Biomonitoring in NHANES

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Exposure Pathway

Source

Water, Air, Food, Soil, Dust, Sediment, Personal Care Products

Exposure Dose

Absorption following:

Internal Dose

Inhalation
Ingestion
Dermal Contact

Target Organ Dose

Metabolism
Distribution
Elimination

Biologically Effective Dose

Elimination

Effect
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.

**Urine**
- Metals (13)
- PAH metabolites
- Phthalate metabolites
- Pesticides
  - Organophosphorus
  - Carbamates
  - Herbicides
- Repellants
- Phytoestrogens

**Blood**
- Lead
- Cadmium
- Mercury

**Serum**
- Dioxins
- Furans
- PCBs
- Organochlorine pesticides
- Cotinine

Released: March 2003
[www.cdc.gov/exposurereport](http://www.cdc.gov/exposurereport)
National Report on Human Exposure to Environmental Chemicals

What it is:
An ongoing (every 2 years) biomonitoring assessment of the exposure of the U.S. population to selected environmental chemicals

Matrices monitored: Urine; blood and its components
Major Findings: U.S. Population-based Reference Ranges

- Geometric means
- 10\textsuperscript{th}, 25\textsuperscript{th}, 50\textsuperscript{th}, 75\textsuperscript{th}, 90\textsuperscript{th}, and 95\textsuperscript{th} percentiles
- Age, sex, race/ethnicity breakout
National Health and Nutrition Examination Survey

- Conducted by the National Center for Health Statistics/CDC
- Population is a stratified, complex, multistage probability sample of the civilian, noninstitutionalized U.S. population
- Estimates are probability based for the U.S. population
- Includes detailed history, physical, and laboratory exam
- Primary focus is generation of clinical data, but exposure data can be linked to clinical data and nutritional status
NHANES 1999-2000

- About 5000 participants annually from 15 locations
- Continuous annual survey
- Includes home interview
- Oversampled African Americans, Mexican Americans, adolescents (12-19 years), older Americans (≥ 60 years); pregnant women. In 2000 also low income whites

More information:
http://www.cdc.gov/nchs/nhanes.htm
Goals of National Report

In American population and subpopulations (age, sex, race/ethnicity)

- Assess exposure to various chemicals (which?)
- Establish national “reference ranges” of these chemicals (blood, urine)
- Track, over time, trends in these “reference ranges”
- Help set priorities on linking exposure to health outcomes
Public Health Uses of *National Report*

- Assess effectiveness of efforts to reduce exposures (lead in gasoline; FQPA; POPs) in all Americans
- In some cases, provide data for establishing source (pattern recognition, e.g., gasoline, dioxins/furans)
- Provide data for risk assessment (dose-response and exposure assessment)
- Provide data for linking environmental exposure data with interactions with genes, nutrition, and demographic data to eventually link with health outcome data
Interpreting Data in the Report

- The presence of a chemical in the body does not mean it causes disease.

- For many chemicals in the Report, more research is needed to interpret these levels.

- The Report provides new exposure data, but does not identify levels that cause disease.
  - Additional studies are needed.
Lead

Blood lead levels (BLLs)
1 year of age and greater
Lead Used in Gasoline Declined from 1976 Through 1980

[Graph showing a decline in gasoline lead from 1976 to 1980.]
Predicted Blood Lead Changes with Decreasing Gasoline Lead

- Lead used in gasoline (thousands of tons)
- Predicted blood lead levels (µg/dL)

Year

- Gasoline lead
- Predicted blood lead
NHANES II Blood Lead Measurements Found A Substantial Decline in Blood Lead Levels, 10 Times More Than Predicted from Environmental Modeling
After NHANES II, EPA Further Restricted Leaded Gasoline and Gasoline Lead Levels Continued to Decline Through 1991
NHANES III (1988-1994) showed blood lead levels continued to decrease as gasoline levels declined.

NHANES II, III, 1999-2000
Major Findings: Decline in Blood Lead Levels among Children

For children 1 through 5 years old

- **NHANES III (1991-94)**
  - Geometric mean BLL 2.7 µg/dL
  - 4.4% had BLLs ≥ 10 µg/dL

- **NHANES 1999-2000**
  - Geometric mean BLL 2.23 µg/dL
  - 2.2% had BLLs ≥ 10 µg/dL
  - Higher prevalence of BLLs in U.S. children occur in urban settings, lower SES, immigrants and refugees

