Prenatal Exposure of the Northern Québec Inuit Infants to Environmental Contaminants

Gina Muckle, Pierre Ayotte, Éric Dewailly, Sandra W. Jacobson, and Joseph L. Jacobson

1Department of Social and Preventive Medicine, Laval University and Public Health Research Unit, CHUQ Research Center (CHUL), 2Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan, USA; 3Department of Psychology, Wayne State University School of Medicine, Detroit, Michigan, USA

Mercury is a heavy metal that enters the environment from both natural and anthropogenic sources. A natural element in the earth’s crust, Hg is converted by bacteria to methylmercury (MeHg) in lakes and oceans and bioaccumulates in the marine food web. Hg is also released into the environment through human activities, mainly burning of fossil fuels and waste incineration. Polychlorinated biphenyls (PCBs) and chlorinated pesticides are organochlorine and methylmercury concentrations may make it easier to identify the specific developmental deficits attributable to each toxicant. Similarly, the weak correlations noted between environmental contaminants and nutrients will facilitate the documentation of possible protective effects afforded by either n-3 PUFA or selenium against neurotoxic contaminants.

Key words: Canada, chlorinated pesticides, environmental contaminants, human exposure, Inuit, lead, mercury, polychlorinated biphenyls, polyunsaturated fatty acids, selenium.

The developmental neurotoxicity of MeHg first became evident during the 1950s at Minamata Bay, Japan, which was heavily contaminated with Hg from industrial effluent entering the bay. A second well-documented MeHg poisoning occurred in Iraq in the 1970s when seed grain contaminated with a MeHg fungicide was used to make homemade bread (10). The neurodevelopmental effects seen in children exposed in utero in both Japan and Iraq included severe sensory and central nervous system impairments (11,12). Three well-designed, prospective, longitudinal studies that examined the effects of prenatal exposure to lower doses of MeHg on childhood cognitive function were performed in New Zealand, Faroe Islands, and Seychelles Islands (13–17). In the Faroe Islands study, MeHg exposure was found to be related to poorer performance in the domains of fine motor function, attention, language, visual–spatial abilities, and verbal memory (15,18). Although no adverse effects were found in the Seychelles study (16,19,20), the New Zealand study, which was similar in exposure and research design, found...
poorer performance in domains similar to those observed in the Faroe study (13,14).

The developmental toxicity of heat-degraded PCBs was first recognized in Japan in the late 1960s and in Taiwan in the late 1970s. In both countries, infants born to women who had consumed rice oil contaminated with mixtures of PCBs and polychlorinated dibenzo-p-dioxins (PCDDs) exhibited skin rashes and poorer intellectual functioning during infancy and childhood (21,22). The effects of prenatal exposure to background levels of PCBs and other OCs from environmental sources have been studied since the 1980s in prospective longitudinal studies. In Michigan, prenatal PCB exposure was associated with poorer visual recognition memory in infancy (23–25), an effect recently confirmed in the Oswego study (26). In North Carolina, deficits in psychomotor development were seen in the most highly exposed children through 24 months of age (27,28). In Michigan, prenatal PCB exposure was linked to poorer intellectual function at 4 and at 11 years (24,29), a finding confirmed at 42 months in the Netherlands (30).

Low levels of postnatal lead exposure have been linked to poor childhood cognitive performance in several studies (31,32). Although prenatal lead exposure at background levels is associated with adverse effects on cognitive function during infancy, these effects have generally been transient and are no longer evident during childhood (33).

