDC’s Guidelines for Children

Acknowledgment: Data from COHP, California Department of Health Services
2001 ABLES Meeting

• ABLES Adult Blood Lead Level Management Guideline Committee convened
• Expert Panel review of Guidelines proposed
• Guidelines development continues
• Search for funding/sponsorship

2002 ABLES Meeting

• Association of Occupational and Environmental Clinics (AOEC)
  – Agreed to sponsor project including convening Expert Panel meeting and facilitation for completion of Guidelines
  – NIOSH provided $20K
  – National Center for Environmental Health contributed additional $15K
Health effects of lead at low dose warrant a reappraisal of the levels of lead exposure that may be safely tolerated in the workplace.

- **Chronic effects of cumulative dose**
  - Hypertension
  - Decrements in renal function
  - Cognitive dysfunction

- **Acute effects of recent dose**
  - Adverse reproductive outcome

The Relationship Between Blood Lead and Blood Pressure in the NHANES II Survey

[Schwartz J Environ Health Persp 78:15-22; 1988]

Representative cross-sectional survey of US Population 20,322 persons examined; PbB obtained on 9932

Mean blood lead in adults 13.1 µg/dl (12.7 -13.7)

Blood lead significantly associated with systolic and diastolic blood pressure, after controlling for age, BMI, demographic, multiple nutritional factors
The Relationship of Bone and Blood Lead to Hypertension. The Normative Aging Study
[ Hu H et al, JAMA 1996; 275:1171-1176]

Case control study: 146 hypertensive men; 444 controls selected from large, ongoing prospective study of aging. Mean age = 66.6 ± 7.2 y

Exposure reflects that of general population. (Mean PbB = 6.3 ug/dL)

Final logistic model (backward elimination) yielded 3 significant risk factors for hypertension:

- Body mass index
- Family history of hypertension
- Tibia bone lead concentration

*From the lowest quintile of bone lead to the highest quintile, the odds of being hypertensive increased by 50 % (O.R. = 1.5 (95% C.I. 1.1 - 1.8)*
Blood Lead Levels and Cardiovascular Mortality: Results from NHANES III
(Schober et al, Environ Health Persp 114:1538-1541; 2006)

12 year longitudinal study of participants in the National Health and Nutrition Examination Survey.
Subjects ≥ 40 years of age (n = 9757)

<table>
<thead>
<tr>
<th>Blood Lead</th>
<th>RR of Cardiovascular Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 µg/dL</td>
<td>1.0</td>
</tr>
<tr>
<td>5 - 9 µg/dL</td>
<td>1.20 (0.93 - 1.55)</td>
</tr>
<tr>
<td>≥ 10 µg/dL*</td>
<td>1.55 (1.16 - 2.07)**</td>
</tr>
</tbody>
</table>

* Median = 11.8 µg/dL  ** Test for trend (P < 0.01)

Blood Lead Below 0.48 μmol/L (10 µg/dL) and Mortality Among US Adults
[Menke et al, Circulation 114:1388-1394; 2006]


<table>
<thead>
<tr>
<th>Cause</th>
<th>Tercile I</th>
<th>Tercile III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BLL ≤ 1.93 µg/dL</td>
<td>BLL ≥ 3.63 µg/dL</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>50 1.0</td>
<td>234 1.89 (1.04 - 3.43)</td>
</tr>
<tr>
<td>Stroke</td>
<td>22 1.0</td>
<td>63 2.51 (1.20 - 5.26)</td>
</tr>
<tr>
<td>Cancer</td>
<td>67 1.0</td>
<td>238 1.10 (0.82 - 1.47)</td>
</tr>
</tbody>
</table>

Hazard Ratios for Mortality, multivariate adjusted*

*Age, race-ethnicity, sex, diabetes, BMI, current/former smoking, alcohol, physical activity, income, CRP, cholesterol, education, urban, menopause, hypertension, renal function
Impairment of renal function with increasing blood lead concentration in the general population

Staessen JA et al. NEJM 327:151-6; 1992
- Random population sample of 965 men and 1016 women (age 20 to 88)
- Blood lead range 1.7 - 72.5 ug/dL; geometric mean = 10 ug/dL
- Significant correlation between age-adjusted creatinine clearance and blood lead
- Relationship persisted after excluding subjects with occupational Pb exposure, or those with highest tercile of PbB (geom. mean 18.4 ug/dL)

Association of Cumulative Lead and Neurocognitive Function in an Occupational Cohort
[Khalil et al, Neuropsych 209:10-19; 2009]

Lead workers and controls previously assessed in 1982 underwent re-testing of neuropsych status, plus bone lead measurement, in 2004.

