Blood Mercury Levels in US Children and Women of Childbearing Age, 1999-2000

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Context Humans are exposed to methylmercury, a well-established neurotoxin, through fish consumption. The fetus is most sensitive to the adverse effects of exposure. The extent of exposure to methylmercury in US women of reproductive age is not known.

Objective To describe the distribution of blood mercury levels in US children and women of childbearing age and the association with sociodemographic characteristics and fish consumption.

Design and Setting The 1999-2000 data from the National Health and Nutrition Examination Survey, a cross-sectional survey of the noninstitutionalized US population.

Participants In 1999-2000, 1250 children aged 1 to 5 years and 2314 women aged 16 to 49 years were selected to participate in the survey. Household interviews, physical examinations, and blood mercury levels assessments were performed on 705 children (56% response rate) and 1709 women (74% response rate).

Main Outcome Measure Blood concentration of total mercury.

Results Blood mercury levels were approximately 3-fold higher in women compared with children. The geometric mean concentration of total blood mercury was 0.34 µg/L (95% confidence interval [CI], 0.30-0.39 µg/L) in children and 1.02 µg/L (95% CI, 0.85-1.20 µg/L) in women. Geometric mean mercury levels were almost 4-fold higher among women who ate 3 or more servings of fish in the past 30 days compared with women who ate no fish in that period (1.94 µg/L vs 0.51 µg/L; $P<.001$).

Conclusions Measures of mercury exposure in women of childbearing age and young children generally fall below levels of concern. However, approximately 8% of women had concentrations higher than the US Environmental Protection Agency's recommended reference dose (5.8 µg/L), below which exposures are considered to be without adverse effects. Women who are pregnant or who intend to become pregnant should follow federal and state advisories on consumption of fish.

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MERCURY IS WIDESPREAD IN the environment, originating from both natural and anthropogenic sources.[1-3] The general population may be exposed to 3 forms of mercury: elemental, inorganic, or organic (predominantly methyl). Elemental and inorganic mercury exposure can result from mercury spills, dental amalgams, exposure at the workplace, environmental exposure to natural weathering of mercury containing ores, and from the burning of coal and incineration of medical wastes. Methylmercury is formed through microbial action from inorganic mercury that has deposited in aquatic environments and bioaccumulates through the food chain so that concentrations are highest in large predatory fish. Exposure occurs primarily through consumption of seafood, freshwater fish, and shellfish.[1,4-6]

Methylmercury exposure is of particular concern because it is a well-established human neurotoxin and the developing fetus is most sensitive

to its adverse effects.[1-3] Toxic effects of methylmercury exposure are known from past poisoning outbreaks, particularly those in Minamata, Niigata, and Kumomoto Prefecture, Japan,[7,8] and in Iraq.[9] Recent epidemiological studies have addressed neurodevelopmental effects in young children from in utero methylmercury exposure in populations in which fish or seafood is a substantial component of the diet and in which exposure levels may be comparable with those levels in high-end consumers in the United States.[10-12]

These data have been used by environmental and public health authorities to define safe levels of mercury exposure and to provide guidance to the public regarding consumption of certain species of fish. For example, the US Food and Drug Administration provides advice to pregnant women and women of childbearing age who may become pregnant to avoid consumption of shark, swordfish, King mackerel, and tile fish.[13] Health Canada and the British Food Standards Agency have also provided guidance.[14,15] Additionally, many state governmental agencies issue fish advisories and bans relating to mercury concentrations for locally caught fish.[16]

Total blood mercury is a reasonable indicator of methylmercury exposure in people who consume fish and have no significant exposure to inorganic or elemental mercury.[1,3-6] Total blood mercury levels also include small amounts of inorganic mercury, such as that from dental amalgams, although inorganic mercury exposure is better measured by levels in urine.[3,17]

In the United States, blood mercury levels have been described in certain groups, including recreational anglers, subsistence fishers, and American Indian and Alaskan Native groups.[18-22] However, information about the distribution of blood mercury levels in the general US population is needed to evaluate the public health significance of mercury exposure and to establish a baseline from which future interventions designed to decrease mercury exposures may be evaluated. Exposure information for women of childbearing age is particularly important because of fetal sensitivity to adverse effects.[1,2] Exposure in young children is of interest because of continuing neurobehavioral development during this life stage.

