# Biomonitoring Methods for Assessing Human Exposure to Perchlorate


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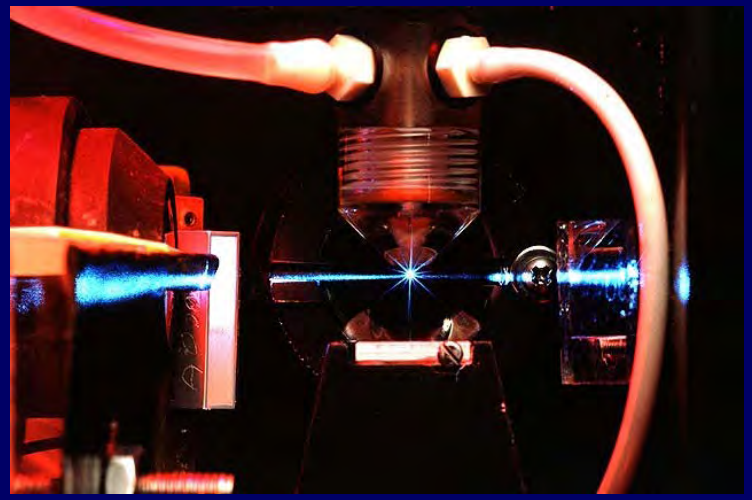
# Overview

