

**“NHANES 1999-2002
Update on Mercury”
&
Northeast Regional
Mercury Conference**

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The Findings and Conclusions in This Presentation
Have Not Been Formally Disseminated by US
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Overview

- Update on all four years of NHANES blood mercury data for adult women.
- *Look at subgroups and absence of trend data.*
- Comparison with exposures associated with US EPA's Reference Dose for methylmercury.

Updated Analysis of NHANES Data on Adult Women's Blood Mercury Concentrations Since January 2004

- Includes two additional years of NHANES data: 2001 and 2002.
- *Data from > 30 additional “stands” or communities.*
- Separate analysis of blood mercury data for women residing in “coastal” areas compared with those living in “noncoastal” geographic residences.
- *Comparison of 1999/2000 and 2001/2002 data for blood organic [Hg].*
- *Assessment of subpopulations' mercury exposures.*

Distribution of Blood Organic Mercury ($\mu\text{g/L}$) *Adult Women – NHANES 1999 thru 2002*

Group	Sample Persons	Arithmetic Mean	95% CI	75th	90th	95th
Total	3,613	1.43	(1.19-1.67)	1.52	3.52	5.8
Mexican/ American	1,099	0.89	(0.77-1.02)	1.02	2.10	3.32
Other Hispanic	218	1.54	(0.84-2.24)	1.72	3.30	4.50
Non- Hispanic Whites	1,368	1.38	(1.07-1.68)	1.42	3.42	6.00
Non- Hispanic Blacks	789	1.61	(1.28-1.94)	1.82	3.62	5.22
Other Race	139	2.46	(1.72-3.19)	3.70	6.70	9.02

Comparison of Blood Organic [Hg] µg/L for Adult Women NHANES 1999-2002 by Income

<i>Annual Income</i>	Sample Persons	Arith. Mean	(95% CI)	75th%	90th %	95th %
Total (All Incomes)	3,613	1.43	(1.35-1.50)	1.52	3.52	5.8
Less Than \$20,000	1,164	1.19	(0.88-1.49)	1.30	2.80	4.22
\$20,000 Or more	2,432	1.52	(1.26-1.79)	1.60	3.92	6.20

Women Statistically More Likely to Have Higher Blood Mercury Concentrations

- “Other” Category which includes Asians, Native Americans, persons of “Island” ethnicity. [Also see Hightower et al. Environmental Health Perspectives *on line, in press, 9/19/2005.*]
- *Women with incomes higher than the “poverty” level.*
- Trends in the NHANES data for adult women are supported by a number of additional studies.

Geographic Differences in Blood Mercury Concentrations of Adult Women – NHANES 1999-2002

- Utilizing NCHS Data Center, divided NHANES data into those stands located in “Coastal” counties – any stand in a county bordering the Atlantic Ocean, the Pacific Ocean, or the Gulf of Mexico – and stands located in “Non-Coastal” counties which were all other areas.

Great Lakes Region: the 4th “Coast”

- Project is currently under development with the Research Data Center of the National Center for Health Statistics.
- Need all six years of data (i.e., 1999 through 2004) to include the Great Lakes region.
- The 2003/2004 data set includes adult males for the first time.

Distribution of Adult Female Subjects with Organic Hg Data– NHANES 1999 through 2002 by Coastal and Non-Coastal Categories

Total = 3,613

Coastal = 1,431

(Atlantic Ocean = 598)

(Gulf of Mexico = 184)

(Pacific Ocean = 649)

Non-Coastal = 2,182

(Midwest = 524)

(North East = 219)

(South = 969)

(West = 470)

Comparison of Blood Organic [Hg] by Coastal and Non-Coastal Residence and by Region for Adult Women Aged 16 through 49 Years, NHANES 1999 through 2002: $\mu\text{g/L}$.

Group	N	Arithmetic Mean	(95th % C.I.)	90th
Total	3,613	1.43	1.2-1.7	3.5
Non-Coastal	2,182	1.03	0.8 - 1.2	2.4
Coastal	1,431	2.21	1.8 - 2.6	5.9
<i>Atlantic</i>	598	2.72	2.4 - 3.1	7.7
<i>Pacific</i>	649	1.73	1.5 - 1.9	4.7
<i>Gulf of Mexico</i>	184	1.31	0.6 - 2.0	3.2

Findings for Fish Intake by Coastal Subpopulations Consistent with Higher Blood Mercury Concentrations

- **In France fish consumption by coastal residents reported to be 3-times higher than fish intake by non-coastal residents (Crepet et al. 42: 179-189, *Regul. Toxicol. Pharmacol.*, 2005).**
- **Observed for fish intake in Florida in the 1990s. 50th percentile intake comparable to 90th percentile intake of NHANES survey (Denger et al., 1994).**

Comparison of Numbers of Women Ages 16 through 49 Years

- 1,707 women in the 1999 and 2000 report had blood organic [Hg] analyses (Mahaffey et al., 2004).
- 1,906 women in the 2001 and 2002 period had blood organic mercury analyses.
- 3,613 women in the 1999 through 2002 report had blood organic [Hg] analyses reported.
- More subjects in the latter two years.