Mean BLL of workers in 1982 = 40 µg/dL; in 2004 = 12 µg/dL (n=83)
Control BLL (1982) = 7.2; (2004) = 3 (n=51)
Mean age of workers in 2004 = 54 ± 9 years; last worked with lead a mean of 6 years prior (interquartile range 0.02 - 16 y).

Tibia bone lead of exposed subjects  57 µg/g ( 20, 86)
               of unexposed subjects  12 µg/g (-8, 32)
Regression Coefficients for \( \Delta \) Cognition by Bone Pb

<table>
<thead>
<tr>
<th>Peak tibia Pb (( \mu g/g ))</th>
<th>Total Cognitive Score</th>
<th>Spatial</th>
<th>Executive Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed</td>
<td>- 0.352*</td>
<td>- 0.338*</td>
<td>- 0.342*</td>
</tr>
<tr>
<td>Nonexposed</td>
<td>- 0.049</td>
<td>0.079</td>
<td>0.166</td>
</tr>
</tbody>
</table>

\*\( P < 0.01 \); Adjusted for age, education, income, BP, yrs employed, yrs since last worked, smoking, etoh, and baseline score

In models, blood lead was not associated with cognitive function

The lead exposed workers experienced 17% greater loss in total cognitive score as compared with nonexposed workers.

[Khalil et al, 2009]

---

Bone lead concentration predicts decrements in cognitive function in older adults

Normative Aging Study (Weisskopf et al, Epidemiology. 18:59; 2007)

N = 1089 older, mainly white men, mean age 68.7 ± 7.4 yrs.
Repeat neuropsych testing over ≈ 3.5 yr interval

Median PbB = 5 \( \mu g/dL \) (IQR 3 - 6)
Bone lead: longitudinal \( \downarrow \) visuospatial performance (N = 761)

Response latency on pattern recognition test

Patella Pb
Lead, diabetes, hypertension and renal function*

- Long term low-level lead accumulation (tibia bone lead) is associated with increased risk of declining renal function particularly among diabetics or hypertensives

*Tsaih SW et al: Environmental Health Perspectives 112:1178-1182, 2004

Case discussion: Lead and chronic disease

- 46 year old man works as radiator repairman, in an automotive repair shop for 14 years.
- 2 year history of crampy abdominal pain and paresthesias in lower extremities
- BLL: January 2008 = 25 ug/dl
  - Recheck March 2008 = 21 ug/dl (Is this significantly lower?)
- PMH: diabetes for > 15 years. HgB A1c 12.2, Cr 1.2
- Medications: amitryptiline, hydrocodone, ibuprofen, gabapentin, metformin, glypizide
- PE: normal exam, including neurological.

Clinical Considerations -

- Are the paresthesias related to his lead exposure?
- With his diabetes, what are the chances of worsening kidney function if exposure continues?
- What does his abdominal pain tell you?
- What else can you recommend?
Recommendations for Medical Management of Adult Lead Exposure

Michael J. Kosnett,1 Richard P. Wodson,2 Stephen J. Rothenberg,2,4 Karen L. Hopkins,5 Barbara L. Materna,6 Brian S. Schwartz,7,8 Howard Hu,9 and Alan Woolt10


Michael.Kosnett@uchsc.edu

CALIFORNIA DEPT. of PUBLIC HEALTH
LEAD MANAGEMENT GUIDELINES

Medical Guidelines
for the Lead-Exposed Worker

Located at:
http://www.cdph.ca.gov/programs/olppp/Pages/default.aspx
Although the OSHA lead Standard needs to be updated, the current Standard gives physicians discretion to order medical removal (MRP) at any level of lead exposure.

OSHA, 1977

“... if the examining physician recommends special protective measures for an employee (e.g., use of a powered air purifying respirator) or recommends limitations on an employee’s exposure to lead, then the employer must implement these recommendations. Recommendations may be more stringent than the specific provisions of the standard. The examining physician, therefore, is given broad flexibility to tailor special protective procedures to the needs of individual employees...The return of the employee to his or her former job status, or the removal of special protections or limitations, depends upon the examining physician determining that the employee is no longer at increased risk of material impairment or that special measures are no longer needed.”

