



Recent Publications on the Human Health Effects of Mercury

ENVIRONMENT AND HEALTH PROGRAM

Identifying adverse neurodevelopmental effects in a fish-consuming population

Myers GJ, Davidson PW, Cox C, Shamlaye CF, Palumbo D, Cernichiari E, et al. 2003. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study. *The Lancet* 361(9370):1686–1692.

INTRODUCTION: Exposure to methylmercury (MeHg) before birth can adversely affect children's neurodevelopment. The most common form of prenatal exposure is maternal fish consumption, but whether such exposure harms the fetus is unknown. We aimed to identify adverse neurodevelopmental effects in a fish-consuming population. **METHODS:** We investigated 779 mother-infant pairs residing in the Republic of Seychelles. Mothers reported consuming fish on average 12 meals per week. Fish in Seychelles contain much the same concentrations of MeHg as commercial ocean fish elsewhere. Prenatal MeHg exposure was determined from maternal hair growing during pregnancy. We assessed neurocognitive, language, memory, motor, perceptual-motor, and behavioral functions in children at age 9 years. The association between prenatal MeHg exposure and the primary endpoints was investigated with multiple linear regression with adjustment for covariates that affect child development. **FINDINGS:** Mean prenatal MeHg exposure was 6.9 parts per million (SD=4.5 ppm). Only two endpoints were associated with prenatal MeHg exposure. Increased exposure was associated with decreased performance in the grooved pegboard using the non-dominant hand in males and improved scores in the hyperactivity index of the Conner's teacher rating scale. Covariates affecting child development were appropriately associated with endpoints.

Investigating fish consumption patterns of WIC participants in East Harlem, New York City

Bienenfeld LA, Golden AL, Garland EJ. 2003. Consumption of fish from polluted waters by WIC participants in east Harlem. *Journal of Urban Health* 80(2):349–358.

To minimize exposure to neurotoxins such as mercury, polychlorinated biphenyls (PCBs), dioxins, and pesticide residues, the New York State Department of Health issues

health advisories about consumption of certain fish and shellfish caught from polluted local waters. Fetal exposure causes cognitive developmental deficits in children. Consumption of fish was assessed. We surveyed 220 WIC (Special Supplemental Nutrition Program for Women, Infants, and Children) participants. Of the participants, 10% ate fish and shellfish caught in local polluted waters. Statistically significant factors associated with eating local, noncommercial fish included male gender and knowledge of the health advisory. Locally caught fish and crabs are consumed; thus, in utero and childhood exposure to these neurotoxins occurs. Interventions to promote safer choices of fish are needed.

Describing the distribution of blood mercury levels in U.S. children and women of childbearing age and the association with sociodemographic characteristics and fish consumption

Schober SE, Sinks TH, Jones RL, Bolger PM, McDowell M, Osterloh J, et al. 2003. Blood mercury levels in U.S. children and women of childbearing age, 1999–2000. *Journal of the American Medical Association* 289(13):1667–1674.

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 U.S. population. **PARTICIPANTS:** In 1999–2000, 1,250 children aged 1 to 5 years and 2,314 women aged 16 to 49 years were selected to participate in the survey. **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 three or more servings of fish in the past 30 days compared with women who ate no fish in that period (1.94

$\mu\text{g/L}$ vs. $0.51 \mu\text{g/L}$; $p < 0.001$). **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 U.S. Environmental Protection Agency's recommended reference dose ($5.8 \mu\text{g/L}$), 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.

Studying mercury levels in high-end consumers of fish

Hightower JM, Moore D. 2003. Mercury levels in high-end consumers of fish. *Environmental Health Perspectives* 111(4):604–608.

Consumption of food containing mercury has been identified as a health risk. The U.S. Environmental Protection Agency (U.S. EPA) and the National Academy of Sciences recommend keeping the whole blood mercury level $< 5.0 \mu\text{g/L}$ or the hair level $< 1.0 \mu\text{g/g}$. This corresponds to a reference dose (RfD) of $0.1 \mu\text{g/kg}$ body weight per day. All patients in a 1-year period ($n=720$) who came for an office visit in a private internal medicine practice in San Francisco, California, were evaluated for mercury excess using the current RfD. One hundred twenty-three patients were tested (93 females, 30 males). Of these, data were statistically analyzed for 89 subjects. Mercury levels ranged from 2.0 to $89.5 \mu\text{g/L}$ for the 89 subjects. The mean for 66 women was $15 \mu\text{g/L}$ [standard deviation (SD)=15], and for 23 men was $13 \mu\text{g/L}$ (SD=5); 89% had levels exceeding the RfD. Subjects consumed 30 different forms or types of fish. Swordfish had the highest correlation with mercury level. Sixty-seven patients with serial blood levels over time after stopping fish showed a decline in mercury levels; reduction was significant ($p < 0.0001$). A substantial fraction of patients had diets high in fish consumption; of these, a high proportion had blood mercury levels exceeding the maximum level recommended by the U.S. EPA and National Academy of Sciences. The mean level for women in this survey was 10 times that of mercury levels found in a recent population survey by the U.S. Centers for Disease Control and Prevention. Some children were > 40 times the national mean.