Neurotoxic effects of MeHg might be attenuated by protective effects of nutrients such as selenium, and adverse effects from OCs might be attenuated by a high intake of N-3 polyunsaturated fatty acids (n-3 PUFA). Increased intake of Se and n-3 PUFA would be expected in a population who consume relatively large quantities of fish and marine mammals. Although the effects of Se on MeHg toxicity have not been well documented in humans, there is evidence from over 40 animal studies that Se can influence the deposition of Hg in the body and protect against its toxicity (34). n-3 PUFA, especially DHA, are essential for brain development (35). DHA deficiency impairs learning and memory in rats (36), and rodents and non-human primates fed diets severely deficient in n-3 PUFA show altered visual function and behavioral problems (37). Supplementation of n-3 PUFA can enhance visual acuity and brain development in preterm human infants (38,39), although it is not clear whether increased levels of these nutrients can benefit full-term infants (40). Therefore, n-3 PUFA may protect against neurotoxicity associated with prenatal exposure to environmental contaminants.

We are currently conducting a prospective longitudinal study to examine the effects of pre- and postnatal exposure to OCs and MeHg on cognitive and behavioral development in a sample of Inuit infants in northern Quebec (Nunavik). Whereas Dewailly et al. (6,7) examined contaminant exposure in Nunavik Inuit adults, here we focus specifically on levels of exposure in infants during the period of development when humans appear to be most vulnerable. We report on the concentrations of OCs, Hg, and lead in biological samples from our Nunavik cohort of mothers and newborns and compare their levels with those found in other developmental studies. In addition, we examine the degree to which exposure to neurotoxins tends to be elevated in the same individuals. Finally, in view of the unique source of exposure to OCs and heavy metals in this population (marine food web), we document circulating levels of Se and n-3 PUFA, which may afford protection against exposure to neurotoxins.

Materials and Methods

Population. Pregnant Inuit women from Nunavik were invited to participate in a study focusing on infant health and development. The Nunavik region is located north of the 55th parallel, about 1,500 km from Montreal and 2,000 km from the Great Lakes in the United States (Figure 1). About 7,660 Inuit live in 14 villages scattered along a 2,000-km seashore line along Hudson Bay, Hudson Strait, and Ungava Bay. The study participants were living in Puvirnituq (50%), Inukjuak (37%), and Kuujjuarapik (13%), the three largest communities on the Hudson Bay coast.

Procedures and variables. From November 1995 to March 2001, a midwife or nurse in each of three targeted communities gave our research assistant the name of each pregnant woman shortly after her first prenatal visit. Our research assistant then contacted the potential participant by telephone and invited her to meet at the community nursing station to learn about the study’s objectives and procedures. Women without telephones (24% of the sample) were contacted by an announcement on the community’s FM radio station asking them to contact our research assistant. A detailed informed consent was obtained from each participating mother. The research procedures were approved by the human subjects committees of Laval University and Wayne State University. Interviews were conducted in the community’s nursing station at mid-pregnancy and at 1, 6, and 11 months post-partum by trained research assistants to assess the mothers’ socioeconomic and personal characteristics. Among the 333 Nunavik women invited to participate in this study through April 2000, 13.5% were excluded because a newborn from the same mother had been previously recruited. 2.4% could not be contacted by our research assistants, and 18.5% refused to participate. Among the women interviewed prenatally, 4.5% were subsequently excluded for miscarriage or perinatal or postnatal mortality; 5.6% for failure to obtain the biological samples needed to document maternal PCB and Hg body burden; 3.4% for relocation to another village; and 2.8% for the adoption of the newborn by residents of another village; 3% chose to withdraw from the study.

A 30-mL blood sample was obtained from the umbilical cord after it was severed. A 12.5-mL blood sample was obtained from each participating mother at delivery or within a few weeks thereafter [median = 6 days; interquartile range (IQR) = 0–6.6 weeks]. Two 5-mm diameter hair samples were collected from the mother, one at the prenatal interview (median = 21 weeks of pregnancy; IQR = 17–28 weeks) and one at the 1-month postnatal interview (median = 35 days; IQR = 17–59 days). A 10-mL milk sample was collected from breast-feeding mothers at the 1-month postnatal interview (median = 35 days; IQR = 17–59 days). PCB congener and chlorinated pesticide concentrations were measured in cord and maternal plasma and breast milk. Hg concentrations were determined in cord and maternal whole blood, as well as in the hair sample collected postnatally, which was cut into three segments of 3 cm in length, with each segment corresponding to a trimester of pregnancy. The hair samples were long enough to represent the whole pregnancy (≥ 9 cm) for all participants except one for whom the sample collected prenatally was used in addition to the postnatal sample. Lead concentrations were measured in cord
blood, Se concentrations in cord and maternal blood, and n-3-PUFA in cord plasma.