- 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?**

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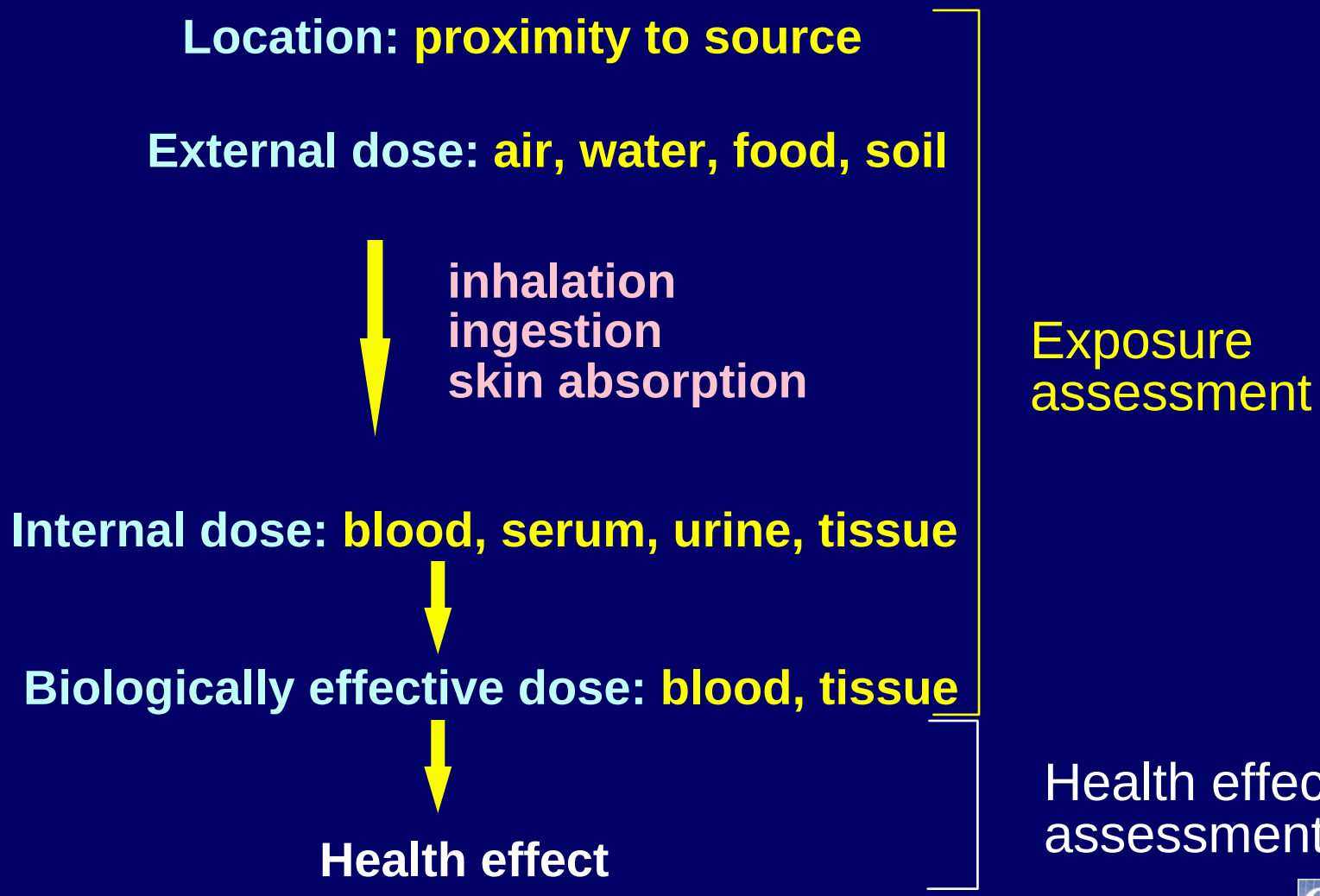
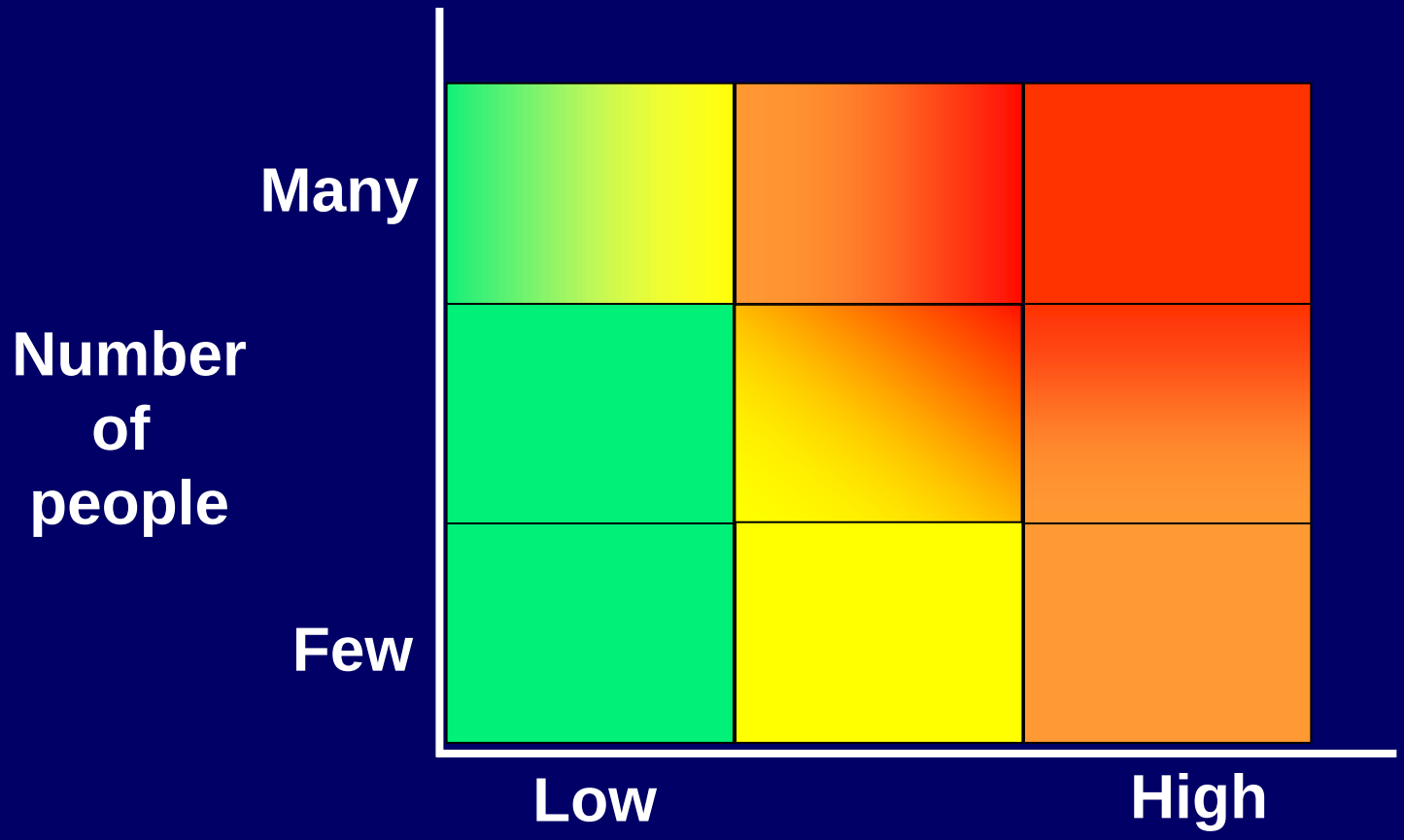
# Exposure and health effects pathway



