BIOMONITORING AND BIOLOGICAL MATRIX CONSIDERATIONS

Kathleen L. Caldwell, PhD
Robert L. Jones, PhD
Inorganic and Radiation Analytical Toxicology Branch
Matrix Decisions

- Whole blood/serum
- Urine
- Adipose tissue
- Hair
- Breast milk
- Saliva and sputum
- Semen
- Exhaled air
### Selection of Matrix: Toxicant Independent

<table>
<thead>
<tr>
<th>Factor</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount (body)</td>
<td>Regulated</td>
<td>Not regulated</td>
</tr>
<tr>
<td>Amount available</td>
<td>Limited</td>
<td>Less limited</td>
</tr>
<tr>
<td>Composition</td>
<td>Varies</td>
<td>Varies widely</td>
</tr>
<tr>
<td>Collection</td>
<td>Invasive</td>
<td>Non-invasive (generally)</td>
</tr>
<tr>
<td>Storage</td>
<td>Depends</td>
<td>Generally stable</td>
</tr>
</tbody>
</table>
## Final Selection of Matrix

<table>
<thead>
<tr>
<th>Factor</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toxicant Independent Factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed Amount (body)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Amount available</td>
<td>Limited</td>
<td>Less limited</td>
</tr>
<tr>
<td>Composition</td>
<td>Varies</td>
<td>Varies widely</td>
</tr>
<tr>
<td>Collection</td>
<td>Invasive</td>
<td>Non-invasive</td>
</tr>
<tr>
<td>Storage</td>
<td>Depends</td>
<td>Stable</td>
</tr>
<tr>
<td><strong>Toxicant Dependent Factors - Persistent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>Outstanding</td>
<td>Good</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Excellent</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>Toxicant Dependent Factors – NonPersistent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>Excellent</td>
<td>Poor to Excellent</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Very poor</td>
<td>Poor to Excellent</td>
</tr>
</tbody>
</table>
Research studies (separate from NER) are required to determine which blood and urine levels are safe and which are associated with disease.
Analyte / Matrix Issues

- Decide on the analytes of importance (e.g. toxic or essential metals, pesticides, PCBs, etc.)

- The two primary matrices used for biomonitoring are blood (or its components) and urine
Example: Thallium

- **Key characteristics**
  - Mimics K\(^+\) in toxicity and pharmacology similar to K\(^+\)

- **Absorption**
  - High, following ingestion, inhalation, dermal

- **Distribution**
  - Widely, especially tissues with high blood flow

- **Metabolism**
  - Nil, but entero-hepatic circulation occurs

- **Elimination**
  - Feces (~50%) and urine (~25%) relatively rapid (days)

Urine is an ideal matrix for thallium measurement
Example: Arsenic

- **Key characteristics**
  - Inorganic (trivalent) is toxic acutely (and chronically)

- **Absorption**
  - Moderate following ingestion

- **Distribution**
  - Widely, especially RBCs, liver, kidney, muscle, skin, brain

- **Metabolism**
  - Methylation; (pentavalent is reduced to trivalent)

- **Elimination**
  - Slow urinary elimination (days)

- Total As and speciation urine methods are available
Public Health Use of the Reports

Provide unique exposure information to scientist, physicians, and health officials to help prevent exposure to some environmental chemical or biochemical indicators of diet and nutrition.

## Urinary Antimony

Geometric mean and selected percentiles of urine concentrations (in μg/L) for the U.S. population from the National Health and Nutrition Examination Survey.