**Laboratory procedures.** Analyses of OCs, Hg, lead, and Se were performed at the laboratory of the Centre de Toxicologie du Québec, which is accredited by the Canadian Association for Environmental Analytical Laboratories. Blood samples containing EDTA as the anticoagulant were centrifuged and the plasma was collected in glass vials prewashed with hexane. Plasma samples were stored at −80°C until analysis. A 1:1.3 mixture of ammonium sulfate:ethanol:hexane was first added to the plasma to extract OCs. The extracts were then concentrated and purified on two Florisil columns (60–100 mesh; Fisher Scientific, Nepean, Ontario, Canada). The 14 most prevalent PCB congeners (IUPAC nos. 28, 52, 99, 101, 105, 118, 128, 138, 156, 170, 180, 183, and 187) and 11 chlorinated pesticides or their metabolites [aldrin, α-chlordane, γ-chlordane, p,p′-dichlorodiphenyldichloroethane (DDE), hexachlorobenzene (HCB), β-hexachlorocyclohexane (HCH), mirex, cis-nonachlor, trans-nonachlor, oxychlordane] were measured with the purified extracts with an HP 5890 high-resolution gas chromatograph equipped with dual-capillary columns (HP Ultra I and Ultra II) and dual Ni-63 electron capture detectors (Hewlett-Packard, Palo Alto, CA, USA). Quality control procedures were described previously (41). Percent recovery ranged from 89% to 100%, and the detection limit was approximately 0.02 µg/L for all compounds. Coefficients of variation (n = 20, different days) ranged from 2.1% to 9.1%. Biases—the difference between the measurement of the concentration of reference material and the concentration found using the analytic method—ranged from −10.9% to 3.8%.

The same OCs were measured in milk samples using a similar procedure. Compounds were initially extracted from milk using a mixture of acetone/hexane, followed by a second extraction with hexane alone. Combined organic phases were washed with deionized water, concentrated, and purified on activated Florisil columns. A mixture of dichloromethane/hexane was used to elute the compounds, which were separated and quantified by HRGC as described above. Detection limits varied from 0.6 to 2.0 µg/kg for the various OCs. We used two certified milk reference materials (CRM 188 and 450) to assess precision and accuracy of the method. Coefficients of variation varied from 10% to 20% and biases from 5% to 15%, depending on the specific organochlorine. Because OCs distribute mainly in body fat, concentrations in plasma and milk samples are reported in micrograms per kilogram of lipids. We measured total cholesterol, free cholesterol, and triglycerides in plasma samples by standard enzymatic procedures, but determined phospholipids according to the enzymatic method of Takayama et al. (42), using a commercial kit (Wako Pure Chemical Industries, Richmond, VA, USA). We estimated the concentration of total plasma lipids according to the formula developed by Phillips et al. (43). We weighed an aliquot of the milk fat extract to determine the concentration of lipids in milk samples.