We present data from the 1999-2000 National Health and Nutrition Examination Survey (NHANES) on the distribution of blood mercury levels and the association with sociodemographic covariates and fish and shellfish consumption in a representative sample of young children and women of reproductive age.

METHODS
NHANES Sample Design
The NHANES protocol is designed to monitor the health and nutritional status of the US population. In 1999, NHANES became a continuous survey, fielded on an ongoing basis. Each year of data collection is based on a representative sample covering all ages of the civilian, noninstitutionalized population.[23] Public use data files will be released in 2-year groupings (cycles). Two or more years of data are necessary to have adequate sample sizes for subgroup analyses. Our study is based on the first 2 years of the continuous NHANES (1999-2000).

The survey consisted of interviews conducted in participants' homes and standardized physical examinations conducted in specially outfitted mobile examination centers. The household interview included questions about sociodemographic characteristics, health history, health-related behaviors, and access to health care. During the physical examination, blood was obtained by venipuncture for all survey participants 1 year or older.

The NHANES sample was selected through a complex, multistage design that included selection of primary sampling units (counties), household segments within the counties, and finally sample persons from selected households. In 1999 and 2000, blacks, Mexican Americans, persons aged 12 to 19 years, and persons 60 years or older were oversampled to obtain reliable estimates of health and nutritional measures for these population subgroups. Low-income whites were oversampled in 2000. In addition, in 1999 and 2000, all women who indicated that they were pregnant in the screening interview were selected to increase the sample size for pregnant women. The 1999-2000 NHANES was conducted in 26 locations throughout the United States.

The 1999-2000 NHANES protocol was approved by an institutional review board. Signed informed consent was obtained for all participants. Parents or guardians provided consent for children younger than 18 years. All received remuneration for their participation from $30 to $100, depending on age and examination content and additional money to cover transportation costs.

Blood Mercury Measurements
Whole blood specimens were analyzed for total mercury and inorganic mercury for children aged 1 to 5 years and women aged 16 to 49 years. Specimens were analyzed using automated cold vapor atomic absorption spectrophotometry by the Division of Laboratory Sciences at the National Center for Environmental Health of the Centers for Disease Control and Prevention. The detection limit was 0.14 µg/L for total mercury and 0.4 µg/L for inorganic mercury. Throughout this study, conversion to SI (nmol/L) is $\times 4.99$.

Mercury was measured by a Flow Injection Mercury System 400 (Perkin-Elmer, Shelton, Conn) with an AS-91 autosampler.[24] All solutions were made of analytical grade chemicals. Ultrapure water at 3 to 18 MΩ (Milli-Q Systems, Bedford, Mass) was used for solution preparation. Matrix-matched calibration methods were used. All blood collection materials were prescreened for mercury contamination before use. All blood samples were kept frozen from the time of aliquoting until the analysis.

The total blood mercury analysis used a Maxidigest MX 350 (Prolabo, Fontenay-sous-Bois, France) in-line microwave digester connected to the Flow Injection Mercury System 400. The inorganic mercury analysis used stannous chloride as the reducing agent and the total mercury analysis used sodium borohydride as the reducing agent. The blood mercury analysis requires 0.2 mL of blood for the total and an additional 0.2 mL of blood for the inorganic analysis.

For both total and inorganic mercury measures, National Institute of Standards Technology Standard Reference Material 966 was used as a bench-quality control material as well as 3 levels of in-house blood pools traceable to

the reference material for daily quality control. One of 2 different levels of a blind quality-control material was inserted in every analytical group of samples for an additional quality-control check. All quality-control specifications were met in the analyses of the NHANES samples.

Fish and Shellfish Consumption

After completion of a 24-hour dietary-recall interview conducted in the mobile examination center, survey participants (or proxy respondents for the children) were asked about fish and shellfish consumption during the past 30 days. Respondents were shown cards listing various species of fish or shellfish and were asked, "During the past 30 days, did you eat any types of fish (or shellfish) listed on this card? Include any foods that had fish (or shellfish) in them such as sandwiches, soups, or salads." The list of fish and shellfish included other and unknown categories.

Covariates

Race and ethnicity was categorized as non-Hispanic white, non-Hispanic black, and Mexican American. Persons not classified into 1 of these groups were included in total population estimates. A participant's age was defined as his/her age in years at the time of the household interview.

To define pregnancy status, women 12 years or older were asked in a private interview conducted in the mobile examination center whether they were currently pregnant. Also, we used data from a pregnancy test that was conducted to exclude pregnant women from a dual-energy radiograph absorptiometry examination. This test was conducted for women 18 years or older in 1999 and those 8 years or older in 2000.

