

# Prenatal Methylmercury Exposure and Children: Neurologic, Developmental, and Behavioral Research

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Mercury is present in the earth's crust and is methylated by bacteria in aquatic environments to methylmercury (MeHg). It is then concentrated by the food chain so predatory fish and sea mammals have the highest levels. Thus, consuming seafood leads to exposure. MeHg readily crosses the placenta and the blood-brain barrier and is neurotoxic. The developing fetal nervous system is especially sensitive to its effects. Prenatal poisoning with high dose MeHg causes mental retardation and cerebral palsy. Lower level exposures from maternal consumption of a fish diet have not been consistently associated with adverse neurodevelopmental outcomes. However, most studies have considerable uncertainty associated with their results. Two large controlled longitudinal studies of populations consuming seafood are underway that are likely to determine if any adverse effects can be identified. No adverse associations have been found in the Seychelles, where exposure is mainly from fish consumption. In the Faroe Islands where exposure is primarily from consumption of whale meat and not fish, adverse associations have been reported. The Seychelles population consumes large amounts of marine fish containing MeHg concentrations similar to commercial fish in the United States. Current evidence does not support the hypothesis that consumption of such fish during pregnancy places the fetus at increased neurodevelopmental risk. — *Environ Health Perspect* 106(Suppl 3):841–847 (1998). <http://ehpnet1.niehs.nih.gov/docs/1998/Suppl-3/841-847myers/abstract.html>

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## Introduction

Prenatal exposure to methylmercury (MeHg) is primarily dietary (1). MeHg is present in all fresh and marine fish, and pregnant women who consume a high fish diet expose their fetus to this neurotoxin. Several episodes of fetal MeHg poisoning have been reported (2–5), and confirm that the developing fetal brain is especially susceptible. The clinical findings following poisoning are microcephaly, cerebral palsy, seizures, and mental retardation. In all poisonings the source was dietary, but only in Minamata (6) and Niigata (7), Japan, was fish consumption involved. The fish

consumed in Japan contained very high MeHg levels from local pollution. In Minamata, Japan, children showed severe neurodevelopmental impairment even though the mothers experienced minimal or no clinical symptoms (2). No other children symptomatic with fetal poisoning from fish consumption have been described since the Minamata and Niigata episodes.

Following an outbreak of MeHg poisoning in Iraq, a dose-response relationship was determined, indicating that exposures in the range of 10 to 20 ppm might adversely affect the fetus (8). This level of

exposure occurs regularly in populations that consume large amounts of fish (9).

Some studies undertaken in populations consuming large amounts of fish found an association between fetal exposure and outcome measures (3,8,10–14), but others did not (15–20). In 1990 an expert committee for the World Health Organization reviewed the available evidence and concluded “a prudent interpretation of the Iraqi data implies that a 5% risk may be associated with a peak mercury level of 10–20 µg/g in the maternal hair” (1).

In this paper we review fetal MeHg exposure and discuss the outcome measures used to determine if an association actually does exist in fish-eating populations.

## Environmental Mercury

Inorganic mercury occurs naturally in the earth's crust and is widespread in the environment. Volcanic emissions contribute to mercury in the atmosphere, as does human activity such as incineration of household waste, burning of fossil fuels, cremation, and smelting (1). Mercury use in the electrical industry, medical and laboratory instrumentation, paper mills, the extraction of gold, and dental amalgams also contributes to its presence in the environment (21).

In aquatic environments common bacteria methylate mercury. Human activities such as dams that enlarge aquatic environments leach mercury from the earth and facilitate both methylation and the movement of MeHg into the food chain (22). After MeHg enters living organisms it is passed up the food chain, and animals at the top such as predatory fish and large sea mammals accumulate the highest levels.