# Priority Matrix for Chemical Exposures

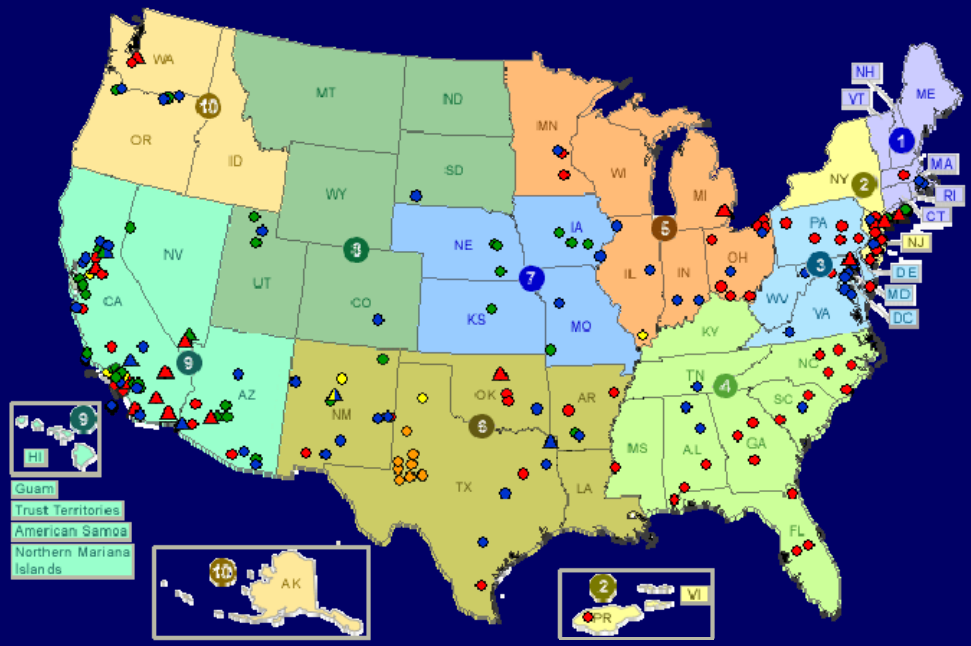


# Uses of Perchlorate


- 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

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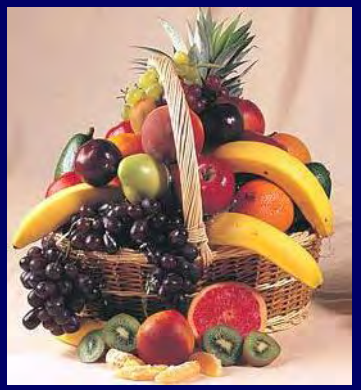
# Potential sources for human exposure to perchlorate