We determined total mercury concentrations in samples of cord and maternal blood and maternal hair by cold vapor atomic absorption spectrometry. Samples were digested with nitric acid and mercury was reduced by adding anhydrous stannous chloride (SnCl2) and cadmium chloride (CdCl2). Metallic mercury was volatilized and detected by atomic absorption spectrometry (Model 120; Pharmacia, Piscataway, NJ, USA). The detection limit for blood mercury analysis was 1.0 nmol/L. Quality control procedures were described previously (41). Coefficients of variation (n = 50, different days) at levels of 40 and 90 nmol/L (in-house reference materials) were 5% and 5.5%, respectively. Relative biases were 2.4% and −0.4%, respectively. The detection limit for hair mercury analysis was 1 nmol/g. We obtained accuracy and precision data using certified reference material from Health Canada’s hair mercury inter-laboratory comparison program. Coefficients of variation (n = 50, different days) were 4.8% for the 12.3 µg/g reference specimen (CRM 397) (44) and 4.3% for the 4.42 µg/g reference specimen (CRM 13) (45). The relative biases were −2.2% and +1.9%, respectively.

We diluted an aliquot of whole blood with a mixture of nitric acid, ammonium phosphate, and Triton X-100 and analyzed it for lead by graphite furnace atomic absorption with Zeeman background correction (model ZL 4100; Perkin Elmer, Norwalk, CT, USA). The detection limit of the method is 50 nmol/L. We used four reference specimens of 2.8, 2.1, 1.2, and 0.3 nmol/L to calibrate the analytic method for lead; the corresponding coefficients of variation were 2.4%, 2.9%, 2.3%, and 5.0%, and relative biases were +2.0%, +2.2%, −0.8%, and −0.2%, respectively (n = 10).

We determined blood Se concentrations with inductively coupled plasma mass spectrometry (ICP-MS) using state-of-the-art instrumentation (PE Elan 6000; Perkin Elmer). Samples were diluted and aspirated into the instrument. We performed matrix-matched calibration using a pool of normal blood. We obtained accuracy and precision data using reference material from our ICP-MS comparison program. The detection limit was 0.1 µmol/L. The coefficient of variation (n = 37, different days) at a level of 2.7 µmol/L was 5.9%, and the bias was −0.4%.

The fatty acid composition of plasma phospholipids was determined by the Lipid Analytical Laboratory at the University of Guelph (B.J. Holub). A 200-µL aliquot of plasma was extracted following the addition of chloroform:methanol (2:1, v/v), in the presence of a known amount of internal standard (diheptadecanoyl phospholipid).

**Table 1. Characteristics of participants.**

| Characteristics | Total no. | Mean | SD | Range | No. Percent |
|-----------------|-----------|------|----|-------|-------------|
| Marital status (% single) | 175 | 53 | 30.3 |
| Age | 175 | 24.6 | 5.67 | 14.1–40.7 |
| Education | 175 | 8.8 | 1.62 | 6.0–14.0 |
| Marital status (% single) | 175 | 53 | 30.3 |
| Socioeconomic status | 172 | 25.6 | 10.39 | 8.0–50.0 |
| Unskilled laborers | 55 | 32.0 |
| Semiskilled workers | 51 | 29.7 |
| Skilled craftsmen, clerical, and sales | 52 | 30.2 |
| Technical, small business | 14 | 8.1 |
| Language of interview | 175 | 121 | 68.2 |
| English | 23 | 13.1 |
| Inuktitut | 31 | 17.7 |
| Breast-feeding status (% breast-fed) | 146 | 140 | 95.9 |

*Hollingshead Index (46) for the mother and her partner or, if she was not self-supporting, for her primary source of support (usually her parents). *Among nonadopted infants.

**Table 2. Concentrations of mercury in blood and hair.**

| Mercury concentrations | No. | Arithmetic mean | Geometric mean | SD | Range | IQR |
|------------------------|-----|-----------------|----------------|----|-------|-----|
| Cord blood (µg/L) | 95 | 22.7 | 18.5 | 0.4 | 2.8–97.0 | 12.0–27.2 |
| Maternal blood (µg/L) | 130 | 12.6 | 10.4 | 0.4 | 2.6–44.2 | 6.6–17.0 |
| Maternal hair (µg/g) | 123 | 4.5 | 3.7 | 1.9 | 0.3–14.0 | 2.5–6.2 |
| Maternal hair, first trimester (µg/g) | 124 | 4.6 | 3.6 | 2.1 | 0.4–16.3 | 2.3–6.6 |
| Maternal hair, second trimester (µg/g) | 125 | 4.4 | 3.7 | 1.9 | 0.3–12.8 | 2.4–6.0 |