Most marine fish contain less than 0.5 ppm MeHg, but sharks, sailfish, marlin, and other billfish frequently have levels of over 1 ppm (23). Marine mammals such as dolphins and whales have even higher levels (24). When local waters are polluted with MeHg, levels in both fresh and marine fish may be much higher. Fish from Minamata Bay was reported to contain up to 40 ppm and above 10 ppm in polluted Canadian waters (25,26). Individuals who eat fish regularly even when there is no local pollution can have hair mercury levels ranging up to 30 ppm or higher (1,9).

## Methylmercury in the Human Body

Dietary MeHg in the human is almost totally absorbed in the gastrointestinal tract

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Abbreviations used: Bender, Bender Visual Gestalt Test; BNT, Boston Naming Test; BSID, Bayley Scales of Infant Development; CVAA, cold-vapor atomic absorption; CVLT, California Verbal Learning Test; DDST or DDST-R, revised Denver Developmental Screening Test; FACT, Functional Acuity Contrast Test; MSCA, McCarthy Scales of Children's Abilities; NES, Neurobehavioral Examination System; PCB, polychlorinated biphenyl; PLS, Preschool Language Scale; WISC-R, Revised Wechsler Intelligence Scale for Children.

and rapidly enters the bloodstream (1). About 95% is taken up by red blood cells, and then distributed throughout the body over the next 3 to 4 days. The brain is the primary target organ. In pregnant women, MeHg readily crosses the placenta and has a high affinity for fetal hemoglobin. Levels in fetal blood are about 25% higher than in the mother (27).

In adults, the neurotoxicity includes neuronal destruction, with the early effects predominantly on the occipital cortex and cerebellum (28). However, in the fetus, exposure leads to diffuse disruption of normal developmental processes such as neuronal migration and organization of gray matter (29). In experimental animals, neurotoxicity has been reported with measured levels of total mercury in brain as low as 1800 parts ppb (30,31). Neuropathologic studies in the Seychelles of neonates dying of illnesses not believed to be related to mercury exposure found brain mercury levels up to 295 ppb (32). No neuropathologic changes were associated with MeHg exposure at that level.

### Measuring Human Exposure

Prenatal MeHg exposure is generally determined by measuring total mercury in a segment of the mother's hair that was growing during pregnancy. MeHg enters hair follicles in direct proportion to its level in blood and is incorporated into the hair shaft (1). Once in the hair shaft, the mercury content does not appear to change. Inorganic mercury such as the vapor released from dental amalgams does not appear to be taken up by hair follicles or incorporated into the hair shaft (21). Human hair grows at about 1.1 cm per month, and the segment that was growing during pregnancy can be determined with some accuracy. By measuring the mercury in short segments of hair, the exposure history for the entire pregnancy can be recapitulated.

Fetal exposure can also be determined by measuring total mercury in cord blood samples at birth. Blood provides an excellent measure of recent exposure. After fish or seafood has been consumed, the blood level of mercury rises then decreases, with an average half-time of 52 days (33,34). Consequently, exposure levels earlier in pregnancy remain unknown.

Multiple analytic methods have been used to determine the mercury content of various tissues, but cold-vapor atomic absorption (CVAA) measuring total mercury in maternal hair has been the standard in nearly all clinical studies. With

CVAA both the inorganic and organic components can be determined. Over 80% of mercury in human hair is organic (35). Neuropathologic evidence confirms that there is a good correlation between levels of total mercury measured in neonatal brain and in the corresponding maternal hair (36).

### Human Effects of High-Level Exposure

The toxicity of MeHg in adults was not fully appreciated until 1940, after an industrial poisoning (37). Although poisoning with MeHg is uncommon, a number of episodes have occurred (2-5,38). The poisonings that occurred at Minamata and Niigata, Japan, and in Iraq led to severe neurologic damage and sometimes death in both adults and children (3,8,28). Prenatal MeHg poisoning, or Minamata disease, clinically presents as mental retardation, cerebral palsy, microcephaly, and seizures (2). The fetus appears especially sensitive to this toxin. During the Minamata outbreak a number of mothers had only transient paresthesias or were asymptomatic even though the children were severely affected (2).