Response Rates

A total of 12 160 persons were selected to participate in the NHANES in 1999-2000, of whom 9282 participated in both the interview and physical examination for an overall examination response rate of 76.3%. Of 1250 children

aged 1 to 5 years who were selected to participate in the survey, 1012 (81%) completed both the household interview and examination components. Of the examined children, 705 participated in the phlebotomy component and had blood available for assessment of mercury levels, resulting in a response rate of 56%. For women aged 16 to 49 years, 2314 were selected to participate and 1819 (79%) completed the interview and examination. Blood mercury data were available for 1709 women for a response rate for the mercury analyses of 74%.

Statistical Analyses

The distribution of blood mercury levels in children and women were described through the calculation of percentiles and geometric means. Estimates were produced using weights for each person to account for differential probabilities of selection and for nonresponse. Sample weights were poststratified to US Census Bureau estimates of the population. Standard errors were calculated with SUDAAN version 6.40 (Research Triangle Institute, Research Triangle Park, NC), statistical procedures for analyses of data from complex sample surveys. The SEs were calculated using the delete 1 jackknife method and t statistics were calculated to test that differences between geometric mean blood mercury levels between subgroups were statistically significant (ie, to test the null hypothesis that there was no difference in geometric means). Confidence intervals (CIs) were calculated for geometric means and percentiles. $P < .05$ was considered statistically significant.

Logarithmically transformed total blood mercury levels were regressed against age, fish consumption, and shellfish consumption as independent variables using multivariate linear regression to examine whether these variables were independently associated with blood mercury levels. Regressions were performed separately for the 3 major race and ethnic groups in the survey. t Statistics were calculated to test the null hypotheses that the β coeffi-

cients were not different from zero. For results that were below the limit of detection, a value equal to the detection limit divided by the square root of 2 was used to calculate geometric means and regression coefficients.

RESULTS

Total mercury concentrations in blood were less than the limit of detection for 19% of children aged 1 to 5 years and for 6% of women aged 16 to 49 years. Inorganic mercury levels were less than the limit of detection for 99% of the children and for 97% of the women.

The geometric mean concentration of total blood mercury was 0.34 µg/L (95% CI, 0.30-0.39 µg/L) in children aged 1 to 5 years and 1.02 µg/L (95% CI, 0.85-1.20 µg/L) in women aged 16 to 49 years. Geometric means and selected percentiles with 95% CIs of total blood mercury levels by selected characteristics are shown in TABLE 1 for children aged 1 to 5 years and in TABLE 2 for women aged 16 to 49 years.

Geometric mean total mercury levels in non-Hispanic black and Mexican American children were higher than in non-Hispanic white children; the differences were small but statistically significant (Table 1). Children who had eaten fish in the last 30 days had geometric mean blood mercury levels approximately twice as high as those of children who had eaten no fish during the same period ($P < .001$). Shellfish consumption had little effect on blood mercury levels in children.

Among women aged 16 to 49 years, non-Hispanic blacks had higher geometric mean mercury levels compared with non-Hispanic whites and Mexican Americans (Table 2). The higher percentiles of blood mercury levels were similar between non-Hispanic blacks and whites. Among women aged 20 to 49 years, geometric mean mercury levels were significantly higher among those with an education beyond high school compared with those who had a high school education or less. Age was associated with blood mercury levels; women aged 30 to 49 years had higher concentrations

than women 16 to 29 years ($P<.001$). The blood mercury levels of the 286 pregnant women in the 1999-2000 NHANES sample were not different than those of women who were not currently pregnant. Blood mercury levels increased with more frequent fish or shellfish consumption. Geometric mean mercury levels were almost 4-fold higher among women who ate 3 or more servings of fish in the past 30 days compared with women who ate no fish in that period (1.94 µg/L vs 0.51 µg/L; $P<.001$).

Results of multivariate linear regression analyses for women 16 to 49 years are shown in TABLE 3. Log-transformed values of blood mercury concentrations were used as the dependent variable and were modeled separately for each of the 3 major race and ethnicity groups. Age was positively associated with blood mercury levels in all 3 race and ethnic groups. The effect of fish consumption on blood mercury levels was observed in each race and ethnic group. The difference in mercury levels between black women who ate no fish and those who ate 1 to 2 servings in the past month was less than in the other 2 race and ethnic groups. Shellfish consump-

tion in the past month (any vs none) was independently associated with blood mercury levels in non-Hispanic whites and Mexican Americans but not in non-Hispanic blacks. The proportion of variation explained by these models is low (R^2=29%, 18%, and 19%, respectively, in non-Hispanic whites, non-Hispanic blacks, and Mexican Americans).