<table>
<thead>
<tr>
<th>Survey years</th>
<th>Geometric mean (95% conf. interval)</th>
<th>50th (95% confidence interval)</th>
<th>75th (95% confidence interval)</th>
<th>90th (95% confidence interval)</th>
<th>95th (95% confidence interval)</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>99-00</td>
<td>.132 (.120-.145)</td>
<td>.130 (.120-.150)</td>
<td>.220 (.200-.230)</td>
<td>.330 (.300-.350)</td>
<td>.430 (.390-.470)</td>
</tr>
<tr>
<td></td>
<td>01-02</td>
<td>.134 (.126-.142)</td>
<td>.130 (.130-.140)</td>
<td>.190 (.180-.200)</td>
<td>.270 (.250-.310)</td>
<td>.350 (.320-.400)</td>
</tr>
<tr>
<td></td>
<td>03-04</td>
<td>*</td>
<td>.080 (&lt;LOD-.090)</td>
<td>.130 (.120-.150)</td>
<td>.200 (.190-.220)</td>
<td>.280 (.250-.320)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6-11 years</td>
<td>99-00</td>
<td>.176 (.154-.200)</td>
<td>.190 (.160-.210)</td>
<td>.260 (.230-.280)</td>
<td>.350 (.300-.400)</td>
<td>.440 (.320-.600)</td>
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<tr>
<td></td>
<td>01-02</td>
<td>.146 (.134-.160)</td>
<td>.150 (.130-.160)</td>
<td>.200 (.180-.210)</td>
<td>.270 (.240-.330)</td>
<td>.340 (.280-.440)</td>
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<tr>
<td></td>
<td>03-04</td>
<td>.099 (.087-.114)</td>
<td>.100 (.070-.120)</td>
<td>.160 (.120-.200)</td>
<td>.240 (.190-.310)</td>
<td>.310 (.230-.330)</td>
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<tr>
<td>12-19 years</td>
<td>99-00</td>
<td>.158 (.141-.178)</td>
<td>.170 (.150-.180)</td>
<td>.240 (.210-.270)</td>
<td>.350 (.290-.420)</td>
<td>.460 (.350-.510)</td>
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<tr>
<td></td>
<td>01-02</td>
<td>.169 (.156-.184)</td>
<td>.160 (.130-.160)</td>
<td>.240 (.220-.260)</td>
<td>.350 (.320-.410)</td>
<td>.460 (.400-.500)</td>
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<td>03-04</td>
<td>.105 (.095-.115)</td>
<td>.100 (.090-.120)</td>
<td>.150 (.140-.160)</td>
<td>.230 (.200-.270)</td>
<td>.290 (.250-.370)</td>
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<td>20 years and older</td>
<td>99-00</td>
<td>.123 (.112-.137)</td>
<td>.120 (.110-.130)</td>
<td>.200 (.180-.220)</td>
<td>.310 (.290-.350)</td>
<td>.430 (.390-.470)</td>
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<tr>
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<td>01-02</td>
<td>.128 (.119-.136)</td>
<td>.130 (.120-.130)</td>
<td>.180 (.170-.190)</td>
<td>.250 (.220-.300)</td>
<td>.330 (.280-.390)</td>
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<tr>
<td></td>
<td>03-04</td>
<td>*</td>
<td>.070 (&lt;LOD-.080)</td>
<td>.120 (.100-.140)</td>
<td>.190 (.170-.210)</td>
<td>.270 (.220-.320)</td>
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<tr>
<td>Gender</td>
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<td></td>
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<tr>
<td>Males</td>
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<td>.143 (.131-.157)</td>
<td>.150 (.130-.160)</td>
<td>.240 (.220-.260)</td>
<td>.350 (.300-.390)</td>
<td>.470 (.390-.570)</td>
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<tr>
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<td>01-02</td>
<td>.145 (.136-.154)</td>
<td>.140 (.130-.150)</td>
<td>.200 (.190-.210)</td>
<td>.310 (.280-.330)</td>
<td>.390 (.350-.440)</td>
</tr>
<tr>
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<td>03-04</td>
<td>.095 (.088-.103)</td>
<td>.090 (.080-.100)</td>
<td>.140 (.130-.160)</td>
<td>.220 (.200-.250)</td>
<td>.320 (.270-.350)</td>
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<tr>
<td>Females</td>
<td>99-00</td>
<td>.122 (.109-.137)</td>
<td>.120 (.110-.140)</td>
<td>.200 (.180-.220)</td>
<td>.300 (.280-.340)</td>
<td>.400 (.350-.460)</td>
</tr>
<tr>
<td></td>
<td>01-02</td>
<td>.125 (.117-.133)</td>
<td>.120 (.120-.130)</td>
<td>.180 (.160-.190)</td>
<td>.240 (.220-.280)</td>
<td>.320 (.260-.360)</td>
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<td>03-04</td>
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<td>&lt; LOD</td>
<td>.120 (.090-.140)</td>
<td>.180 (.150-.220)</td>
<td>.230 (.190-.330)</td>
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<tr>
<td>Race/ethnicity</td>
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<td>Mexican Americans</td>
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<td>.140 (.120-.170)</td>
<td>.210 (.180-.240)</td>
<td>.300 (.260-.390)</td>
<td>.430 (.330-.560)</td>
</tr>
<tr>
<td></td>
<td>01-02</td>
<td>.142 (.130-.154)</td>
<td>.130 (.130-.150)</td>
<td>.200 (.170-.230)</td>
<td>.260 (.240-.320)</td>
<td>.360 (.300-.400)</td>
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<tr>
<td></td>
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<td>.093 (.079-.110)</td>
<td>.090 (&lt;LOD-.120)</td>
<td>.140 (.120-.160)</td>
<td>.190 (.160-.260)</td>
<td>.270 (.210-.330)</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>99-00</td>
<td>.175 (.148-.207)</td>
<td>.180 (.150-.200)</td>
<td>.260 (.230-.300)</td>
<td>.400 (.310-.490)</td>
<td>.490 (.410-.710)</td>
</tr>
<tr>
<td></td>
<td>01-02</td>
<td>.180 (.164-.197)</td>
<td>.170 (.160-.190)</td>
<td>.250 (.220-.280)</td>
<td>.360 (.320-.410)</td>
<td>.460 (.370-.530)</td>
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<td></td>
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<td>.110 (.100-.120)</td>
<td>.160 (.150-.190)</td>
<td>.230 (.200-.280)</td>
<td>.310 (.250-.360)</td>
</tr>
<tr>
<td>Non-Hispanic whites</td>
<td>99-00</td>
<td>.128 (.115-.144)</td>
<td>.130 (.110-.140)</td>
<td>.210 (.190-.230)</td>
<td>.330 (.280-.350)</td>
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</tbody>
</table>