*Average of concentrations found at first, second, and third trimesters of pregnancy.
Total phospholipids were isolated from the lipid extract by thin-layer chromatography using heptane:isopropyl ether:acetic acid (60:40:3, v/v/v) as the developing solvent. After transmethylolation using BF3/methanol, the fatty acid profile was determined by capillary gas-liquid chromatography. Fatty acid concentrations in plasma phospholipids were expressed as percentages of the total area of all fatty acids peaks from C14:0 to C24:1 (percent weight).

Results

Sample sociodemographic characteristics are summarized in Table 1. A large proportion of women were single, 15% were younger than 18 years, and 5% were older than 35. Only 17% of participants had obtained their high-school diploma. Twenty-three percent of the participating women were primiparous, and 32% had already delivered three or more children. Most of the interviews were conducted in English. Most women (90%) smoked during pregnancy (data not shown). Descriptive statistics for the blood and hair Hg analyses are presented in Table 2. The average Hg concentration is 1.8 times higher in cord blood than in maternal blood, and the average hair Hg concentrations are similar during all three trimesters of pregnancy. The intercorrelations among blood and hair Hg concentrations are presented in Table 3. The cord blood–maternal blood correlation is very high, and even a little higher when only maternal blood samples collected within 1 month of delivery are considered (n = 51, r = 0.93). Cord blood Hg concentrations are moderately related to maternal hair Hg concentrations. Given that the cord blood Hg concentration primarily reflect recent exposure, it is not surprising that the cord blood Hg concentrations are more strongly related to third-trimester hair Hg concentrations than to those measured in samples corresponding to earlier trimesters. Cord blood lead concentrations average 0.2 µmol/L, which corresponds to 41.4 µg/L (n = 95, geometric mean = 0.2 µmol/L, geometric standard deviation (SD) = 2.0, range = 0.0-0.9, IQR = 0.1-0.3 [data not shown]).

Tables 4, 5, and 6 show the descriptive statistics for the 14 PCB congeners and 11 chlorinated pesticides in cord plasma, maternal plasma, and breast milk. The most prevalent congeners in all three media are 153, 138, and 180. These three congeners represent about 66% of the total concentration of the 14 PCB congeners in all three media. The next most prevalent congeners are 99, 118, 170, and 187, and the least prevalent are 52, 101, 105, 156, 183, and 187. The intercorrelations among congeners detected in at least 70% of cord plasma and breast milk samples are presented in Table 7. These intercorrelations are very high in cord plasma, ranging from 0.71 to 0.98 (median r = 0.90). The intercorrelations in maternal plasma are similar (median r = 0.90; range = 0.62–0.99 [data not shown]). The magnitude of the intercorrelations among the seven congeners that are readily detected in cord and maternal plasma is similar in breast milk, but the intercorrelations with the lowest chlorinated congeners (52, 101, and 105) are somewhat weaker. On the basis of these data, it seems reasonable to use PCB congener 153, the most prevalent congener, as a marker for exposure to the environmental PCB mixture in the Arctic.

The predominant chlorinated pesticides are p,p'-DDE, HCB, oxychlordane, and trans-nonachlor (Tables 4, 5, and 6). The pesticide p,p'-DDT, which is much less persistent than its main metabolite, p,p'-DDE, constitutes a very small proportion (< 8%) of the total DDT (p,p'-DDT + p,p'-DDE) concentrations in biologic samples. The intercorrelations among the chlorinated pesticides detected in at least 70% of samples are presented in Table 8 for the cord plasma and breast milk samples. These intercorrelations are strong in both cord plasma (median r = 0.76) and breast milk (median r = 0.79). The chlorinated pesticides measured in both media are strongly associated with PCB congener 153, except for p,p'-DDE where the association is moderate, presumably because the p,p'-DDT concentration is low, close to the detection limit, and is more transitory and more specifically reflective of recent exposure.