Only one study examining milder effects of fetal poisoning was reported from Japan (39). Harada reported an increased incidence of mental retardation, sensory disturbances, and dysarthria in school children from the Minamata area compared to other areas in Japan. The methodology used in that study was not reported.

After the Iraq poisoning of 1971 to 1972, children exposed prenatally were identified. Over 80 children who were *in utero* when their mothers consumed bread made from MeHg-treated seed grain were examined (3). The poisoning involved a high level of exposure over a period of 2 to 3 months. This acute exposure produced sharp peaks of mercury when the maternal hair was measured longitudinally. The index of exposure used in the Iraq studies was the highest level of total mercury measured (8). Two neurodevelopmental end points were determined: motor retardation (defined as the age mothers said their child started walking), and a score of neurologic impairment derived from findings on the neurologic examination (3). The most prominent abnormal findings on the neurologic examination were an increase in muscle tone and deep tendon reflexes, and extensor plantar responses. A dose-response relationship for MeHg exposure was described based on these findings. That

relationship suggested that fetal exposure in the maternal hair mercury range of 10 to 20 ppm may be associated with clinically detectable findings (8,40).

There was considerable uncertainty about the lowest level at which the increased risk might occur as only three children had delays in walking and six had abnormal neurologic examinations with an MeHg exposure below 50 ppm in maternal hair (8,40,41). Of those children, three with abnormal neurologic examinations had exposure levels of 1 ppm (3,8). Because of the small number of abnormal subjects in the low-exposure range, it was not possible to tell if the relationship was continuous or if a threshold was present.

The confidence limits for the Iraq analysis were sensitive to the background response rate. Because the true background rate of neurodevelopmental delay unrelated to MeHg exposure in the Iraqi population was unknown, the analysis was done considering several background rates. When a zero background rate of delayed walking was assumed, the confidence interval for the estimated lowest effect level was 7.3 to 14 ppm. If one assumed a 4% background rate, the confidence interval was 9.0 to 190 ppm (8). Using an estimated background level of 9% for abnormal neurological signs, the confidence interval was 10 to 287 ppm. All of the analyses had lower confidence limits that included the range of MeHg exposures previously reported in human populations that regularly consume fish.

### Human Effects of Exposure from Fish Consumption

Exposure to MeHg occurs in all individuals who eat fish or fish products. Clinically diagnosed poisoning from consuming fish has been reported only from Japan where MeHg levels in fish were very high. The dose-response analysis from Iraq, however, clearly raised concern that lower prenatal exposures might be associated with adverse neurodevelopmental effects. Consequently, studies were undertaken to see if adverse effects could be confirmed in such populations. Initial studies from Canada and New Zealand (10-12), and more recently from the Faroe Islands (13,14), have supported the Iraq conclusions. However, studies from Peru and the Republic of Seychelles have not found adverse associations (15-19). The studies have varied in multiple ways including the end points evaluated. Table 1 lists the general categories of end points evaluated. Those reported by the authors to show an association with prenatal MeHg

**Table 1.** Categories of tests used to detect an association between prenatal MeHg exposure and neurodevelopment in reported studies. Further details and references are in the text.

Testing category	Iraq	Canada	New Zealand	Peru	Faroe Islands	Seychelles	
						Main	Pilot
Neurologic	+	+	-	-	-	-	-
Developmental milestones	+			-	-	-	-
Developmental screening	-	+			-	-	+
Psychological			+		+	-	+
Academic/Educational			-			-	-
Behavioral						-	+
Neuropsychologic					+	+	
Neurophysiologic					+		

+, studies in this category were done and an association with prenatal MeHg exposure was reported by the authors; -, studies in this category were done and no association with prenatal MeHg exposure was reported by the authors.

exposure are marked. No consistent pattern of associations is readily apparent.