COMMENT

These results extend recently released estimates of blood mercury levels in US women and children[25] and, for the first time, describe how blood mercury levels vary by fish and shellfish consumption in a nationally representative sample of 2 population subgroups. Diet is the primary source of methylmercury in US individuals.[1] In this study, blood mercury levels were associated with self-reported fish consumption in the past 30 days in both children and women, and among women, increased with number of fish meals consumed. Shellfish consumption, independent of fish consumption, was associated with blood mercury levels in women but not in children.

Blood mercury levels were 3 times higher in women than in young chil-

dren. The difference between women and young children may be due to differences in toxicokinetics, dose-body size relationships, dose frequency, or unknown sources of mercury exposure in adults. However, there was no difference between women and children in the number of fish servings in the last 30 days. Among women of reproductive age, mercury levels were slightly higher in older women, a difference of 0.4 µg/L between women aged 16 to 29 years and those 30 to 49 years. Age remained an independent predictor of blood mercury levels when fish consumption was included in multivariate analyses. Self-reported fish consumption alone does not explain the association between age and total blood mercury.

Blood mercury levels varied by race and ethnicity in both children and women. Among women, blood mercury levels in non-Hispanic blacks were higher compared with non-Hispanic whites and Mexican Americans. This may be due to differences by race and ethnicity in the fish species, portion size consumed, or geographic variation.

The NHANES protocol provides the first US population-based estimates of blood mercury levels in women and

Table 1. Geometric Means and Selected Percentiles of Total Blood Mercury Concentrations (µg/L) for Children Aged 1 to 5 Years by Selected Variables

| | No. of Children | Geometric Mean (95% CI) | P Value* | Selected Percentile, Geometric Mean (95% CI) | | | | | | |
				5th	10th	25th	50th	75th	90th	95th
Total†	705	0.34 (0.30-0.39)		. . .	. . .	. . .	0.26 (0.22-0.31)	0.59 (0.51-0.67)	1.31 (0.69-1.92)	2.28 (2.00-2.56)
Race and Ethnicity										
Mexican Americans	274	0.45 (0.39-0.52)	<.001	. . .	. . .	0.18 (0.15-0.22)	0.38 (0.29-0.47)	0.86 (0.70-1.02)	1.49 (1.06-1.93)	2.27 (1.99-2.55)
Non-Hispanic whites‡	173	0.27 (0.23-0.32)		. . .	. . .	. . .	0.18 (0.15-0.22)	0.43 (0.34-0.51)	1.04 (0.78-1.30)	1.58 (0.25-2.91)§
Non-Hispanic blacks	172	0.56 (0.44-0.67)	<.001	. . .	. . .	0.23 (0.15-0.30)	0.57 (0.45-0.68)	0.92 (0.75-1.09)	1.90 (1.27-2.54)	2.67 (1.95-3.40)
Fish Consumption in Past 30 Days										
Yes	382	0.44 (0.35-0.53)	<.001	. . .	. . .	0.13 (. . . to 0.18)	0.38 (0.30-0.46)	0.89 (0.53-1.26)	2.20 (0.17-4.23)§	3.17 (1.65-4.70)
No	285	0.24 (0.21-0.27)		. . .	. . .	. . .	0.18 (0.15-0.20)	0.36 (0.25-0.46)	0.72 (0.56-0.88)	0.94 (0.80-1.09)
Shellfish Consumption in Past 30 Days										
Yes	179	0.45 (0.32-0.58)	.03	. . .	. . .	0.15 (. . . to 0.22)	0.39 (0.25-0.54)	0.92 (0.37-1.47)	1.79 (1.08-2.50)	2.75 (2.29-3.21)
No	487	0.32 (0.27-0.37)		. . .	. . .	. . .	0.23 (0.19-0.28)	0.54 (0.44-0.63)	1.17 (0.83-1.51)	2.25 (1.74-2.75)