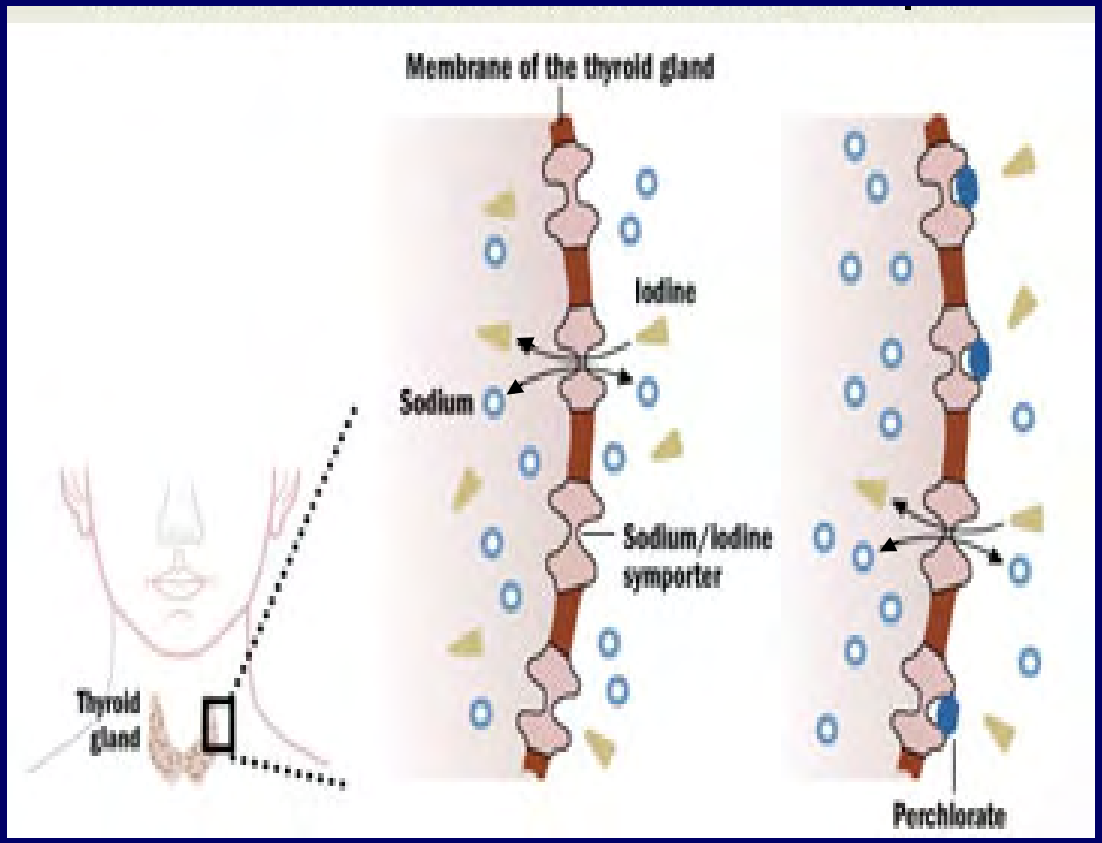
- Direct consumption of contaminated water
- Crops grown with contaminated water or fertilizer
  - Food crops
  - Forage crops



# Widespread perchlorate contamination of certain foods

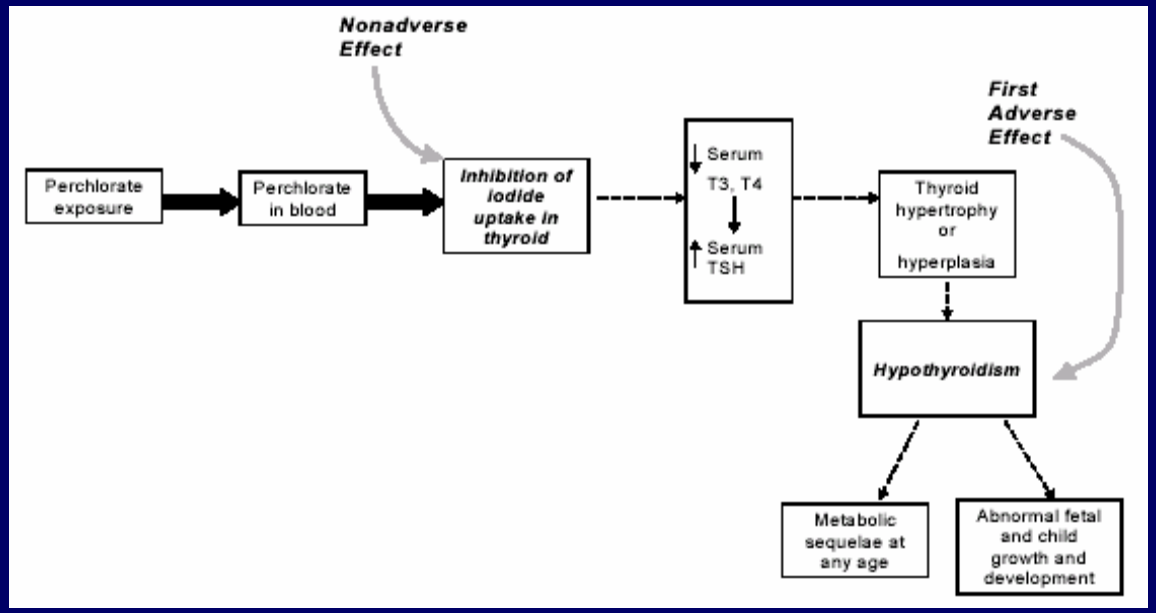
- Multiple studies report perchlorate in milk, grains, fruits and vegetables.
  - FDA 2003, 2004
  - Kirk, *et al.* 2003, 2005
  - Sanchez, *et al.* 2005
  - Jackson, *et al.* 2005

