Biomonitoring of Bisphenol A Exposures in Human Populations

National Center for Environmental Health

Centers for Disease Control and Prevention

Atlanta, GA USA

"The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy"

Biomonitoring

Assessment of internal dose by measuring the parent chemical (or its metabolite or reaction product) in human blood, urine, milk, saliva, adipose, or other tissue.

Quality of Biomonitoring Data

- Analytical method
  - Characterization & validation
  - Quality Assurance / Quality Control
- Sampling & handling
  - Contamination
    - Reagent blanks (analysis)
    - Field blanks (collection)

Optimal Characteristics of an Analytical Method

- Sensitive
- Specific
  - (Enzyme-linked immunosorbent assay vs. isotope dilution-mass spectrometry)
- Accurate
- Precise/Reproducible
- Rugged
- Minimal specimen volume*
- Multianalyte*
- High throughput*
- Quality Assurance / Quality Control*

*Biomonitoring

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Quantitative Measurement of Bisphenol A

- Enzymatic deconjugation
- Solid phase extraction
- Chromatographic separation
- Quantification using isotope dilution mass spectrometry

Kuklenyik et al. Anal Chem. 2003, 75:6820-5.
Ye et al. Anal. Chem. 2005, 77:5407-13.

Validated Collection Protocols

- Situations when contamination is of concern:
  - Biomarker is the parent compound
  - Trace levels
  - Ubiquitous
- Field blanks

Bisphenol A – Some Known Uses*

- Polycarbonate plastic (major)
- Epoxy resins
- Polyvinyl chloride (PVC)

*** European Union. (2003) Risk assessment report on bisphenol A. http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/bisphenolareport325.pdf. Accessed on June 6, 2008.**

Center for Disease Control and Prevention's Phenols (Bisphenol A) Program

- National Health and Nutrition Examination Survey (NHANES)
  - NHANES III (1988-1994)
  - NHANES 2003-2004
  - Urine concentrations
- Specific investigations
  - Human milk concentrations
  - Serum concentrations

NHANES III (1988-1994)*

394 archived urine specimens

- Adults (convenience sample)
- Sampling period: 1988–1994
- Detection frequency for bisphenol A was 95%. (Analytical method's limit of detection = 0.1 μg/L)
- Bisphenol A (total) concentrations
  Median = 1.3 μg/L
  95th percentile = 5.2 μg/L

***NHANES: National Health and Nutrition Examination Survey**

Calafat et al. EHP 2005, 113:391-5

NHANES 2003-2004*

2,517 urine specimens

- Representative general U.S. population (≥ 6 years old)
- Detection frequency for bisphenol A was 92.6%
  (Analytical method's limit of detection = 0.4 µg/L)
- Bisphenol A (total) concentrations
  Median = 2.7 µg/L (95%CI 2.4-3.0)
  95th percentile = 15.9 µg/L (95%CI 14.4-17.2)

Comparisons based on adjusted geometric means of bisphenol A concentration.

- [Females] > [Males]
- [Children, 6-11 years] > [Adolescents, 12-19 years] > [Adults, ≥20 years]
- [Non-Hispanic whites] ~ [non-Hispanic blacks] > [Mexican Americans]

***NHANES: National Health and Nutrition Examination Survey, CI: confidence interval, µg/L: microgram per liter**

Covariates in adjusted analysis: Age, gender, race/ethnicity, household income, urine creatinine concentration.

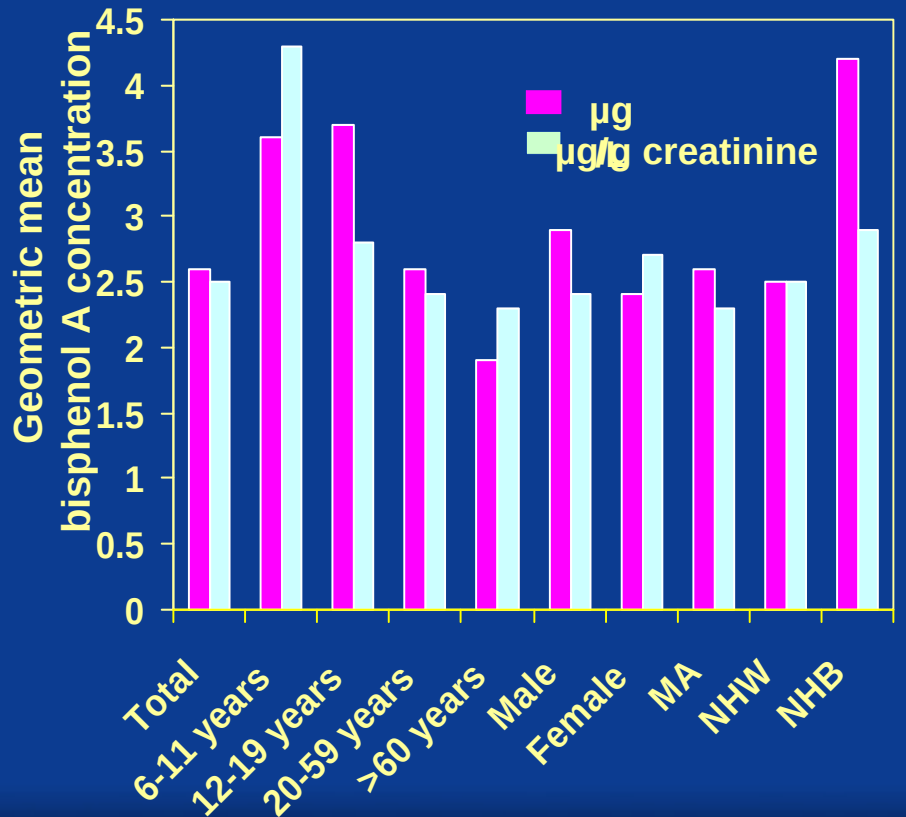
Calafat et al. EHP 2008, 116:39-44

Widespread Exposure to Bisphenol A: NHANES 2003-2004*

- Detected bisphenol A in 92.6% of the urine specimens from 2,517 participants aged 6 years and older. (Analytical method's limit of detection = 0.4 µg/L)
- Bisphenol A (total) concentration at the 95th percentile