(Geltman et al., 2001)
Dioxin-Like Chemicals

PCDDs

PCDFs

Coplanar Polychlorinated Biphenyls

Mono-orthochlorinated PCBs
Distribution and Storage of Dioxin-like Chemicals

- Because they are lipophilic, they tend to “travel” with lipids
  - Lipid Content
    - Blood Serum ~0.6%
    - Mother’s milk 3-4%
    - Adipose tissue ~95%

- Therefore, need to adjust for lipid content in biological matrix
Organohalogen Compounds in Breast Milk in Sweden

Age $\geq 20$ years
Dioxin concentration data: Age Range (5\textsuperscript{th}, 50\textsuperscript{th}, 95\textsuperscript{th}): 21, 42, 76 years
$N \approx 1300$
Serum $\approx 5$ mL per person
NHANES 1999-2000
PCDDs, PCDFs, PCBs – 95th Percentile

- Age 20 years and older (median age = 42 years)

- PCBs (total): ~2.7 ng/g serum

- Dioxin TEQ: 40-50 pg/g lipid
  - PCDD ~ 42%
  - PCDF ~ 16%
  - PCBs (coplanar) ~ 19%
  - PCBs (mono-ortho) ~ 23%
95th Percentile Dioxin TEQ Concentrations. NHANES 1999-2000

TEQ = 40-50 pg/g lipids*
N = 105
Age Range (5th, 50th, and 95th) = 39, 71, 85 years

Needham et al. Neurotoxicology (2005) online
* Range dependent on method used for imputing concentrations < LOD
Serum Pools: NHANES 2001-2002

- 34 People per pool (Total 1,734 people; 51 pools)
- Unweighted; used for estimates of the “means”
- 0.75mL Serum per person
- 25.5 g Serum per pool
  - 2 g BFRs/PCBs/Persistent Pesticides
  - 22 g PCDDs/PCDFs/cPCBs; PCNs
  - 0.5 g Total Lipids
  - 0.4 g Perfluorinated chemicals
Serum Pools: NHANES 2001-2002

- Age, Race, Sex
- Note: Data do not include mono-ortho PCB concentrations
## NHANES 2001-2002 Pools

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Gender</th>
<th>Age Group (years)</th>
<th>Number of Pools</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>12-19</td>
<td>20-39</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>M</td>
<td>2 (3)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2 (3)</td>
<td>4</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>M</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Mexican-American</td>
<td>M</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

( ) for perfluorinated chemicals
Mean and Range of TEQs by Age Group, Race and Sex

Race/Ethnicity, Age, & Gender

Mexican-American

Non-Hispanic Black

Non-Hispanic White
Perfluorochemicals (PFCs) in the Environment

- Produced since 1950's for use in:
  - Surface treatments: soil and stain resistant coatings on textiles, carpet, leather
  - Paper protection: provides oil, grease and water resistance on paper products including those for food use
  - Performance chemicals including insecticide, fire fighting foams, industrial surfactants, acid mist suppression

- 3M phased out its fluorochemistry in May 2000
Some Potential Sources of Perfluorochemicals in the Environment

- Packaging materials
  - Food contact
- Stain-resistant coatings on textiles, carpet & leather
- Fire fighting foams
- Pesticides
- Dietary sources
- Degradation products
  - Perfluorocetyl compounds
  - Fluoropolymers (e.g., telomers)
Perfluorinated Chemicals

Sulfonamides

- $\text{CF}_3(\text{CF}_2)_7\text{S}-\text{N} \rightarrow \text{CH}_2\text{CH}_2\text{COOH}$
- $\text{CF}_3(\text{CF}_2)_7\text{S}-\text{N} \rightarrow \text{CH}_2\text{CH}_2\text{OH}$
- $\text{CF}_3(\text{CF}_2)_7\text{S}-\text{N} \rightarrow \text{H}$

Sulfonic acids (e.g., PFOS)

- $\text{CF}_3(\text{CF}_2)_n\text{S} \rightarrow \text{OH}$

Carboxylic acids (e.g., PFOA)

- $\text{CF}_3(\text{CF}_2)_n\text{C} \rightarrow \text{OH}$
Mean and Range of PFOS by Age Group, Race and Sex

Race/Ethnicity, Age, & Gender

Mexican-American

Non-Hispanic Black

Non-Hispanic White
Mean and Range of PFOA by Age Group, Race and Sex

Race/Ethnicity, Age, & Gender
Cotinine

- Nicotine metabolite that tracks exposure to tobacco smoke
- For nonsmokers, tracks exposure to secondhand smoke

Percentage of the population

ETS exposure (nonsmokers)

Smokers

Serum cotinine (ng/mL)
Second Report Results

  - Measured as serum cotinine
  - Children: 58% decreased
  - Adolescents: 55% decreased
  - Adults: 75% decreased
50th & 95th Percentile of Cotinine by Age Group, Race & Sex