Abbreviation: CI, confidence interval; ellipses, less than the limit of detection.
SI conversion factor: To convert mercury to nmol/L, multiply values by 4.99.
*t Test comparing geometric mean with referent.
†Total includes other race and ethnic groups and those missing information for other variables.
‡Referent for comparison of geometric means.
§Estimate does not meet minimum standard of statistical reliablility (relative standard error >30%).

children. Previously, estimates were available only for nonrepresentative groups. Tentative reference values for typical concentrations of blood mercury among nonoccupationally exposed people have been estimated by Brune et al[26] based on a review of 132 data sets worldwide. In the studies with fish consumption information, the average blood mercury level was 2.0 µg/L in those who ate no fish and 8.4 µg/L in those eating more than 2 to 4 fish meals per week. In the 1999-2000 NHANES, women who consumed no fish had a geometric mean level of 0.51 µg/L and among 71 women who reported eating 9 or more fish meals in the past month, the geometric mean was 3.13 µg/L (95% CI, 2.10-4.16). In 1 study,[21] the geometric mean blood mercury level was approximately 1 µg/L in a sample of 143 pregnant women, comparable with the estimate for women of childbearing age in the 1999-2000 NHANES.

Population-based estimates of blood mercury levels are available from the 1990-1992 German Environmental Survey,[27] which were lower than the 1999-2000 NHANES estimates. German adults who reported never eating fish had a geometric mean blood mercury of 0.30 µg/L, although those consuming fish more than once a week showed a geometric mean of 0.77 µg/L. In Germany, as in the United States, frequency of fish consumption was a predictor of blood mercury in adults, and children had lower blood mercury concentrations than adults.

Other studies describe blood mercury levels in individuals or groups who consume fish frequently. For example, the median blood mercury level was 7.1 µg/L in 236 individuals included in a screening program to evaluate blood mercury levels in individuals who ate fish caught from mercury

Table 2. Geometric Means and Selected Percentiles of Total Blood Mercury Concentrations (µg/L) for Women Aged 16 to 49 Years by Selected Variables