  -15.9 µg/L (95%CI 14.4-17.2)

  -11.2 µg/g creatinine (95%CI 9.8-12.4)



***NHANES: National Health and Nutrition Examination Survey, MA: Mexican Americans, NHW: non-Hispanic whites, NHB: non-Hispanic blacks, CI: confidence interval, µg/L: microgram per liter, µg/g: microgram per gram**

Calafat et al. EHP 2008, 116:39-44

Urinary Conjugates of Bisphenol A (BPA) in Humans*

Compound	Frequency of detection (%)	Median (μg/L)	Range (μg/L)	% Total BPA (%)
BPA free	10	<0.3	<0.3-0.6	9.5
BPA glucuronide	90	1.4	<0.3-19.0	69.5
BPA sulfate	47	0.3	<0.3-1.8	21
BPA total	97	2.1	<0.3-19.8	

***N = 30 adults (unknown collection procedures) , µg/L: microgram per liter. Analytical method's limit of detection for BPA = 0.3 µg/L.**

Ye et al. Anal. Bioanal. Chem. 2005, 383:638-44

Serum Concentrations of Selected Phenol Conjugates in Humans*

Compound	Detection frequency (%)	Mean (µg/L)	Median (µg/L)	Range (µg/L)	Mean percent of total as Conjugates (%)
Bisphenol A (free)	7+	<0.3	<0.3	<0.3 -1.4	0
Bisphenol A (total)	7	<0.3	<0.3	<0.3 -1.5	
Methyl paraben (free)	60	1.3	0.2	<0.1-9.8	90
Methyl paraben (total)	100	42.4	10.9	0.4-301	
Propyl paraben (free)	47	0.4	<0.2	<0.2-2.3	87
Propyl paraben (total)	80	8.0	1.4	<0.2-67.4	
Triclosan (free)	0	<1.1	<1.1	<1.1	~100
Triclosan (total)	67	9.3	<1.1	<1.1-13.7	

*** N = 15 adults (commercial specimens; unknown specimen collection procedures), µg/L: microgram per liter**

+ Bisphenol A (free) was detected in 1 of 15 participants.

Ye et al. Talanta. In press. 2008.

Phenols Measured in Human Milk*

Compound (µg/L)	Participants A	B	C	D
Methyl paraben (free)	<LOD	0.32	3.04	<LOD
Methyl paraben (total)	0.53	0.70	3.00	0.73
Propyl paraben (free)	<LOD	<LOD	0.32	<LOD
Propyl paraben (total)	<LOD	<LOD	0.33	<LOD
Triclosan (free)	2.81	<LOD	13.8	<LOD
Triclosan (total)	3.39	<LOD	14.5	<LOD
Bisphenol A (free)	0.45	0.79	1.54	0.41
Bisphenol A (total)	0.91	0.80	1.62	0.73
Benzophenone-3 (free)	<LOD	1.24	<LOD	<LOD
Benzophenone-3 (total)	<LOD	1.28	<LOD	<LOD

* N = 4 adults (unknown specimen collection procedures). Concentrations in µg/L: microgram per liter, LOD: Analytical method's limit of detection.

Ye et al. Anal. Chim. Acta. In press. 2008.

These Data Suggest …

- High prevalence of exposure to bisphenol A in the general U.S. population
- Bisphenol A is mostly excreted in the urine as a glucuronide conjugate
- Bisphenol A distributes into human milk

Analytical Chemistry and Biomonitoring

Analyte

- Validated method
  - Analytical standard
  - Quality Assurance / Quality Control
  - Laboratory blanks

Exposure Biomarker

- Validated method
  - Analytical standard
  - Quality Assurance / Quality Control
  - Laboratory blanks
- Pharmacokinetics
- Collection/handling
  - Field blanks

Analyte vs. Exposure Biomarker

Many analytes (e.g., bisphenol A) can be measured, but additional information is needed to demonstrate their utility as exposure biomarkers

- Pharmacokinetic data
  - Concentration vs. applied dose
- Sampling considerations
  - Stability (biological matrix / analyte)
  - Potential for contamination
    - Environment and other tissues / fluids
    - Field and laboratory blanks

Biomonitoring of Bisphenol A Summary

- High prevalence of exposure to bisphenol A in the general U.S. population
- Need for increased attention on field sampling protocol.
- Additional information needed:
  - Extent of contamination during field sampling
  - Biomonitoring data from vulnerable populations
  - Biomonitoring data from toxicology studies

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For further information

Centers for Disease Control and Prevention: Third National Report on Human Exposure to Environmental Chemicals (NCEH Pub. No. 05-0570), 2005. US Department of Health and Human Services, Atlanta.

http://www.cdc.gov / ExposureReport/

Centers for Disease Control and Prevention: National Biomonitoring Program.

http://www.cdc.gov / Biomonitoring/

Email: cdcinfo@CDC.GOV