Biomonitoring Methods for Assessing Human Exposure to Perchlorate

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“The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and do not represent any agency determination or policy.”
Overview

- Biomonitoring
- Analytical Methods
- Exposure Studies
  - Atlanta
  - National health study (NHANES)
Biomonitoring

Assessment of internal dose exposure by measuring a toxicant (or its metabolite or reaction product) in human blood, urine, saliva, adipose, or other tissue.
Biomonitoring Questions

- **What** toxicant exposure has occurred (is occurring)?
- **Who** has been exposed (is being exposed)?
- **How much** has each person been exposed?
- **Does exposure correlate with a health effect?**
Exposure and health effects pathway

Location: proximity to source

External dose: air, water, food, soil

- inhalation
- ingestion
- skin absorption

Internal dose: blood, serum, urine, tissue

Biologically effective dose: blood, tissue

Health effect
Priority Matrix for Chemical Exposures

Number of people

Many

Few

Concentration in the body
(relative to health threshold level)

Low  High
Uses of Perchlorate

- Component of Solid Fuel for Rockets and Missiles
- Explosives, Fireworks, Road Flares, Air Bags
  Tanning and Leather Finishing
- Naturally occurs in Chile and West Texas
Perchlorate contamination of water is widespread in the US

- **Drinking water**
  - Thirty-plus U.S. states

- **Ground water**
  - Aquifers associated with disposal sites
  - Natural sources

- **Lakes and rivers**
  - Lake Mead
  - Colorado River

[http://www.epa.gov/fedfac/documents/perchlorate_map/nationalmap.htm](http://www.epa.gov/fedfac/documents/perchlorate_map/nationalmap.htm)
Potential sources for human exposure to perchlorate

- Direct consumption of contaminated water
- Crops grown with contaminated water or fertilizer
  - Food crops
  - Forage crops
Widespread perchlorate contamination of certain foods

- Multiple studies report perchlorate in milk, grains, fruits and vegetables.
  - FDA 2003, 2004
  - Kirk, et al. 2003, 2005
  - Sanchez, et al. 2005
  - Jackson, et al. 2005
Perchlorate can inhibit the sodium-iodide symporter
Key Question

Does exposure to relatively low levels of perchlorate in the environment significantly impair thyroid function?

Health Implications of Perchlorate Ingestion, National Research Council 2005
Potentially Susceptible Populations

- Neonates
- The developing fetus - pregnant woman dyad
- Women of reproductive age
- Populations with low intake of iodine
- Genetically susceptible populations?
Analytical Methodology
Biomonitoring for Perchlorate: Assessing Human Exposure

- **Urine**
  - Dilute and shoot
  - Method published in February 2005 in *Analytical Chemistry*

- **Blood Serum**
  - C18 SPE: approx 90% recovery
  - Also monitors iodide, thiocyanate, nitrate

- **Breast Milk**
  - C18 SPE: approx 85% recovery
  - Also monitors iodide, thiocyanate, nitrate

- **Infant Formula**
- **Amniotic Fluid**
Analytical Approach

1. Spike sample with stable isotope internal standards
2. Ion Chromatography
   • Chromatographic resolution
3. Electrospray Ionization
4. Tandem Mass Spectrometry
   • Sciex 4000 triple quadrupole
   • Mass spectral resolution
5. Quantify using stable isotope dilution
Method Summary

• Highly Selective and Sensitive Method
• Chromatographic resolution of isobaric interference $H^{34}\text{SO}_4^-$
• Linear calibration curve ($R^2 > 0.99$) from 0.05 – 100 ng/ml
• Lowest Reportable Level of 0.05 ng/ml in urine
• Rugged and Rapid Method
  – Analysis 75 unknowns per day
• Method published in Feb 2005 in Analytical Chemistry
Perchlorate Biomonitoring Applications

- Atlanta Convenience Population
- NHANES (work in progress)
Atlanta Convenience Population

- Anonymously collected spot urine samples for method validation
- 62 men and women residing in the Atlanta area
- No questionnaire data
- Not a representative population
- Atlanta area tap water perchlorate 0.2 ppb
Distribution of Perchlorate in Human Urine