### Neurologic Testing

The neurologic examination readily detects the consequences of Minamata disease. Findings include microcephaly, increases in muscle tone and deep tendon reflexes, and extensor plantar responses. It was reasonable to suspect that minor degrees of each of these findings might be present with exposure to lower levels of MeHg, and in Iraq an association was present. Subsequent studies from Canada, Peru, and the Seychelles included a standard neurologic examination in an effort to confirm the Iraq findings.

The neurologic examination of children and its interpretation is a specialized area. A pediatric neurologist should perform the evaluation, as neurologic findings differ in normal children depending upon the age at evaluation, and abnormalities can be difficult to interpret. For example, pediatric neurologists consider extensor plantar responses normal up to 2 years of age (42). They also consider subtle differences in muscle tone and deep tendon reflexes difficult to recognize in young children.

In Iraq, Canada, Peru, and the Seychelles, a pediatric neurologist performed the neurologic examination. The age at which the children were examined varied in each study. In the Seychelles, children were examined between 6 and 105 weeks of age in the pilot study, but in the main study all were examined during the 6th month of life. In the other studies, examinations were generally performed from 4 months up to several years of age. In both Peru and the Seychelles the neurological examinations were done by the same neurologic team that examined the children in Iraq (15,16,18).

The Canadian study included a team of four pediatric neurologists (12). They found no association between neurologic

abnormalities in general and the level of prenatal exposure to MeHg. However, when males were evaluated separately, an association was seen between exposure and changes in muscle tone and deep tendon reflexes. This association was present only when both increases and decreases in muscle tone and deep tendon reflexes were combined. The authors noted that their results differed from those in Iraq, even though there was an association with the neurologic findings (12).

No association was found between abnormal neurologic findings and prenatal MeHg exposure in the Seychelles (16,18). During evaluations of the main cohort, the pediatric neurologist made a special effort to record subtle findings, but no association with exposure was detected (18).

In New Zealand and the Faroe Islands, a variation of the standard neurologic testing was included (10,13,14). In New Zealand the visual and sensory systems of the children were tested clinically by a nurse when the children were 4 years of age. Vision was tested using the Sheridan-Gardner Letter Matching Test and the Stycar Miniature Toy Test. Sensory tests included finger identification, localization of tactile stimuli, and temperature recognition. No association between either visual or sensory testing and prenatal MeHg exposure was found.

In the Faroe Islands, a functional neurologic test developed by Lier and Michelsen (43) was administered. An experienced pediatrician gave the test when the children were 7 years of age (13,14). No association between MeHg exposure and test items was reported (13,14). Some of the functional neurologic tests (diadochokinesia, reciprocal coordination, finger opposition, catching a ball, and finger agnosia) were associated with the neurobehavioral tests (finger tapping, continuous performance, and hand-eye coordination).

The association between neurologic findings and prenatal MeHg exposure has not been confirmed in fish-eating populations even when examinations were performed carefully by experienced clinicians under optimum circumstances.

### Developmental Milestones

Delayed developmental milestones such as the age at which a child begins to sit without support, crawl, take steps alone, or say words are well-known markers of developmental problems. Milestone data increase in reliability the closer it is obtained to the time that the child achieves the skill. In Iraq, there was an association between prenatal MeHg exposure and whether the child first walked before or after 18 months of age. The data for that analysis were collected when the children's mean age was 30 months (3). Two subsequent studies have examined developmental milestones in relation to prenatal MeHg exposure (20,44).

In the Faroe Islands the ages at which children first sat without support, crept, and stood with support were examined (44). Data were obtained from the district health nurses who visited the children regularly during the first year of life. The authors reported that children with higher mercury concentrations in their hair at 12 months of age reached these milestones earlier. They attributed the precocious development to the benefits of breastfeeding.