Ng/mL

MA 95th
MA 50th
NHB 95th
NHB 50th
NHW 95th
NHW 50th

Male
Female
Male
Female
Male
Female
Male
Female
Male
Female

3-11
12-19
20-39
40-59
60+
Second Report Results

- DDT banned in U.S. in 1973
- Pesticide DDE is 3 times higher in Mexican-Americans (3.9; 1.6; 1.3 ng/g)
- Also measurable in 12-19 year olds (born after ban) (0.6 vs. 1.8 ng/g)
- May be persisting in environment or from imported food
50th & 95th Percentile of DDE by Age Group, Race & Sex
Third *National Report* on Human Exposure to Environmental Chemicals

Includes chemicals from Second *National Report* (1999-2000) + the following in NHANES 2001-2002

- Organochlorine pesticides: aldrin, dieldrin, endrin
- OP pesticides: additional metabolites
- Pyrethroids: 5 metabolites
- Herbicides: mercapturate metabolites of acetochlor and metolachlor
- PAHs: 1-, 2-, and 4-hydroxychrysene; 4- and 9-hydroxyphenanthrene; 9-hydroxyfluorene; 3-hydroxybenzo(a)pyrene
- Additional PCDDs and PCBs
- Additional phthalate metabolites (e.g., oxidative metabolites of DEHP and DnOP)
Seveso, Italy Scenario

- Saturday – July 10, 1976
  - Explosion in a TCP reactor
  - Atmospheric release of kilogram amount of 2,3,7,8-TCDD

- People potentially exposed
  - A Zone – 736
  - B Zone – 4,737
  - R Zone – 31,800

- Highest measured level
  - 56,000 ppt (Oct. 1976)
Chlorpyrifos

- Organophosphorus pesticide
- Many food uses
- Termiticide
- Use in and around homes and non-residential settings - eliminated
Limitation: Specificity of Analysis

Chlorpyrifos (R’=ethyl) and Chlorpyrifos-methyl (R’=methyl)
Metabolism and Env’l Degradation

3,5,6-TCPy is “specific” metabolite
Dialkyl phosphates are “nonspecific” metabolites
50th & 95th Percentile of 3,5,6-TCPy by Age Group, Race & Sex

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male 95th</th>
<th>Male 50th</th>
<th>Female 95th</th>
<th>Female 50th</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-11</td>
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<td>12-19</td>
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<tr>
<td>40-59</td>
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</tr>
</tbody>
</table>
Map of Seveso Showing Contaminated Area
Seveso, Italy

- Acute exposure
- Wide range of exposure
- Both genders
- Adults and children
- Serum specimens saved from 1976-1985 medical exams
2378-TCDD Levels in Persons in Seveso, Italy Study

Seveso, Italy: Serum TCDD Levels (1976) by Zone of Residence

<table>
<thead>
<tr>
<th>Zone</th>
<th>Population</th>
<th>N</th>
<th>Range</th>
<th>Median</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>736</td>
<td>296</td>
<td>ND-56,000</td>
<td>447</td>
</tr>
<tr>
<td>B</td>
<td>4,737</td>
<td>80</td>
<td>ND-725</td>
<td>94</td>
</tr>
<tr>
<td>R</td>
<td>31,800</td>
<td>48</td>
<td>ND-545</td>
<td>48</td>
</tr>
<tr>
<td>Non ABR</td>
<td>182,843</td>
<td>11*</td>
<td>ND (&lt;12)-169</td>
<td>15</td>
</tr>
</tbody>
</table>

*Pools of 4-10 individuals per pool

Change in Sex Ratio with Exposure to Dioxin

- Seveso, Italy Dioxin Explosion
  - July 10, 1976 factory explosion
  - A Zone (736 people)
- Normal sex ratio (106 M and 100 F)

Change in Sex Ratio with Exposure to Dioxin

- 74 Total births from 9 months after accident to December 1984 (~1 half-life of serum TCDD)
  - Excess of females (26 M vs. 48 F)
  - $^2 (P < 0.001)$
- From 1985 to 1994
  - 60 Males and 64 Females

Sex Distribution of Children Born April 1977 – December 1984 to Parents with Measured Serum TCDD Levels (ppt) in Zone A – Seveso, Italy

Father’s TCDD Level  | 2340 | 1490 | 1420 | 509 | 444 | 436 | 208 | 176 | 104 | 65 | 55 | 30 | 29
Mother’s TCDD Level  | 960  | 485  | 463  | 257 | 126 | 434 | 245 | 238 | 1650 | 27 | 28 | 37 | ND