	No. of Women	Geometric Mean (95% CI)	P Value*	5th	10th	25th	50th	75th	90th	95th
							Selected Percentile, Geometric Mean (95% CI)			
Total†	1709	1.02 (0.85-1.20)		. . .	0.17 (0.14-0.21)	0.42 (0.29-0.55)	0.94 (0.73-1.15)	2.07 (1.50-2.64)	4.84 (4.11-5.57)	7.13 (5.79-8.48)
Race and Ethnicity										
Mexican Americans	579	0.82 (0.68-0.96)	.23	. . .	0.20 (0.14-0.26)	0.38 (0.28-0.47)	0.84 (0.74-0.93)	1.44 (1.05-1.83)	2.50 (1.86-3.15)	3.91 (2.71-5.11)
Non-Hispanic whites‡	578	0.96 (0.76-1.16)		. . .	0.16 (. . . to 0.20)	0.38 (0.29-0.47)	0.86 (0.71-1.00)	1.83 (1.44-2.22)	4.89 (3.18-6.59)	7.08 (5.39-8.77)
Non-Hispanic blacks	364	1.35 (1.08-1.61)	.01	0.16 (. . . to 0.26)	0.33 (0.25-0.42)	0.64 (0.44-0.84)	1.34 (1.09-1.58)	2.59 (1.95-3.24)	4.74 (3.26-6.23)	6.55 (3.41-9.69)
Education, y§										
≤12	615	0.93 (0.75-1.12)	.004	. . .	0.19 (. . . to 0.25)	0.37 (0.31-0.44)	0.84 (0.70-0.98)	1.83 (1.49-2.17)	4.15 (2.09-6.20)	6.69 (3.86-9.53)
>12	578	1.20 (0.98-1.42)		. . .	0.19 (0.14-0.25)	0.54 (0.45-0.62)	1.15 (0.96-1.33)	2.64 (1.72-3.55)	5.62 (3.79-7.45)	8.43 (5.23-11.63)
Age, y										
16-29	950	0.79 (0.64-0.95)	<.001	. . .	. . .	0.31 (0.24-0.39)	0.73 (0.55-0.91)	1.58 (1.30-1.87)	3.75 (1.62-5.88)	6.22 (5.63-6.82)
30-49	759	1.19 (0.96-1.43)		0.14 (. . . to 0.18)	0.23 (0.15-0.31)	0.52 (0.38-0.67)	1.11 (0.89-1.33)	2.41 (1.53-3.29)	5.25 (4.05-6.44)	7.94 (3.65-12.22)
Pregnancy Status										
Pregnant	286	0.97 (0.68-1.27)	.69	. . .	0.15 (. . . to 0.22)	0.38 (0.20-0.55)	0.89 (0.63-1.16)	1.95 (. . . to 4.06)‖	4.83 (4.02-5.64)	5.98 (4.56-7.40)
Not pregnant	1417	1.02 (0.85-1.20)		. . .	0.17 (0.14-0.21)	0.42 (0.30-0.55)	0.94 (0.74-1.15)	2.05 (1.52-2.59)	4.80 (4.10-5.50)	7.17 (4.81-9.54)
Fish or Shellfish Consumption in Past 30 Days										
No fish or shellfish‡	429	0.42 (0.36-0.49)		. . .	. . .	0.16 (. . . to 0.21)	0.36 (0.30-0.41)	0.75 (0.62-0.87)	1.46 (1.28-1.64)	1.95 (1.05-2.85)
Only shellfish	201	0.76 (0.58-0.94)	<.001	. . .	0.14 (. . . to 0.31)‖	0.39 (0.27-0.50)	0.71 (0.55-0.87)	1.38 (1.16-1.60)	2.27 (2.02-2.51)	2.91 (2.07-3.74)
Only fish	438	1.04 (0.81-1.27)	<.001	. . .	0.24 (0.15-0.33)	0.51 (0.40-0.62)	1.00 (0.79-1.20)	1.91 (1.36-2.46)	4.07 (2.89-5.25)	6.00 (3.36-8.64)
Both fish and shellfish	574	1.73 (1.41-2.04)	<.001	0.30 (0.21-0.39)	0.41 (0.29-0.54)	0.82 (0.72-0.93)	1.54 (1.25-1.82)	3.78 (2.71-4.85)	6.95 (5.97-7.94)	10.81 (7.15-14.47)
No. of Fish Meals in Past 30 Days										
0‡	630	0.51 (0.43-0.59)		. . .	. . .	0.20 (0.15-0.26)	0.48 (0.37-0.59)	0.90 (0.70-1.09)	1.81 (1.36-2.25)	2.42 (1.70-3.14)
1-2	565	1.05 (0.84-1.26)	<.001	0.14 (. . . to 0.21)	0.27 (0.15-0.40)	0.53 (0.43-0.62)	0.95 (0.73-1.17)	1.82 (1.38-2.27)	4.03 (2.05-6.00)	6.12 (2.18-10.07)‖
≥3	448	1.94 (1.52-2.35)	<.001	0.27 (0.16-0.39)	0.44 (0.21-0.68)	0.96 (0.74-1.17)	1.78 (1.44-2.12)	4.19 (3.32-5.06)	7.41 (4.82-10.01)	10.91 (8.42-13.39)
No. of Shellfish Meals in Past 30 Days										
0‡	868	0.69 (0.57-0.81)		. . .	. . .	0.27 (0.21-0.33)	0.64 (0.52-0.77)	1.39 (1.06-1.71)	2.73 (1.59-3.88)	4.47 (3.40-5.54)
1-2	468	1.08 (0.90-1.25)	<.001	. . .	0.23 (0.16-0.29)	0.51 (0.42-0.61)	1.02 (0.75-1.29)	2.12 (1.63-2.62)	4.44 (3.20-5.69)	6.22 (5.49-6.94)
≥3	308	2.10 (1.66-2.54)	<.001	0.43 (0.36-0.50)	0.56 (0.42-0.70)	0.91 (0.60-1.22)	1.79 (1.55-2.04)	4.54 (3.65-5.43)	8.87 (6.19-11.56)	11.88 (11.09-12.66)

Abbreviation: CI, confidence interval; ellipses, less than the limit of detection.
SI conversion factor: To convert mercury to nmol/L, multiply values by 4.99.
*t Test comparing geometric mean with referent.
†Total includes other race and ethnic groups and those missing information for other variables.
‡Referent for comparison of geometric means.
§For women 20 to 49 years.
‖Estimate does not meet minimum standard of statistical reliability (relative standard error >30%).