Limit of detection (LOD, see Data Analysis section) for Survey years 99-00, 01-02, and 03-04 are 0.04, 0.04, and 0.07, respectively. < LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. * Not calculated: proportion of results below limit of detection was too high to provide a valid result.
CASE STUDY: INVESTIGATION OF ANTIMONY EXPOSURE IN FIRE FIGHTERS - FLORIDA, 2009
Background on HHE

- October 2008: HHE request from the Fire Chief at Fire Department (FD) A in Florida
- Concerned possible outbreak of antimony toxicity as a result of wearing uniform pants made from FireWear® fabric
- FireWear fabric: antimony trioxide as a flame retardant
**FireWear fabric**

- Consists of 55% FFR (fibrous flame retardant) fiber and 45% cotton

- FFR fiber: acrylonitrile, vinylidene chloride, and antimony trioxide

- Meet requirements set by National Fire Protection Association (NFPA)

- Worn by various FDs nationwide
Background on HHE

• Index fire fighter: unexplained neurologic symptoms since October 2007

• Saw local physician in August 2008 who performed heavy metals testing on a hair sample

• Revealed hair elevated antimony level

• Local union encouraged all fire fighters in FD-A to undergo testing for antimony
Antimony Toxicity
• Acute exposure: abdominal pain, cough, loss of appetite, itching, irritation of skin, eyes, nose, throat
• Chronic exposure: headache, sleeplessness, dizziness, metallic taste, lung disease, weight loss, nausea, vomiting, diarrhea
• Neurological effects not observed in humans

Reported Symptoms: Fire Dpt A
• 45 workers’ compensation claims filed
• Fatigue (38%)
• Headache (27%)
• Muscle cramps (16%)
• Joint pain (13%)
• No symptoms (38%)
Widespread Concern About Outbreak

Fire-Resistant Clothing Suspected in Heavy Metal Poisoning

Firefighters poisoned by chemical in pants fabric

Chemical concerns cause two more fire departments to stop using fire-resistant pants

Firefighters Blame FireWear Uniform Pants For Sickness

Sick firefighters blame chemical in pants

Firefighters may be wearing a health hazard

Firefighter Clothing May Be Toxic
Objectives and Study population of HHE

- Determine extent of antimony exposure among fire fighters
- Determine whether urine concentrations of antimony differed among fire fighters wearing and not wearing FireWear pants

- Fire Department A (unexposed)
  - No longer wearing FireWear pants
  - Employs 199 fire fighters
  - Invited 112 participants