# 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?

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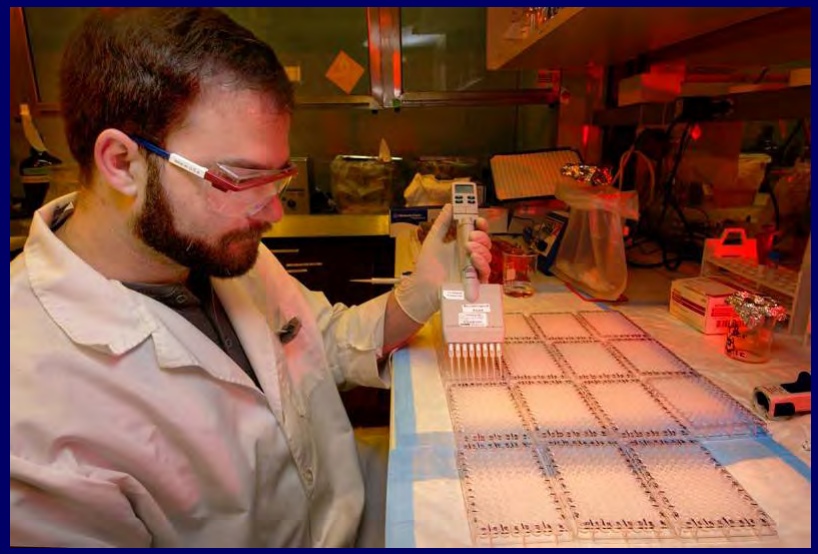
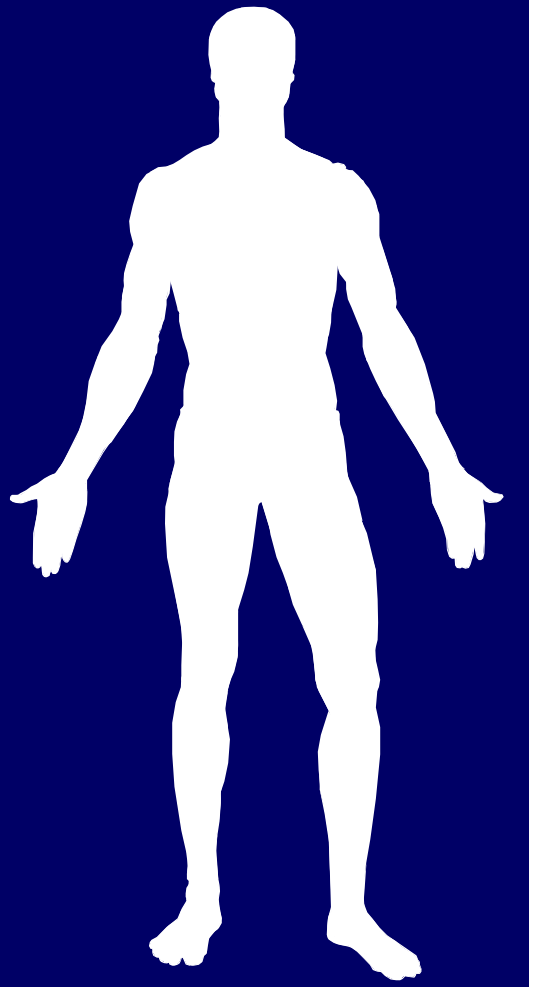
# Analytical Methodology