In the Seychelles, the age at which children first walked independently and said two words other than "mama" and "dada" was examined (20). These were the same two end points assessed in the Iraq study. Data on development were obtained from mothers when the children were evaluated at 19 months of age. Developmental milestones in this cohort were also precocious. In one model that included an interaction between MeHg and gender, the interaction was not significant, but in males there was an association between exposure and age at walking. The association was not present when statistical outliers were excluded. Seychellois males were precocious in walking (mean age 10.6 months vs 11.7 months in U.S. males), but a 10-ppm increase in maternal hair mercury was associated with a 2-week delay in walking. The authors concluded that there was no definite association between MeHg exposure and either milestone. No studies in fish-eating populations have confirmed the delays in developmental milestones found in Iraq.

### Neurophysiologic and Neurobehavioral Testing

In the Faroe Islands, neurobehavioral and neurophysiologic testing were conducted when study children were examined at 7 years of age (13,14). Visual and auditory evoked potentials, postural stability, and variability of the R-R interval on electrocardiograms were measured. Postural stability, visual evoked potentials, and cardiac variability was reported to have no association with prenatal MeHg exposure (14). However, associations were found between fetal MeHg exposure and brainstem auditory evoked potentials. There were delays in peaks III and V at higher MeHg exposures, but no association with interpeak latencies.

The neurobehavioral tests were part of a computerized test battery called the Neurobehavioral Examination System (NES). The NES assesses motor speed, sustained attention, and motor coordination, and includes finger tapping and tests of continuous performance and hand-eye coordination. In addition, the Functional Acuity Contrast Test (FACT), a test of visual contrast sensitivity, was administered. There was an association between the FACT and tests on the NES (13). Dahl and colleagues (13) reported associations with fetal exposure as follows "none of the above predictors was clearly related to prenatal mercury exposure ( $p < 0.05$ ). On the other hand, increased mercury exposure was associated with decreased performance on all NES parameters, in most cases statistically significant." The authors cautioned (13) that "...the deficits associated with a doubling of mercury exposure are limited..." (13). They also stated "...PCB [polychlorinated biphenyl] exposure cannot so far be ruled out as a potential underlying cause of the observed association between prenatal mercury exposure and neurobehavioral dysfunction..." Grandjean and colleagues (14) reported the results of NES testing in more detail. They found that the maximum number of finger taps in 15 sec was inversely associated with MeHg exposure, as was the average reaction time and the total number of missed responses on the continuous performance task. No association with the hand-eye coordination task was present. The sophisticated neurophysiologic and neurobehavioral test battery used in the Faroe Islands was reported (13,14) to show an inverse association between prenatal MeHg exposure and both neurophysiologic and neurobehavioral test outcomes. The Faroe Islands diet also

exposes residents to PCBs, but the authors measured PCBs and considered them in their analyses. They concluded that the associations were mainly with MeHg.

### Developmental Screening Tests

Developmental screening tests were included in the New Zealand, Canadian, and Seychelles studies. All three studies used either the original or the revised Denver Developmental Screening Test (DDST or DDST-R). The New Zealand investigators examined 31 children whose mothers had a hair mercury value during pregnancy of 6 ppm or greater, and a reference group of 30 children whose mothers' hair mercury values were less than 6 ppm (10). The authors reported 52% of the high group and 17% of the low group had abnormal or suspect scores on the DDST, and that an association between DDST scores and fetal exposure appeared to be present (10). The high percentage of questionable and abnormal scores, the mixing of ethnic groups, and the nonstandard grouping of the scores raised questions about this association, as discussed previously (15,16,18).

In the Seychelles study, an association between fetal MeHg exposure and scores on the DDST-R was found in the pilot study (16). This association was greater in males and when the children's age at evaluation was younger. In the main study when evaluations were conducted under more optimal conditions, no association was present (18). In the Canadian study, no association between the DDST scores and MeHg exposure was reported (12).

### Psychologic Testing

Experimental animals exposed to MeHg at relatively low doses have shown global cognitive delays, visual perceptual problems, and alterations in visual memory (31,45,46). Psychologic testing examines cognitive abilities and has been an important part of test batteries. In New Zealand, at 6 years of age the children were given psychologic tests that examined language development, intelligence, and fine and gross motor coordination (11). The test battery included the Test of Language Development, the Peabody Picture Vocabulary Test, the McCarthy Scales of Children's Abilities (MSCA), and the Revised Wechsler Intelligence Scale for Children (WISC-R).