PCB and chlorinated pesticide concentrations are lowest in cord plasma and highest in breast milk. For example, the average cord plasma concentration of congener 153 is 84.4% of its average concentration in maternal plasma, and its average concentration in maternal plasma is 83.6% of that in breast milk. Although concentrations differed among the three media, correlations...
among PCB congener 153 concentrations in cord plasma, maternal plasma, and breast milk are very high (cord plasma—maternal plasma, $r = 0.93$; cord plasma–breast milk, $r = 0.91$; maternal plasma–breast milk, $r = 0.95$). The strength of these associations does not change when the same Pearson correlation analyses are performed using only the maternal plasma samples collected within 1 month after delivery (data not shown).

The intercorrelations between PCB congener 153 and Hg are modest: cord PCB–cord Hg, $r = 0.24$; cord PCB–average hair Hg, $r = 0.34$; maternal PCB–average hair Hg, $r = 0.17$. The associations between concentrations of lead and Hg in cord blood are also low (0.21–0.29). The intercorrelations between cord blood lead and OC concentrations are even weaker, whether OCs are also low (0.21–0.29). The intercorrelations among the environmental contaminants, Se and DHA are presented in Table 10. When compared with cohorts with relatively high exposure, the Hg exposure in Nunavik Inuit is lower. Because the intercorrelation between cord Hg and cord OC concentrations is low in the Nunavik cohort, it

Table 5. Descriptive statistics for PCB congeners and chlorinated pesticides concentrations detected in at least 70% of maternal plasma samples ($n = 159$).

| PCBs (µg/kg) | Percent detected | Arithmetic mean | Geometric mean | SD | Range | IQR | Total PCBs |
|-------------|------------------|-----------------|----------------|----|-------|-----|------------|
| Congener 28 | 17.6             | 24.4            | 19.1           | 2.0| 3.3–124.8 | 6.1 |
| Congener 52 | 56.6             |                 |                |    |        |     |            |
| Congener 99 | 100              | 24.4            | 19.1           | 2.0| 3.3–124.8 | 6.1 |
| Congener 101| 82.3             |                 |                |    |        |     |            |
| Congener 105| 74.2             | 4.4             | 3.4            | 2.0| 0.95–25.8 | 1.1 |
| Congener 118| 98.7             | 18.1            | 14.3           | 2.0| 1.3–100.9 | 4.7 |
| Congener 128| 15.1             |                 |                |    |        |     |            |
| Congener 138| 100              | 73.8            | 57.8           | 2.0| 10.2–387.1 | 18.6 |
| Congener 153| 100              | 137.4           | 105.3          | 2.1| 18.9–709.0 | 34.6 |
| Congener 156| 93.7             | 8.5             | 6.4            | 2.1| 1.1–44.6  | 2.1 |
| Congener 170| 99.4             | 23.3            | 18.9           | 2.2| 1.3–148.3 | 5.9 |
| Congener 183| 96.9             | 9.4             | 7.4            | 2.0| 1.3–44.8  | 2.4 |
| Congener 187| 100              | 26.6            | 21.3           | 1.9| 3.3–127.8 | 6.7 |
| Σ 14 congeners$^a$ | 397.3 | 313.2 | 2.0 | 71.3–1951.3 | 197.9–489.2 |

Table 6. Descriptive statistics for PCB congeners and chlorinated pesticides concentrations detected in at least 70% of breast milk samples ($n = 116$).