# 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**



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# 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

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# Method Summary

- Highly Selective and Sensitive Method
- Chromatographic resolution of isobaric interference $H^{34}SO_4^-$
- 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

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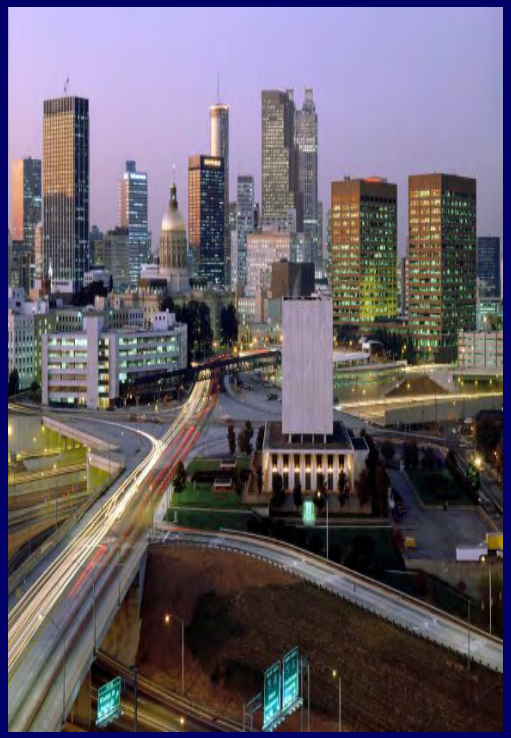
# Perchlorate Biomonitoring Applications

- Atlanta Convenience Population
- NHANES (work in progress)