Number of Years of NHANES Data Needed for Comparisons

- Generally recommended that at least three years of data be utilized for national estimates.
- Estimates based today utilize four years of NHANES data: 1999, 2000, 2001 and 2002.

Comparison of Coastal and Non-Coastal Residence of Women Participating in NHANES by Release Year

Counts Based on 24-Hour Dietary Recall Data

1999 and 2000 Release

- Coastal
n = 744 or 42.9%
% Fish Consumers: 18.3
Mean g Eaten (consumers only): 58.0
- Non-Coastal
n = 991 or 57.1%
% Fish Consumers: 10.6
Mean g Eaten (consumers only): 48.1

2001 and 2002 Release

- Coastal
n = 676 or 35.0%
% Fish Consumers: 16.7
Mean g Eaten (consumers only): 59.9
- Non-Coastal
n = 1,257 or 65.0%
% Fish Consumers: 13.0
Mean g Eaten (consumers only): 69.3

Question

- Does the decline reported in blood mercury between the 1999/2000 release and the 2001/2002 release reflect the ratio of coastal to non-coastal residences or other study design considerations?

Question

- How should we interpret exposure data based on women's blood mercury levels compared with EPA's Reference Dose for methylmercury?

What is EPA's RfD for Methylmercury Based On?

- It's not a LOAEL.
- It's not a NOAEL.
- It's a Benchmark Dose (BMD). A dose that produces a predetermined change in response rate of an adverse effect compared to background. Specifically a BMD Lower Confidence Limit (BMDL) in which the point of departure is set at a level in which there is a 5% increase in the prevalence of the endpoint against a population prevalence of 5% for the adverse effect, i.e., the prevalence of the adverse effect doubles.

BMDL for Methylmercury: Adverse Neurological Effects

- Methylmercury exposure associated with doubling the prevalence of children scoring in the lowest 5th percentiles on tests of neuro-development.
- Using IRIS language: “BMDs are calculated under the assumption that 5% of the responses will be abnormal in unexposed subjects ($P_0=0.05$), assuming a doubling of the excess risk (BMR = 0.05).
- Means that at the BMDL the prevalence of neurological deficits increases from 5% to 10%.
- Dose calculated in $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ for the mother that will produce a cord blood concentration measured in $\mu\text{g}/\text{L}$.

Are there estimated BMDLs lower than the 58 $\mu\text{g/L}$ recommended by the NAS?

BMDL for Methylmercury (IRIS, EPA, 2001)

**Utilized A Number of Endpoints from Three Major Cohort Studies:
Faroës, Seychelles, & New Zealand**

- Median Values, Calculated as $\mu\text{g Hg/L}$
cord blood

Faroës

**BMDL_{05} ppb mercury = 48 $\mu\text{g/L}$ cord
blood**

Integrative

**BMDL_{05} ppb mercury = 32 $\mu\text{g/L}$ cord
blood**

New Zealand

**BMDL_{05} ppb mercury = 24 $\mu\text{g/L}$
cord blood**

Distribution of Blood Mercury Concentrations for Adult Women and Comparison with NAS's and US EPA's Benchmark Dose

- Based on cord blood mercury concentration.
- *BMDL: 58 $\mu\text{g Hg /L}$ cord blood.*
- To calculate a Reference Dose the NAS's "Committee on Toxicology of Methylmercury" recommended use of an UF of not less than 10.
- *Five years ago there was minimal recognition of extent to which methylmercury is concentrated across the placenta.*

Comparison of UF for Methylmercury Risk Assessment between 2000/2001 and 2005

- The UF is for variability and uncertainty. The UF was 10 in 2000/2001 as recommended by NAS and used by EPA. No change in the past five years.
- However, there are additional data regarding maternal-fetal methylmercury kinetics between 2001 and 2005.
- What do these advances in understanding physiology mean for the exposure assessment part of risk assessment?

Exposure Analysis

- Stern and Smith (2003) compared cord blood with maternal blood [Hg] concluding that the mean cord blood was 70% higher than maternal blood [Hg]. Based on a meta-analysis of 10 separate data sets for cord:maternal [Hg] analyses.
- Subsequent to this publication there have been at least 3 additional studies published describing geographically diverse populations yielding very similar results.