Looking at whether a high dietary intake of mercury from fish consumption causes an increase in coronary heart disease in men

Yoshizawa K, Rimm EB, Morris JS, Spate VL, Hsieh CC, Spiegelman D, et al. 2002. Mercury and the risk of coronary heart disease in men. *The New England Journal of Medicine* 347(22):1755–1760.

BACKGROUND: A high dietary intake of mercury from consumption of fish has been hypothesized to increase the risk of coronary heart disease. **METHODS:** Using a nested case-control design, we investigated the association between mercury levels in toenails and the risk of coronary heart disease among male health professionals with no previous history of cardiovascular disease or cancer who were 40 to 75 years of age in 1986. Each patient was matched according to age and smoking status with a randomly selected control subject. **RESULTS:** The mercury level was significantly correlated with fish consumption (Spearman $r=0.42$, $p < 0.001$), and the mean mercury level was higher in dentists than in nondentists (mean, 0.91 and $0.45 \mu\text{g/gram}$, respectively; $p < 0.001$). After age, smoking, and other risk factors for coronary heart disease had been controlled for, the mercury level was not significantly associated with the risk of coronary heart disease. When the highest and lowest quintiles of mercury level were compared, the relative risk of coronary heart disease was 0.97 in the highest level (95% confidence interval, 0.63 to 1.50; p -value for trend=0.78). **CONCLUSIONS:** Our findings do not support an association between total mercury exposure and the risk of coronary heart disease, but a weak relation cannot be ruled out.

Mercury exposure diminishes cardiovascular benefits associated with eating fish

Guallar E, Sanz-Gallardo MI, van't Veer P, Bode P, Aro A, Gomez-Aracena J, et al., Heavy Metals and Myocardial Infarction Study Group. 2002. Mercury, fish oils, and the risk of myocardial infarction. *The New England Journal of Medicine* 347(22):1747–1754.

A study of middle-aged European and Israeli men found a direct association between measured mercury levels in toenails and first heart attack. Adjusting for traditional risk factors and antioxidant levels, the highest 20% exposure group had a 2.2-fold increased risk of heart attack compared to the lowest 20% exposure group. When examining the effects of a specific fatty acid (DHA) on cardiovascular disease, the researchers found a significant trend toward lower heart attack incidence with increasing DHA levels only when adjusted for mercury levels. Researchers concluded that high mercury levels may diminish the cardioprotective effect of fish intake.

Measuring mercury levels in infertile men and women

Choy CM, Lam CW, Cheung LT, Briton-Jones CM, Cheung LP, Haines CJ. 2002. Infertility, blood mercury concentrations and dietary seafood consumption: a case-control study. *BJOG: an International Journal of Obstetrics and Gynecology* 109:1121–1125.

A study of 157 infertile couples and 26 fertile couples in Hong Kong compared blood mercury levels and evaluated possible sources of mercury exposure in couples with high levels. Researchers found that infertile couples had higher mercury levels than fertile couples; infertile males with abnormal semen and infertile females with unexplained infertility also had higher blood mercury levels than their fertile counterparts. Blood mercury concentrations in infertile couples also increased with seafood consumption.

Measuring maternal seafood diet, methylmercury exposure, and neonatal neurologic function

Steuerwald U, Weihe P, Jorgensen PJ, Bjerve K, Brock J, Heinzow B, et al. 2000. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. *The Journal of Pediatrics* 136(5):599–605.

OBJECTIVE: To determine whether neonatal neurologic function is adversely affected by seafood contaminants from maternal diet during pregnancy. **STUDY DESIGN:** One hundred eighty-two singleton term births were evaluated in the Faroe Islands, where marine food includes pilot whale. Maternal serum, hair, and milk and umbilical cord blood were analyzed for contaminants. Levels of essential fatty acids, selenium, and thyroid hormones were determined in cord blood. Each infant's neurologic optimality score was determined at two weeks of age adjusted for gestational age, and predictors were assessed by regression analysis. **RESULTS:** Exposures to methylmercury and polychlorinated biphenyls were increased in relation to maternal seafood intake, as were [omega] 3 fatty acid concentrations in cord serum. Thyroid function was normal. After adjustment for confounders, a 10-fold increase of the cord-blood mercury concentration was associated with a decreased neurologic optimality score of 2.0 ($p=0.03$). This effect corresponds to a decrease in gestational age of about 3 weeks. Other indicators of the seafood diet had no effect on this outcome. **CONCLUSIONS:** Prenatal exposure to methylmercury from contaminated seafood was associated with an increased risk of neurodevelopmental deficit. Thus in this North Atlantic population, methylmercury constituted an important neurologic risk factor, although effects of other seafood components were not detectable.