The authors reported normal values for all the administered tests. However, they noted an association between prenatal MeHg exposure and decreased performance

on the tests. The child's ethnic background and social class also influenced test results. The authors stated that at an MeHg exposure of 13 to 15 ppm in maternal hair (corresponding to peak hair mercury values of about 20–25 ppm) the child's performance on the tests started to decline. This level of exposure was similar to the one found in the Iraq dose-response relationship. Children with questionable or abnormal scores on the DDST at 4 years of age tended to have lower scores on psychologic testing at 6 years of age. However, differences among ethnic groups and the small sample size make the results from New Zealand difficult to interpret.

During the Seychelles pilot study, children were given the MSCA and the Preschool Language Scale (PLS) at approximately 66 months of age (17). On analysis an association was found between prenatal MeHg exposure and four of the seven end points from these tests. The General Cognitive Index and Perceptual Performance scales from the MSCA, and the Total Language and Auditory Comprehension scores from the PLS showed an association. The significance of three associations was dependent on statistical outliers and influential points, and only Auditory Comprehension from the PLS was associated when these were removed.

During the 6.5-month enrollment of the main cohort in Seychelles, children were tested for visual novelty preference using the Fagan procedure (17). Deficits in novelty preference had previously been noted with increasing prenatal MeHg exposure in experimental animals (47,48). During the 19- and 29-month evaluations, the Bayley Scales of Infant Development (BSID) were administered (19). At 66 months of age, children were tested using the MSCA and the Bender Visual Gestalt Test (Bender). Through 29 months of age, no association between prenatal MeHg exposure and visual recognition memory or the Mental or the Psychomotor scale from the BSID was found. The results of the 66-month testing have not been published in detail, but analyses have been completed and no negative correlation with prenatal MeHg exposure was found (49).

### Educational and Academic Achievement Testing

In New Zealand and the Seychelles, educational testing was included in the test battery. In New Zealand at 6 years of age, the children were given three tests of academic attainment that examined the

components of reading, word recognition, and number concepts (11). The tests used were the Clay Diagnostic Survey, the Burt Word Recognition Test, and the Key Math Diagnostic Arithmetic Test. No association between scores on these outcomes and prenatal MeHg exposure was reported.

In the Seychelles, during both the pilot and main studies, the children were given the Woodcock-Johnson Test of Achievement when they were 66 months of age (17,49). This test examines acquisition of language and numerical concepts. No association with MeHg was found.

### Behavioral and Neurobehavioral Testing

In New Zealand, the Faroe Islands, and the Seychelles, specific behavioral testing was conducted. In New Zealand at 6 years of age, the children were given the Everts Behavior Rating Scale (11). This test was widely used at the time in New Zealand and was completed by the child's teacher. No statistically significant differences were found between scores on this test and prenatal MeHg exposure. However, children with higher MeHg exposure generally had a higher proportion of low scores, especially for adaptability and task application.

During the Seychelles main study, six items from the Infant Behavior Scale of the BSID were recorded during the 29-month evaluation (19). On one item the tester rated the activity level of the child during the examination. Activity level scores showed an inverse association with prenatal MeHg exposure. Changes in activity were only present in males. The interpretation of this finding was unclear. When the main cohort children were 66 months of age, each parent or caregiver completed the Child Behavior Checklist. This test measures a number of social and functional behaviors; no association with exposure was present (49).

In the Faroe Islands the Nonverbal Analogue Profile of Mood States was administered during the 7-year evaluation (14). This test measures a child's ability to recognize different moods. No association with MeHg exposure was found.