| PCBs (µg/kg) | Percent detected | Arithmetic mean | Geometric mean | SD | Range | IQR | Total PCBs |
|-------------|------------------|-----------------|----------------|----|-------|-----|------------|
| Congener 28 | 41.0             |                 |                |    |       |     |            |
| Congener 52 | 83.8             | 7.1             | 4.2            | 3.0| 0.4–45.1 | 1.5 |
| Congener 99 | 98.3             | 35.5            | 27.4           | 2.1| 2.7–166.8 | 7.5 |
| Congener 101| 88.9             | 6.4             | 4.3            | 2.6| 0.3–38.2 | 1.3 |
| Congener 105| 85.5             | 4.9             | 3.2            | 2.5| 0.3–42.6 | 1.0 |
| Congener 118| 100              | 23.1            | 18.6           | 1.9| 3.7–108.1 | 4.9 |
| Congener 128| 56.4             |                 |                |    |       |     |            |
| Congener 138| 99.1             | 96.7            | 78.2           | 1.9| 14.0–408.9 | 20.4 |
| Congener 153| 100              | 164.4           | 131.6          | 1.9| 21.7–727.9 | 34.6 |
| Congener 156| 92.3             | 12.0            | 8.3            | 2.6| 0.3–53.5 | 2.5 |
| Congener 170| 97.4             | 25.3            | 18.5           | 2.3| 10.0–100.3 | 5.3 |
| Congener 180| 99.1             | 61.1            | 48.0           | 2.0| 10.5–214.2 | 12.9 |
| Congener 183| 99.1             | 10.9            | 8.8            | 1.9| 1.7–43.8  | 13.6 |
| Congener 187| 100              | 30.7            | 25.6           | 1.8| 6.2–97.8  | 6.5 |
| Σ 14 congeners$^a$ | 474.5 | 385.9 | 1.9 | 75.7–1915.8 | 253.7–579.4 |

Discussion

These data confirm that prenatal exposure to Hg among the Inuit of Nunavik is higher than that observed in general population samples in Canada and the United States ($47,48$). Hg concentrations reported in other cohorts are presented in Table 10. When compared with cohorts with relatively high concentrations that were selected to examine the neurobehavioral effects of prenatal Hg exposure, the Hg exposure in Nunavik Inuit is similar to that observed in the Faroe Islands first and second cohorts ($18,48$), slightly lower than in the Seychelles Islands cohorts ($17,20$), and substantially lower than in the highest exposed group in the New Zealand study ($14$). Hg exposure in the Inuit is also markedly lower than in another northern Québec aboriginal population, the Cree, in 1977–1978, but slightly higher than the average concentration observed in the same population more recently in 1992 ($49,50$). Compared with Greenlandic Inuit from the Disko Bay region ($9$), the Nunavik Hg exposure is lower. Because the intercorrelation between cord Hg and cord OC concentrations is low in the Nunavik cohort, it

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$^a$ Sum of all 14 congeners including congeners not detected in at least 70% of samples.
should be possible to identify the specific deficits attributable to each of these environmental contaminants in this cohort.

The intercorrelations among the Hg measures reflecting the third-trimester exposure—the cord blood, maternal blood, and maternal third-trimester hair Hg concentrations—are high, suggesting that all three measures provide reliable assessments of third-trimester fetal exposure. A similar high cord–maternal blood intercorrelation was recently reported for the Greenlandic Inuit (5). The cord and maternal blood Hg measures are less strongly related to the first- and second-trimester hair Hg values. Hair Hg is approximately 90% MeHg, the most toxic form of Hg, and has the advantage of providing a historical record of MeHg exposure (3,4). These data suggest that potential neuropsychological deficits caused by the impact of Hg on third-trimester brain development may be detected more easily using analyses examining the developmental effects of prenatal OCs and Hg exposure.