Reaffirming the risk of mercury exposure in utero to the developing nervous system

Committee on the Toxicological Effects of Methylmercury, National Research Council. 2000. *Toxicological Effects of Methylmercury*. Washington, DC: National Academy Press.

In its study, the National Research Council Committee on the Toxicological Effects of Methylmercury reviewed the

epidemiological and toxicology literature up to 2000. The committee determined that from a public health perspective, the use of a positive study (i.e., the Faroe Islands research indicating mercury-related impairments in children) was the best choice in deriving a safe exposure level (e.g., a reference dose, or RfD). Following this approach, the committee reaffirmed the validity of the U.S. EPA RfD ($0.1 \mu\text{g}/\text{kg}$ body weight/day). Based on population levels, fertility rates, and estimates of the number of women of childbearing age in the top 5% of fish consumption, the committee estimated 60,000 newborns annually are at risk for neurodevelopmental effects due to in utero mercury exposure in the U.S. The report also reviewed evidence of associations between dietary exposure to methylmercury and abnormal cardiac function in both children and adults.

Studying high mercury exposures and neurodevelopmental effects in children in the Amazon

Grandjean P, White RF, Nielsen A, Cleary D, de Oliveira Santos EC. 1999. Methylmercury neurotoxicity in Amazonian children downstream from gold mining. *Environmental Health Perspectives* 107(7):587–591.

In widespread informal gold mining in the Amazon Basin, mercury is used to capture the gold particles as amalgam. Releases of mercury to the environment have resulted in the contamination of freshwater fish with methylmercury. In four comparable Amazonian communities, we examined 351 of 420 eligible children between 7 and 12 years of age. In three Tapajós villages with the highest exposures, more than 80% of 246 children had hair-mercury concentrations above $10 \mu\text{g}/\text{g}$, a limit above which adverse effects on brain development are likely to occur. Neuropsychological tests of motor function, attention, and visuospatial performance showed decrements associated with the hair-mercury concentrations. Especially on the Santa Ana form board and the Stanford-Binet copying tests, similar associations were also apparent in the 105 children from the village with the lowest exposures, where all but two children had hair-mercury concentrations below $10 \mu\text{g}/\text{g}$. Although average exposure levels may not have changed during recent years, prenatal exposure levels are unknown, and exact dose relationships cannot be generated from this cross-sectional study. However, the current mercury pollution seems sufficiently severe to cause adverse effects on brain development.

Analyzing the influence of prenatal mercury exposure on children's test performance in New Zealand

Crump KS, Kjellstrom T, Shipp AM, Silvers A, Stewart A. 1998. Influence of prenatal mercury exposure upon scholastic and psychological test performance: bench-

mark analysis of a New Zealand cohort. *Risk Analysis* 18(6): 701–713.

This paper presents benchmark (BMD) calculations and additional regression analyses of data from a study in which scores from 26 scholastic and psychological tests administered to 237 6- and 7-year-old New Zealand children were correlated with the mercury concentration in their mothers' hair during pregnancy. The original analyses of five test scores found an association between high prenatal mercury exposure and decreased test performance, using category variables for mercury exposure. Our regression analyses, which utilized the actual hair mercury level, did not find significant associations between mercury and children's test scores. However, this finding was highly influenced by a single child whose mother's mercury hair level (86 mg/kg) was more than four times that of any other mother. When that child was omitted, results were more indicative of a mercury effect and scores on six tests were significantly associated with the mothers' hair mercury level. BMDs calculated from five tests ranged from 32 to 73 mg/kg hair mercury, and corresponding BMDLs (95% lower limits on BMDs) ranged from 17 to 24 mg/kg. When the child with the highest mercury level was omitted, BMDs ranged from 13 to 21 mg/kg, and corresponding BMDLs ranged from 7.4 to 10 mg/kg.

Documenting developmental delays in children exposed to mercury in utero

Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, et al. 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicology and Teratology* 19(6):417–428.

A cohort of 1,022 consecutive singleton births was generated during 1986–1987 in the Faroe Islands. Increased methylmercury exposure from maternal consumption of pilot whale meat was indicated by mercury concentrations in cord blood and maternal hair. At approximately seven years of

age, 917 of the children underwent detailed neurobehavioral examination. Neuropsychological tests included Finger Tapping; Hand-Eye Coordination; reaction time on a Continuous Performance Test; Wechsler Intelligence Scale for Children Revised Digit Spans, Similarities, and Block Designs; Bender Visual Motor Gestalt Test; Boston Naming Test; and California Verbal Learning Test (Children). Clinical examination and neurophysiological testing did not reveal any clear-cut mercury-related abnormalities. However, mercury-related neuropsychological dysfunctions were most pronounced in the domains of language, attention, and memory, and to a lesser extent in visuospatial and motor functions. These associations remained after adjustment for covariates and after exclusion of children with maternal hair mercury concentrations above 10 µg/g (50 nmol/g). The effects on brain function associated with prenatal methylmercury exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe.

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