- All samples contained perchlorate
- Log normal dist
- Min. 0.66 µg/L
- Geo. Mean 3.7 µg/L
- Max. 21 µg/L
Toxicological Perspectives

- 2002 Greer, et al, Human Exposure Study: ‘No Effect Level’ 5.2 µg/kg-day
- 2004 Mass DEP Proposed Reference Dose (RfD) 0.03 µg/kg-day
- 2005 NAS: RfD 0.7 µg/kg-day
- 2005 ATSDR Toxicological Profile: Minimal Risk Level (MRL) 0.7 µg/kg-day

Compare with urinary perchlorate levels:
  - Assume 70 kg weight, 1.44 g creatinine/day
Atlanta Convenience Population
Toxicological Perspective

- Urinary perchlorate (µg/g creatinine)
  - 260
  - 100
  - 34
  - 10
  - 1.5
  - 1

Greer, et al ‘No Effect Level’

NAS RfD

Mass DEP RfD
Atlanta Study Summary

- All samples contain measurable levels of perchlorate
- Perchlorate ranges from 1 – 35 µg/g creatinine; median = 7.8 µg/g
- Perchlorate exposure was less than NAS RfD for the majority of study participants
- Significant perchlorate exposure likely from non-tap water sources
National Health and Nutrition Examination Survey (NHANES)
NHANES

CDC survey designed to collect data on the health and nutritional status of a representative U.S. population (4000 - 5000 people/year)
NHANES

- Thorough interview and physical exam, including blood and urine collection
- Biomarkers of exposure to environmental chemicals quantified in blood and/or urine
Perchlorate NHANES

- Establish a reliable reference range for urinary perchlorate based on a representative US population
- Opportunity to link exposure data with thyroid function data
- Explore source apportionment – drinking water vs. food
- Monitor exposure trends
# Relevant NHANES Analytes

**1999 - 2006**

<table>
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<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Perchlorate in urine</td>
<td>1/3 subset, 6+</td>
<td>1/3 subset, 6+</td>
<td>complete set, 6+</td>
<td></td>
</tr>
<tr>
<td>Perchlorate in tap water</td>
<td></td>
<td></td>
<td></td>
<td>½ subset, 12+</td>
</tr>
<tr>
<td>Iodine in urine</td>
<td>1/3 subset, 6+</td>
<td>1/3 subset, 6+</td>
<td>1/3 subset, 6+</td>
<td>1/3 subset, 6+</td>
</tr>
<tr>
<td>total T4 in serum</td>
<td>1/3 subset, 12+</td>
<td>1/3 subset, 12+</td>
<td>?</td>
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<tr>
<td>TSH in serum</td>
<td>1/3 subset, 12+</td>
<td>1/3 subset, 12+</td>
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<tr>
<td>Thiocyanate in urine</td>
<td></td>
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<td>complete set, 6+</td>
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<tr>
<td>Nitrate in urine</td>
<td>1/3 subset, 6+</td>
<td></td>
<td>complete set, 6+</td>
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</tbody>
</table>
NHANES timeline
2001 - 2002

  - Urinary perchlorate
  - Urinary iodide
  - Urinary thiocyanate and nitrate
  - Smoking status
  - Relevant questionnaire data
  - Serum TSH
  - Serum total T4
National Report on Human Exposure to Environmental Chemicals

• To provide the public, federal partners, and policy makers with U.S. population exposure levels of important environmental chemicals.

• 2001 Report: 27 chemicals
• 2003 Report: 116 chemicals
• 2005 Report: 148 chemicals

• [www.cdc.gov/exposurereport](http://www.cdc.gov/exposurereport)

• Partnership between NCEH lab and NCHS/NHANES
Conclusions

• Measuring perchlorate in biological samples provides useful human exposure data.
• Perchlorate exposure was prevalent in an Atlanta convenience population, albeit at doses mostly less than the current EPA RfD.
• NHANES will provide estimates of the prevalence and magnitude of perchlorate exposure in the US, as well as assessment of thyroid impact of exposure to NIS-inhibitors.
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