Assessing Chemical Exposures: A Biomonitoring Update

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Human exposure to chemicals
The human exposure scenario

- Controlled conditions, as in animal studies, do not apply
- Numerous and ever-unknown exposure routes and sources
- Unknown dose, duration and timing
- People exposed to chemical “cocktails” (multiple/mixtures)
- How can we assess exposures?
Approaches to assess exposures

- Questionnaire/Historical Information
- Environmental monitoring
- Personal monitoring
  - Hand wipes
  - Personal samplers
- Biomonitoring

- Combine these approaches with calibrated and validated models
Biomonitoring

- Assessment of internal dose by measuring the parent chemical (or its metabolite or reaction product) in human samples
  - Integrates all sources/routes of exposure
  - Trace concentrations (vs environmental levels)
- We measure concentrations, not exposures
  - Analytical Chemistry foundation
Evaluation of human exposure using Biomonitoring at CDC—Examples

- **Large-scale surveys**
  - National Health and Nutrition Examination Survey (NHANES)
  - Others

- **Epidemiological studies of specific populations**
  - Susceptible/vulnerable
  - Highly exposed (e.g., occupational settings)

- **Emergency investigations**

- **Disease clusters**
NHANES

- **Annual survey (NCHS, CDC)**
  - US Congress funding
  - Clinical & nutritional data

- **Stratified, multistage probability sample of civilian, noninstitutionalized US population**
  - Yearly: ~5,000 persons, ~15 counties
  - Results for 2-year cycles (e.g., 1999-2000)

- **Physical examination, collection of medical history, demographic, socioeconomic & behavioral data**

- **Also collects biological specimens**
  - Clinical chemistry tests
  - Nutritional biomarkers & environmental chemicals

[http://www.cdc.gov/nchs/nhanes.htm](http://www.cdc.gov/nchs/nhanes.htm)
**Biomonitoring in NHANES**

- Limited amount of blood available; urine limited by age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Blood (mL)</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>9</td>
<td>No</td>
</tr>
<tr>
<td>3-5</td>
<td>22</td>
<td>No</td>
</tr>
<tr>
<td>6-11</td>
<td>38</td>
<td>Yes</td>
</tr>
<tr>
<td>12+</td>
<td>89-92</td>
<td>Yes</td>
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</tbody>
</table>

- Yes in 2015+
- Metals & NPs
- Nutrition markers

- POPs (12+), Pb, Cd & Hg (1+), cotinine (3+)
- Nutrition markers

- **Randomly selected subsets of participants**
  - Average sample size ~ 2500 people/chemical for each 2-year cycle
National Reports on Biochemical Indicators of Diet and Nutrition

- Improve laboratory diagnosis and detection of nutrition-related diseases

<table>
<thead>
<tr>
<th>Fat-Soluble Vitamins &amp; Nutrients</th>
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<tbody>
<tr>
<td>• Vitamin A</td>
</tr>
<tr>
<td>• Vitamin E</td>
</tr>
<tr>
<td>• γ-Tocopherol</td>
</tr>
<tr>
<td>• α-Carotene</td>
</tr>
<tr>
<td>• trans-β-Carotene</td>
</tr>
<tr>
<td>• β-Cryptoxanthine</td>
</tr>
<tr>
<td>• Lutein/zeaxanthin</td>
</tr>
<tr>
<td>• trans-Lycopene</td>
</tr>
<tr>
<td>• 25OH-Vitamin</td>
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<tr>
<td>• Fatty Acids</td>
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<table>
<thead>
<tr>
<th>Trace Elements</th>
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<tbody>
<tr>
<td>• Iodine (urine)</td>
</tr>
<tr>
<td>• Iron-Status Indicators</td>
</tr>
<tr>
<td>• Ferritin (serum)</td>
</tr>
<tr>
<td>• Iron (serum)</td>
</tr>
<tr>
<td>• TIBC (serum)</td>
</tr>
<tr>
<td>• Transferrin saturation (serum)</td>
</tr>
<tr>
<td>• Protoporphyrin (erythrocyte)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Water-Soluble Vitamins</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Folate</td>
</tr>
<tr>
<td>• Vitamin B6</td>
</tr>
<tr>
<td>• Vitamin B12</td>
</tr>
<tr>
<td>• Homocysteine</td>
</tr>
<tr>
<td>• Methylmalonic acid</td>
</tr>
<tr>
<td>• Vitamin C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Isoflavones &amp; Lignans</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Genistein</td>
</tr>
<tr>
<td>• Daidzein</td>
</tr>
<tr>
<td>• O-DMA</td>
</tr>
<tr>
<td>• Equol</td>
</tr>
<tr>
<td>• Enterodiol</td>
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<tr>
<td>• Enterolactone</td>
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</tbody>
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http://www.cdc.gov/nutritionreport/
CDC’s National Reports on human exposure to environmental chemicals