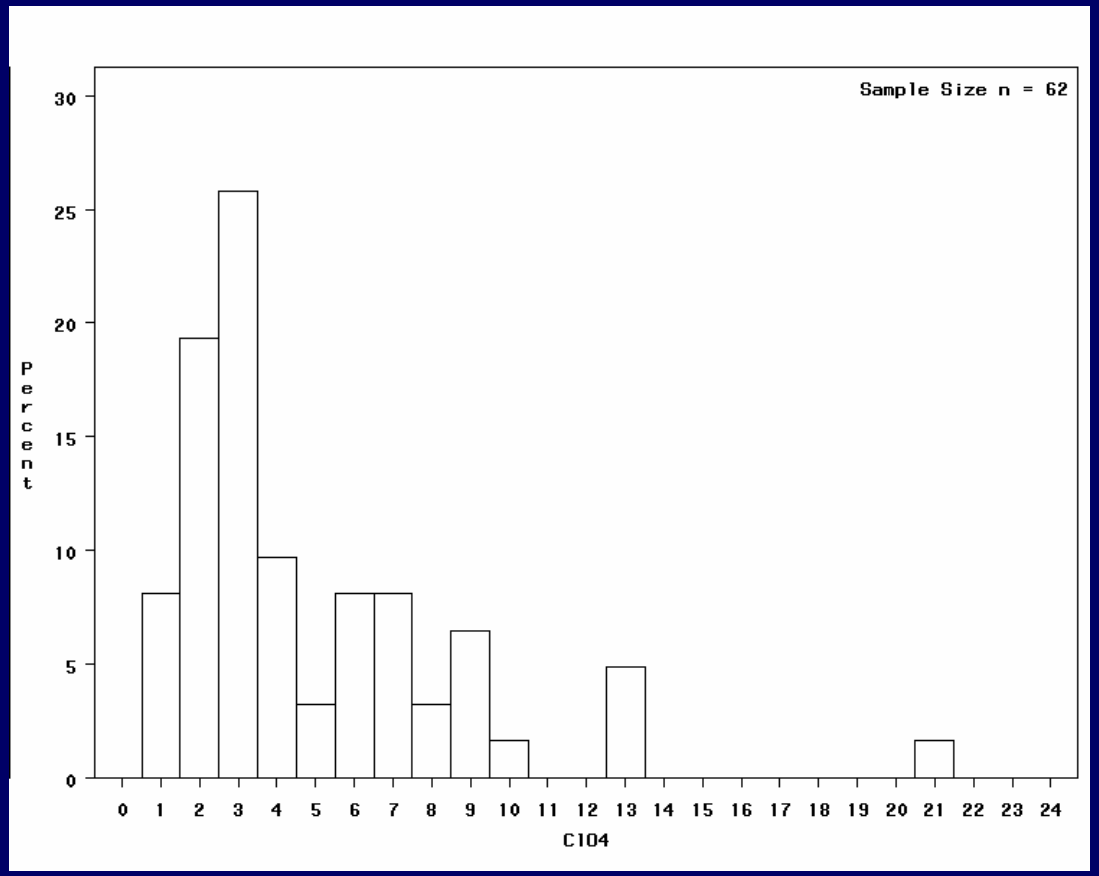
# Atlanta Convenience Population

- 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



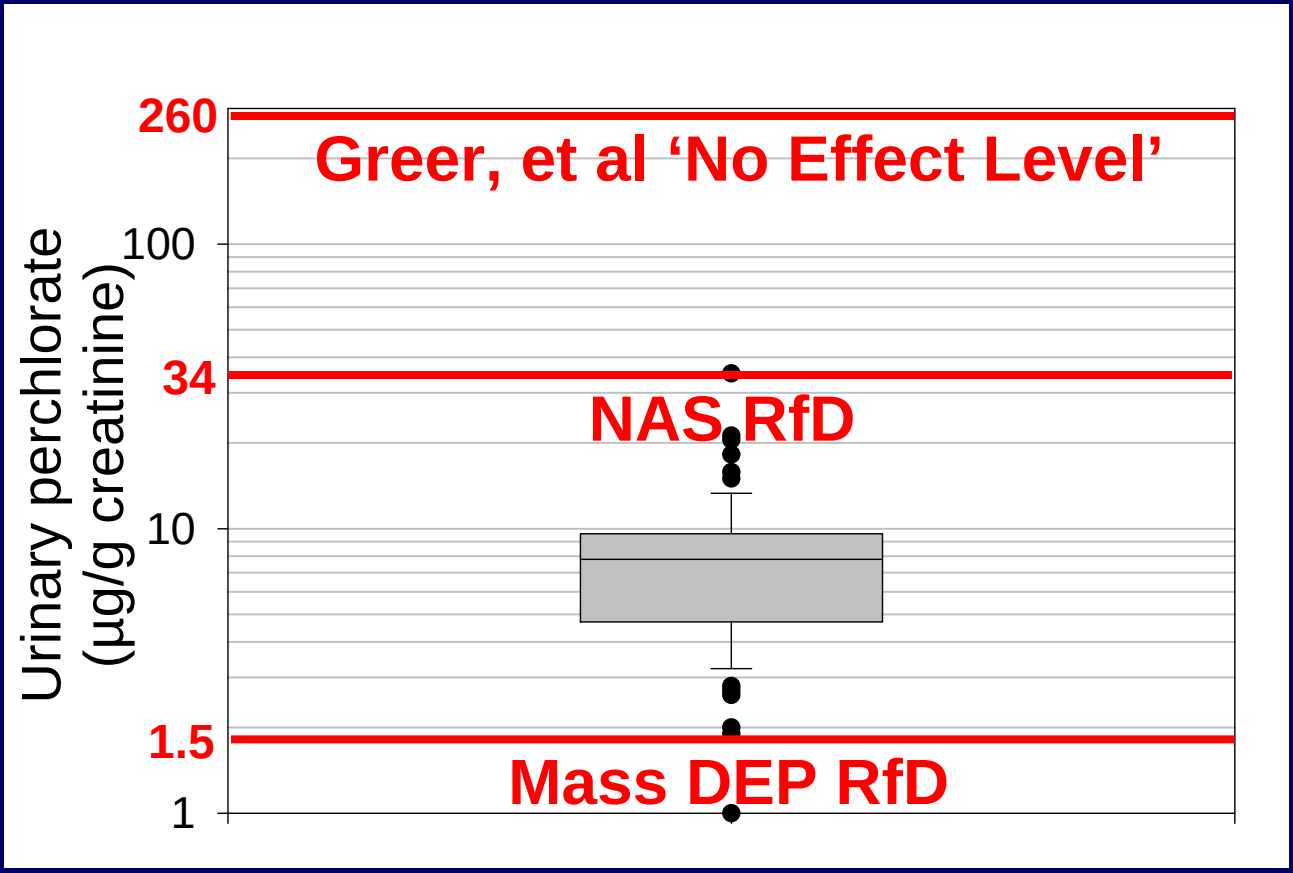
# Toxicological Perspectives

- 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



# 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)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# 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

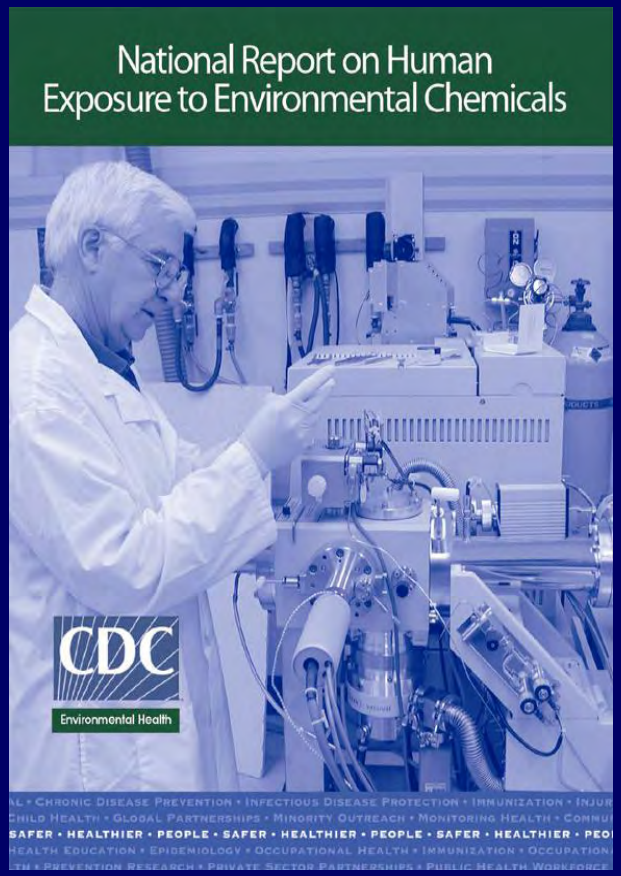
# Relevant NHANES Analytes
# 1999 - 2006

| Analytes | 1999-2000 | 2001-2002 | 2003-2004 | 2005-2006 |
|---|---|---|---|---|
| Perchlorate in urine | | 1/3 subset, 6+ | 1/3 subset, 6+ | complete set, 6+ |
| Perchlorate in tap water | | | | ½ subset, 12+ |
| Iodine in urine | 1/3 subset, 6+ | 1/3 subset, 6+ | 1/3 subset, 6+ | 1/3 subset, 6+ |
| total T4 in serum | 1/3 subset, 12+ | 1/3 subset, 12+ | ? | ? |
| TSH in serum | 1/3 subset, 12+ | 1/3 subset, 12+ | ? | ? |
| Thiocyanate in urine | | 1/3 subset, 6+ | | complete set, 6+ |
| Nitrate in urine | | 1/3 subset, 6+ | | complete set, 6+ |

# NHANES timeline
# 2001 - 2002

- Publish complete data set in 4th Exposure Report (2007), with early release for perchlorate data possible (2006)
  - 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
- 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.

# Acknowledgements


- Liza Valentin-Blasini
- Josh Mauldin
- Amy Delinsky
- David Ashley
- Jim Pirkle

- National Center for Health Statistics

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