Table 3. Estimated β Coefficients From Multiple Linear Regression Analyses of the Natural Logarithm of Blood Mercury Levels (µg/L) Among Women 16 to 49 Years by Race and Ethnicity

Covariates	Race and Ethnicity, β Coefficients (SEs)					
	Non-Hispanic White	P Value	Non-Hispanic Black	P Value	Mexican American	P Value
R^2, %	29		18		19	
Intercept	−1.37 (0.160)		−0.88 (0.210)		−0.94 (0.138)	
Age*	0.01 (0.005)	.01	0.02 (0.006)	<.001	0.01 (0.004)	.08
No. of Fish Meals in Past 30 Days						
≥3	1.16 (0.157)	<.001	0.83 (0.224)	<.001	0.85 (0.145)	<.001
1-2	0.63 (0.131)	<.001	0.24 (0.170)	.16	0.48 (0.106)	<.001
0	0		0		0	
Shellfish Eaten in Past 30 Days						
Yes	0.49 (0.115)	<.001	0.10 (0.157)	.16	0.34 (0.082)	<.001
No	0		0		0	

*Natural logarithm of blood mercury per year of age.

contaminated waters in Arkansas.[18] In a screening program in Louisiana, elevated blood mercury levels (median, 25 µg/L; range, 19.6-35.1 µg/L) were found in 6 persons who were commercial fishermen or their family members.[28] A family in Wisconsin had blood mercury levels of 37 to 58 µg/L that were attributed to consumption of 2 meals per week of imported sea bass.[20] In a study of all clients tested for mercury in an environmental and occupational medicine clinic, regular or high-fish consumption (>2-4 meals per week) explained 10 of 11 cases with mercury levels higher than 15 µg/L.[22]

In 2000, a National Research Council (NRC) committee recommended a benchmark dose level of 58 µg/L mercury in cord blood based on developmental effects from in utero methylmercury exposure.[3] The benchmark dose is the lower 95% confidence limit of the estimated level that would result in a doubling of the proportion of children with an abnormal score on a developmental assessment tool used in the Faroe Islands study.[11] To account for uncertainties in exposure measures and variability in individual response to toxic effects of mercury, the NRC recommended an uncertainty factor of 10 to calculate a reference dose, corresponding to a concentration of 5.8 µg/L mercury in cord blood. In 2003, the US Environmental Protection Agency published its final reference dose for methylmercury, agree-ing with the recommendation of the NRC.[29] In the 1999-2000 NHANES, no women had blood mercury concentrations at the benchmark dose level or higher. However, 7.8% (95% CI, 5.0%-10.5%) had blood mercury levels at 5.8 µg/L or higher. The Agency for Toxic Substances and Disease Registry specifies another risk level, the Minimum Risk Level, based on results from the Seychelles Child Development Study[10] and an uncertainty factor of 4.5.[2] The mercury blood concentration corresponding to the Minimum Risk Level is 13.6 µg/L. Approximately 1% of women aged 16 to 49 years had levels at or higher than the Minimum Risk Level, although this estimate did not meet minimum standards of statistical reliability.

We presented information on total mercury concentrations in blood, primarily representing the distribution of exposure to organic (methyl) mercury, which was supported by the correlation of concentrations of total mercury with fish and shellfish consumption. Fish and shellfish consumption represents the primary source of methylmercury in humans.[1,2] With a meal consisting of fish, more than 95% of methylmercury is absorbed.[30-32] In adults, total mercury concentrations reflect methylmercury exposures during several months but may be influenced by recent fish or shellfish meals. The rate of clearance for methylmercury also affects blood mercury concentrations. Additional evalu-ation of methylmercury biokinetics in children is needed.

That total blood mercury represents predominantly methylmercury is also supported by the fact that 97% of the women in the study had inorganic mercury levels lower than the limit of detection (0.4 µg/L). However, the limit of detection for inorganic mercury was about 3 times higher than the limit of detection for total mercury. Among the 50% of children and 25% of women having a total blood mercury of less than 0.4 µg/L, the amount of inorganic and elemental mercury in blood could not be determined. Among women in this study, 55 had blood concentrations of inorganic mercury higher than the detection limit; 3 of these were clear outliers (>10 µg/L). These individuals did not influence our estimates of the upper percentiles or the prevalence of values 5.8 µg/L or higher when we removed them from the analyses.