<table>
<thead>
<tr>
<th>BLL (µg/dL)</th>
<th>Recommended Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 - 9</td>
<td>Discuss health risks;</td>
</tr>
<tr>
<td></td>
<td>Reduce Pb exposure for</td>
</tr>
<tr>
<td></td>
<td>women who are or may</td>
</tr>
<tr>
<td></td>
<td>become pregnant.</td>
</tr>
<tr>
<td>10 - 19</td>
<td>Educate about ways to</td>
</tr>
<tr>
<td></td>
<td>decrease lead exposure.</td>
</tr>
<tr>
<td></td>
<td>Increase biological</td>
</tr>
<tr>
<td></td>
<td>monitoring. Consider</td>
</tr>
<tr>
<td></td>
<td>removal from exposure</td>
</tr>
<tr>
<td></td>
<td>if BLL stays above 10,</td>
</tr>
<tr>
<td></td>
<td>or if there is a medical</td>
</tr>
<tr>
<td></td>
<td>condition that increases</td>
</tr>
<tr>
<td></td>
<td>risk with continued</td>
</tr>
<tr>
<td></td>
<td>exposure.</td>
</tr>
<tr>
<td>20 - 29</td>
<td>Remove from exposure if</td>
</tr>
<tr>
<td></td>
<td>repeat BLL measured in</td>
</tr>
<tr>
<td></td>
<td>4 weeks remains ≥ 20.</td>
</tr>
</tbody>
</table>
Logistical issues in implementing new “medical removal protection” levels: The need for increased engineering controls and respiratory protection

Toxicokinetic simulation of battery workers*

<table>
<thead>
<tr>
<th>Job Category</th>
<th>% BLL &gt;10</th>
<th>% BLL &gt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grid Casting</td>
<td>57.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Pasting</td>
<td>58.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Cast on strap</td>
<td>57.4</td>
<td>9.2</td>
</tr>
<tr>
<td>HV Welding</td>
<td>59.7</td>
<td>10.2</td>
</tr>
</tbody>
</table>

*Assumes: Pb -Air = 25 µg/m³; Pop Avg BLL = 6 µg/dL

Froines JR et al. Occup Hyg 1:279-292; 1995
Other Interventions for High PbB

- Education about other sources of Lead
  - Smoking
  - Eating in work area
  - Hand hygiene (brush fingertips!)
  - Gum chewing
  - Change to clean clothes before going home
- Work Comp - file Doctor’s First Report, contact Carrier’s Risk Manager
- Blood lead screen of pre-school age children in the household, for Take-Home exposure

Chelation for Lead Intoxication

- Chelating agents decrease lead concentration in blood and certain tissues, and greatly accelerate urinary lead excretion
  - $\text{CaNa}_2\text{EDTA}$ (intravenous or intramuscular)
  - Succimer (DMSA) (oral)
  - DMPS (oral or intravenous)

**HOWEVER,**

- There are no randomized, placebo controlled trials of chelation that indicate it improves the therapeutic outcome of patients
Chelation for Lead Intoxication in Adults

- BLLs (Pbb) ≥ 80 to 100 µg/dL - very often warrant chelation to prevent encephalopathy, which can have an unpredictable sudden onset, with devastating irreversible consequences.
- BLLs 50 to 79 - consider chelation if persistently symptomatic despite MRP.
- BLL’s below 50 essentially never need chelation.

Summary of Key Points

The 1977 OSHA Lead Standards that established a medical removal blood lead level of 50 µg/dL are insufficiently protective and are outdated.

Low to moderate levels of lead exposure are associated with a risk of hypertension, decrement in renal function, cognitive dysfunction, and adverse reproductive outcome.

The goal is to keep long-term BLL < 10; a single level over 30, or two consecutive BLL over 20 merit medical removal.

Chelation is indicated for very high BLL, or symptomatic high levels. However, aspects of the therapeutic efficacy of chelation are unresolved.
Thank you for participating in today’s webinar. At the conclusion of this call you will receive an email with a link to a post-webinar survey.

You will need to complete this survey in order to receive CME for this webinar.

This webinar presentation can be downloaded at www.woema.org