- Ongoing biomonitoring assessment of US population exposure to select metals, POPs, non-persistent chemicals
  - www.cdc.gov/exposurerreport
- Set reference ranges
- Track temporal trends
- Monitor interventions
- Assist with priorities
- Exposure/risk assessment
The Exposure Reports have and don’t have…

- Limited data interpretation
- No health outcomes analysis
  - The presence of a chemical in the body does not mean it causes disease
- No identification of levels that may cause disease
  - Additional exposure-health effect studies
- Per NHANES design:
  - No geographical (local, state or region) information
  - No seasonal data
  - No target populations with potential low/high exposures
    - Collaborative studies
    - National, state or local efforts
      - NYC HANES, Biomonitoring California, other
  - Limited biomonitoring data for the young
Who is exposed? How much? What chemicals?: Exposure to triclosan

- No concentration differences by race/ethnicity or by sex
- Triclosan concentrations increase with household income

Calafat et al. EHP 2008, 116:303-7
Regardless of age, benzophenone-3 geometric mean concentrations are:

- Higher in females than in males
- Higher in non-Hispanic whites than in non-Hispanic blacks

Same trends at the 95th percentile concentrations
Monitor time trends: Human exposure to PFOS

- PFCs Surfactants: Persistent, bioaccumulative & toxic
- PFOS precursors phased out (2000 -2)
  - PFOS human levels reduced by 78% since 1999 -2000
- PFOS precursors still produced in China
FQPA reduced exposure to organophosphate insecticides

- Phase-out residential use of chlorpyrifos (2000-1)

Error bars represent 95% confidence intervals
Prevalence above thresholds: U.S. children with blood lead levels $\geq 5 \mu g/dL$

- Focus to primary prevention
- Reference level set in Oct 2012
- Based on the 97.5th percentile of blood lead distribution in NHANES 1-5 year old children
- CDC will update the reference value every four years using the two most recent NHANES datasets
- Chelation therapy considered when a child has a blood lead test result $\geq 45 \mu g/dL$

http://www.cdc.gov/nceh/lead/ACCLPP/blood_lead_levels.htm
NHANES Biomonitoring data show …

- **Widespread exposure to chemicals/chemical classes**
  - Multiple sources & exposure pathways

- **Differences in prevalence and magnitude of exposure among demographic groups**
  - Children vs adults and adolescents
    - Exposure driven (e.g., lifestyle)
    - ADME related
  - Race/ethnicity & sex differences
    - Exposure and/or genetic factors
  - SES differences
    - Lifestyle, diet, etc

- **Exposure trends**
Non-persistent chemicals & variability in urinary concentrations

- Variability is unavoidable
  - MEP (PCP use): Mostly between-person variability
  - MEHHP: (diet) Mostly within-person variability

- Variability factors
  - Chemical properties
  - Nature of exposure & population
  - Timing of urine collection

Preau et al. EHP 2010, 118(12):1748-54
Can one sample be used to assess exposure?

- Comparable distribution of spot sample concentrations from eight persons over one week and from NHANES 2005–2006 adults
- Range of population average urinary concentrations over time are less variable than suggested by the distribution of spot sample concentrations for compounds with rapid elimination relative to exposure frequency
Population variability

- BPA urinary concentrations are highly variable
  - Short-lived chemical & episodic exposures
- Urinary levels of BPA increased by 1221 per cent in people who ate canned soup compared with those who ate fresh soup

N = 75 persons

Carwile et al. JAMA 2011 306:2218-20
Take home messages – Biomonitoring

- **One tool for exposure assessment**
  - Integrates sources/routes of exposure
  - Trace vs environmental levels
  - Requires complex analytical methods

- **Interpretation of Biomonitoring data**
  - More than a laboratory measurement
  - Multiple samplings may be needed (NPs)
    - Variability
  - Collection & handling considerations (how/when/where?)
    - Stability (analyte & matrix)
    - Potential contamination

- **Used properly, biomonitoring undoubtedly improves exposure assessment**
Take home messages – NHANES

- NHANES can provide ongoing data on the exposure of the U.S. population to select environmental chemicals
- Biomonitoring, clinical and nutritional NHANES parameters can be linked to evaluate health outcomes
- NHANES per design cannot answer all public health issues
  - Need for additional studies to assess exposures in select populations
  - Separate studies of varying exposure levels and health effects are required to determine which blood and urine levels are safe and which may result in disease
- Biomonitoring NHANES data can be/have been used to support public health guidelines
Acknowledgements

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NCHS
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THANK YOU!

For more information please contact Centers for Disease Control and Prevention

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Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

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