Significant occupational exposures to elemental or inorganic mercury are unlikely in this general population sample. Elemental and inorganic mercury exposures from dental amalgams, thimerosol (ethyl mercury), or mercury preservatives (phenyl mercuric acetate) may cause a transient shift in total blood mercury concentrations, because these forms of mercury are more rapidly cleared from blood into the urine. Urinary mercury is the preferred biomarker for low-level exposures to elemental and inorganic mercury.[17] The distribution of urine mercury levels in women aged 16 to 49 years from the 1999-2000 NHANES are far less than levels of concern in occupational settings.[25] Once information from the NHANES dental examination is available, these data can be used to further examine exposure to inorganic and elemental mercury in the US population. Children may be exposed to ethylmercury from thimerosol, a preservative used in vaccines. A recent study suggests that mercury from thimerosol is rapidly eliminated in infants,[33] indicating that thimersol exposure may not significantly contribute to blood mercury levels in children. Cur-

rently, the Centers for Disease Control and Prevention is developing new analytical capacity to directly measure a variety of chemical species of mercury in the ongoing NHANES study.

There are several caveats regarding the NHANES results on blood mercury levels and fish consumption. The number of fish meals consumed in the past 30 days is, at best, a crude measure of methylmercury exposure and likely responsible for the low to modest R^2 values obtained in multivariate analyses. The relatively low R^2 values indicate that the independent variables as currently defined are not useful collectively to predict individual blood mercury levels. Also, self-reported data may underestimate or overestimate the number of fish meals. Portion size also affects exposure to mercury but was not collected. Analyses by species was limited because few people ate the same types of fish. Mercury concentrations clearly differ between and within fish species.[34] The cumulative effect of methylmercury ingestion and the rate of clearance for methylmercury also affect total blood mercury concentrations.

Several additional limitations to these data exist. These measurements cannot be generalized to populations other than children aged 1 to 5 years and women of reproductive age. The 1999-2000 NHANES was not designed to describe geographic variation because of the relatively small number of geographic sites sampled. Furthermore, geographical locations were not selected to address the potential for variability of mercury exposures by region. The oversampling of Mexican American and non-Hispanic blacks is highly correlated with region and this may in part explain the small differences observed between the race and ethnic groups. Income-based information on socioeconomic status is not yet available from 1999-2000 NHANES. Socioeconomic status may be related to fish consumption and may be important for differences between racial and ethnic groups. The survey did not include an oversample of subgroups within the United States that frequently consume

fish such as sports fishermen, certain American Indian or Alaskan Native groups, or those who limit their protein intake to fish.

Blood mercury measures were not available for 44% of children aged 1 to 5 years who were selected to participate in the survey largely due to the high refusal rate for phlebotomy. A potential nonresponse bias was examined by comparing the race and ethnicity of children who had blood mercury measures with those who did not (among all children who were included in the interview portion of the survey). The potential for a nonresponse bias is low because race and ethnicity did not differ between participating and nonparticipating children.

These results support the conclusion from the NRC committee review based on earlier estimates of methylmercury exposure in US populations that in utero methylmercury exposure is low. However, approximately 8% of reproductive-aged women have mercury levels higher than the Environmental Protection Agency's reference dose.

Fish is part of a nutritious diet and is a particularly good source of high-quality protein and essential fatty acids as well as being low in saturated fat. Numerous recommendations support the benefits of fish consumption, especially in prevention of coronary heart disease. The American Heart Association recommends eating 2 servings of fish per week.[35] Although all fish and shellfish contain at least trace amounts of methylmercury, the concentration varies widely. Some fish and shellfish species, such as haddock, tilapia, salmon, cod, pollock, and sole, as well as most shellfish are relatively low in methylmercury.[1,13] Fish species that are predatory and high on the food chain bioconcentrate methylmercury resulting in methylmercury concentrations that are much higher.[1]

The importance of careful choices in fish selected for consumption has been emphasized by recent advisories from the US government as well as other countries.[13-16] Because of wide variations in the concentrations of mercury in fish and

shellfish, it is possible to have the nutritional benefits of moderate fish consumption and avoid fish high in mercury. Government advisories also make clear that it is important to continue efforts to reduce environmental releases of mercury into the air and water. The NHANES data on the distribution of blood mercury levels in women and children will provide a baseline to evaluate continuing efforts to reduce mercury exposure in the United States.

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The history of intellectual growth and discovery clearly demonstrates the need for unfettered freedom, the right to think the unthinkable, discuss the unmentionable, and challenge the unchallengeable. To curtail free expression strikes twice at intellectual freedom, for whoever deprives another of the right to state unpopular views necessarily deprives others of the right to listen to those views.

—C. Vann Woodward (1908-1999)