Studies Published on Cord:Maternal Blood [Hg] Subsequent to Stern & Smith, 2003

- Sakamoto et al. (2004). Range 1.1 to 2.2; $r=0.92$. $x=1.6$ for ratio of cord to maternal RBC-Hg. Japanese 63 maternal-fetal pairs.
- Morrisette et al. (2004). Average cord blood OHg was 1.7 times O Hg in maternal blood. 92 Canadian maternal-fetal pairs.
- Butler et al. (2005). Arithmetic mean ratio (cord:maternal) for methylmercury (1.86; $n=294$ pairs; $r=0.90$) and for total mercury (1.49; $n=320$ pairs; $r=0.95$). Range 1.2 to 1.7 for THg, from 1.3 to 2.0 for MeHg. Canadian: Caucasian, Dene/Métis, Inuit, and Others.

Understanding the BMDL in Biomonitoring Values

- BMDL of 58 $\mu\text{g/L}$ in cord blood is equivalent to 35 $\mu\text{g/L}$ in maternal blood because of bioconcentration of methylmercury across the placenta.
- *When conducting an exposure assessment based on organic blood mercury concentrations for adult women 35 $\mu\text{g/L}$ is associated with fetal methylmercury exposures in the range of the BMDL.*
- Blood mercury concentrations in this range likely reflect exposure from fish or marine mammal consumption, unless there is an indication of some other highly unusual source of exposure.

Based on the Combined NHANES 1999 through 2002 Data for Adult Women and National Center for Health Statistics Data in the US

- During the combined years 1999-2002, among women ages 16 through 49 years who participated in the NHANES, 10.2% had blood mercury concentrations \geq 3.5 $\mu\text{g/L}$.
- The number of women delivering babies during these years* were:

1999:	3,959,417
2000:	4,058,814
2001:	4,025,933
2002:	4,021,726

Average: 4,016,427

Estimate Number of Infants Born to Mothers with Blood Organic Mercury Concentrations \geq 3.5 $\mu\text{g/L}$:

$$10.2\% \times 4,016,427 = 409,676 \text{ or } \sim 410,000$$

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- Martin JA, et al. "Births: Final Data for 2002. National Vital Statistic Reports, Vol. 52, Number 10.
 - http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_10pdf. accessed August 26, 2005

Reasons and Revised Estimates for the Number of Women Estimated to Have Exposures Greater Than US EPA's Reference Dose for Methylmercury

- Number of years of NHANES data.
- Previous estimates (based on NHANES data for 1999 and 2000) of the number of births to women having blood organic mercury concentrations indicative of methylmercury exposures > EPA's RfD, ranged between 300,000 (no bioconcentration) and 600,000 (with bioconcentration) depending on whether placental bioconcentration of CH₃Hg was considered.
- Current estimates (based on NHANES data for 1999 through 2002) of the number of births to women having blood organic mercury concentrations indicative of methylmercury exposures > EPA's RfD, are ~ 220,000 using blood [Hg] of 5.8 µg/L (no bioconcentration) and ~ 410,000 using 3.5 µg/L (with bioconcentration) with no adjustment for placental concentration of methylmercury.
- There is bio-concentration of methylmercury across the placenta based on approximate 30 separate studies of mother-child pairs reported in the peer-reviewed literature.

NHANES is and is not

- Is: Nationally representative data
- Is not: Representative of the highest exposures.
- Published reports of higher exposures to methylmercury within the US and territories include the following:

Mercury Exposure among Groups with Much Higher Fish Consumption than the General Population: United States and Territories

- Health-Aware Urbanites
San Francisco Private Practice
Blood Hg: 89% of 116 patients had blood [Hg] > 5 µg/L. 16% > 20 µg/L. 4 patients > 50 µg/L.

New York City Rehabilitation Clinic – Neuropathies
Blood Hg: 27-96 µg/L.
- Commercial Fishermen and Families
Louisiana - Blood [Hg] ranging from < 0.3 to 35 µg/L. 2% > 20 µg/L.
- Coastal Populations
New Jersey – pregnant women
1% to 2% had hair [Hg] > 4 ppm
- \$ Island Population
Vieques (Puerto Rican women)
Hair Hg: 90th percentile, 9 ppm
3 women had values of 15, 25 and 101 ppm

These data indicate

- *Should use larger sample size for 1999 through 2002 NHANES which is more geographically representative than was 1999 through 2000 NHANES.*
- *Coastal populations, “Other” subpopulations, and women with incomes higher than “poverty level” have higher blood mercury concentrations.*
- *Substantial number of women have blood mercury concentrations (3.5 $\mu\text{g}/\text{L}$) greater than those associated with US EPA’s 2000/2001 RfD based on cord blood mercury (i.e., 5.8 $\mu\text{g}/\text{L}$).*