### Neuropsychologic Testing

In the Faroe Islands and the Seychelles, neuropsychologic tests were administered to the children. Neuropsychologic tests measure specific cognitive functions such as short- or long-term memory, attention, etc. Some tests, such as the MSCA, can provide both overall cognitive assessment

and neuropsychologic information about specific cognitive functions. Neuropsychologic testing refers mainly to how one interprets test results, and subscales from the MSCA provide insight into specific cognitive strategies. Neuropsychologic testing can begin at about 3 years of age, but is most reliably assessed after 5 years of age.

In the Faroe Islands a variety of neuropsychologic tests were included in the evaluations (14). From the WISC-R, the digit span, similarities, and block designs were given. The Bender, Boston Naming Test (BNT), and California Verbal Learning Test (CVLT) were also administered. The authors reported inverse associations between prenatal MeHg exposure (measured in cord blood) and test components from the WISC-R, Bender, BNT, and CVLT. When maternal hair mercury levels during pregnancy were used as the exposure index, no associations with outcomes were significant.

### Discussion

The dose-response analysis from Iraq predicted that prenatal MeHg exposures in the range achieved by regular consumption of fish might affect fetal neurodevelopment. That dose-response analysis was based on delays in developmental milestones and abnormalities on the neurologic examination. Longitudinal studies in both the Faroe Islands and the Seychelles have reported that developmental milestones in their populations are advanced (20,44). Both cohorts exhibited precocious motor development.

Poisoning by MeHg can delay developmental milestones, but exposure to lower doses may be offset by other factors. Grandjean and colleagues (44) proposed that breastfeeding might confer benefits that counteract any deleterious effects of MeHg exposure. At lower doses other dietary constituents such as selenium may also affect the toxicity of MeHg (50). Alternatively, the exposure levels achieved by consuming fish may have no effect on developmental milestones.

Test batteries have become increasingly more sophisticated in efforts to identify adverse effects. Reports from the Faroe Islands indicate that neurobehavioral, neuropsychologic, and neurophysiologic tests show associations with prenatal MeHg exposure. These findings are intriguing, but their relevance to other populations is unclear and they have not been replicated. In the Faroe Islands, exposure to MeHg was primarily from consuming whale meat

and blubber, dietary items not commonly consumed in most countries. Whales contain significant amounts of PCBs and other neurotoxins, and the MeHg concentration in their meat is several times that of most fish. Why these associations are present using mercury values from cord blood, but not from maternal hair, is puzzling (14). Mercury values in cord blood provide excellent data on recent exposure, but no information about levels earlier in pregnancy. Whale meat contains about 1.6 ppm MeHg and an equal amount of inorganic mercury (24). A small number of whale meals over a short time period during pregnancy could produce peaks of exposure that were not apparent at the time of delivery.

The Republic of Seychelles appears to provide a more appropriate sentinel population for the United States. The MeHg exposure in the Seychelles is believed to be only from fish consumption, and the fish contains concentrations of MeHg similar to those found commercially in the United States. The Seychellois do not consume sea mammals and PCB levels are low. The exposure to MeHg from fish in the Seychelles is similar to that of U.S. consumers. However, the average Seychellois consumes fish at 12 meals each week (51), and mercury concentrations in maternal hair are 10 to 20 times those of the U.S. population (49). The main Seychelles study has found no adverse associations with this degree of MeHg exposure from fish through 66 months of age.

### Conclusions

Current evidence does not support the hypothesis that consumption of even large amounts of fish during pregnancy places the fetus at neurodevelopmental risk from MeHg exposure. Moreover, fish is an important nutritional source in many parts of the world. It provides important components for brain development such as calories, omega-3 fatty acids, and antioxidants such as selenium and vitamin E (50). Wheatley and Paradis (52) have also pointed out the importance of the environment and traditional lifestyles such as fishing to the social, cultural, and economic well-being of indigenous people in Canada. In addition, there is a growing body of evidence that fish consumption has cardiovascular protective benefits for adults (53,54). Concern about fetal exposure to MeHg from fish should be tempered by its importance to brain development and other benefits.

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