- Fire Department B (exposed)
  - Wearing FireWear pants at the time
  - Employs 96 fire fighters
  - Invited 42 participants
Laboratory Methods for Antimony

• Collected spot urine samples
• Analyzed at NCEH’s Inorganic Toxicology Lab
• Antimony measured by ICP-DRC-MS
• Adjusted for creatinine

• Compared results with:
  – National reference range for urine antimony (0.120-0.364 μg/g creatinine)
  – Based on 3rd National Report on Human Exposure to Environmental Chemicals, 2005
Geometric Mean Urine Antimony Concentrations

- Upper limit of national reference range
- Geometric mean of general population

Geometric mean urine antimony (μg/g creatinine)

Fire Department A
Fire Department B
Population
Conclusions

- Fire fighters from FD-A and FD-B: urine antimony concentrations below or within normal range for general population

- Pants made from FireWear fabric: no effect on body burden of antimony

- Wearing these pants does not pose a risk for antimony toxicity
Conclusions

Highlights importance of:

- Using validated methods for toxicity determination
- Public health responsibility of effectively communicating accurate information
Appropriate Testing Methods

- Urine testing: reliable and valid test method for measuring antimony concentrations in the body
- CDC has established US population reference values
- Hair testing opposed by American Medical Association (AMA)
- ATSDR panel concluded insufficient data to support use
Hair Testing Limitations

- Accepted standards on methods of collection, storage, analysis lacking
- No regulation and certification of labs
- No established references ranges for hair levels of heavy metals
- Cannot distinguish between internal and external exposure
- Does not predict toxicity or disease
Effective Communication

- Firefighters received reliable and unreliable information from:
  - Personal physicians
  - Internet
  - Media reports
  - Firefighter blogs

- NIOSH contacted by concerned fire fighters, fire chiefs, and union leaders nationwide
Fanning the Flames: An Evaluation of Antimony Exposure in Florida Firefighters, 2009

N de Paris, J Garigliani, R Castellini, R Bernardi, J de Paul, M National Institute for Occupational Safety and Health National Center for Environmental Health Centers for Disease Control and Prevention, Cincinnati, OH and Atlanta, GA

ABSTRACT

INTRODUCTION

METHODS

RESULTS

CONCLUSIONS

RECOMMENDATIONS

Pseudo-Outbreak of Antimony Toxicity in Firefighters --- Florida, 2009

Antimony studies, in combination with biology, have been used as fumes retarders in textiles since the 1940s. Uniforms made from fabric containing antimony are common among firefighters. In a recent report, antimony levels in fabrics from 20 firefighter stations in 10 different locations were evaluated. The results showed that antimony levels in fabrics from firefighter stations ranging from 0.05 to 0.25 mg/g were detected. These levels exceeded the recommended exposure limits of 0.05 mg/g. The study also revealed that antimony levels in fabrics from firefighter stations were significantly higher than those in non-fabric materials. The results indicate a potential health risk to firefighters and those who come into contact with these fabrics. It is recommended that further research be conducted to determine the long-term effects of antimony exposure on firefighters and their families. The study also highlights the need for improved protective gear and safety measures to prevent potential health risks to firefighters.
Effective Communication

NIOSH Research Demonstrates That Uniform Pants Are Safe

Antimony Exposure Among Firefighters: FAQs about the February NIOSH Health Hazard Evaluation in Florida
Effective Communication

ILLNESS AND FIREFIGHTER UNIFORM PANTS? NIOSH INVESTIGATION QUESTIONS AND ANSWERS

FireWear Pants Not The Problem
With one exception, ATSDR is unaware of any conclusive studies that link hair concentrations of contaminants to specific health outcomes.... As the exception, scientists have studied how hair concentrations of methyl mercury in pregnant mothers relate to adverse developmental effects in their children.

http://www.atsdr.cdc.gov/hac/hair_analysis/
Conclusions

• Carefully consider the laboratory criteria when selecting a laboratory.
• Understanding the “Quality Factors” of an Analytical Method as implemented, will assist with lab selection.
• Analytical method general issues will help you in evaluating a lab’s claims for analyte/matrix methods.
• ICP-DRC-MS has great advantages as well as limitations.
Questions?

For more information please contact Centers for Disease Control and Prevention (CDC)
1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: http://www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.