Selenium is widely distributed in the environment, and exists naturally in the form of selenide, elemental Se, selenite, and selenate. Most Se compounds are water soluble. Data on Se in fish and marine mammals are available, especially for specimens collected in the Arctic regions (5). The average whole cord blood concentration found in this study is 50% higher than that observed in southern Quebec between 1993 and 1998 (arithmetic mean = 2.4 µmol/L, geometric mean = 2.3 µmol/L, range = 1.3–4.3, n = 178) (55). It is 1.7 times higher than those found in the cohorts of marine mammal consumers from the Faroe Islands (48,56). These data indicate that we should be able to test hypotheses regarding protective effects of Se on neurodevelopmental end points because we observed elevated levels of this

Table 7. Intercorrelations among PCB congeners detected in at least 70% of cord blood and breast milk samples.

| PCB congeners (µg/kg) | PCB 99 | PCB 101 | PCB 105 | PCB 118 | PCB 119 | PCB 138 | PCB 153 | PCB 156 | PCB 170 | PCB 180 | PCB 183 | PCB 187 |
|----------------------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Cord blood (n = 98)  |        |         |         |         |         |         |         |         |         |         |         |         |
| PCB 99               | 0.91*  | 0.92*   | 0.90*   | 0.76*   | 0.81*   | 0.82*   |         |         |         |         |         |         |
| PCB 118              | 0.90*  | 0.98*   |         | 0.71*   | 0.76*   | 0.80*   |         |         |         |         |         |         |
| PCB 138              | 0.98*  |         |         | 0.89*   | 0.93*   | 0.95*   |         |         |         |         |         |         |
| PCB 153              | 0.91*  | 0.94*   |         | 0.93*   |         |         |         |         |         |         |         |         |
| PCB 170              | 0.96*  |         |         |         |         |         |         |         |         |         |         |         |
| PCB 180              |         |         |         |         |         |         |         |         |         |         |         |         |
| PCB 187              |         |         |         |         |         |         |         |         |         |         |         |         |
| Breast milk (n = 116)|        |         |         |         |         |         |         |         |         |         |         |         |
| PCB 52               | 0.59*  | 0.68*   | 0.51*   | 0.53*   | 0.51*   | 0.52*   | 0.42*   | 0.43*   | 0.41*   | 0.54*   | 0.47*   |         |
| PCB 99               | 0.64*  | 0.75*   | 0.49*   | 0.61*   | 0.75*   | 0.70*   | 0.84*   | 0.77*   | 0.87*   | 0.79*   |         |         |
| PCB 101              | 0.61*  | 0.57*   | 0.51*   | 0.49*   | 0.75*   | 0.70*   | 0.73*   | 0.83*   | 0.63*   | 0.53*   | 0.46*   |         |
| PCB 118              | 0.86*  | 0.68*   | 0.68*   | 0.37*   | 0.55*   | 0.52*   | 0.88*   | 0.86*   | 0.54*   | 0.70*   | 0.57*   |         |
| PCB 138              | 0.87*  | 0.93*   | 0.79*   | 0.93*   | 0.93*   | 0.95*   | 0.96*   | 0.93*   | 0.93*   | 0.93*   | 0.93*   |         |
| PCB 155              | 0.78*  | 0.91*   | 0.61*   | 0.71*   | 0.73*   | 0.86*   | 0.80*   | 0.62*   | 0.66*   | 0.58*   | 0.57*   |         |
| PCB 156              | 0.86*  | 0.83*   | 0.74*   | 0.74*   | 0.94*   | 0.83*   | 0.80*   | 0.74*   | 0.74*   | 0.74*   | 0.74*   |         |
| PCB 170              | 0.94*  | 0.86*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   | 0.87*   |         |
| PCB 180              | 0.92*  | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   | 0.94*   |         |
| PCB 183              | 0.96*  |         |         |         |         |         |         |         |         |         |         |         |
| PCB 187              |         |         |         |         |         |         |         |         |         |         |         |         |

Values shown are Pearson r. *p < 0.000.

Table 8. Intercorrelations among chlorinated pesticides and PCBs detected in at least 70% of cord plasma and breast milk samples.

| Pesticides (µg/kg) | β-HCH | cis-Nonachlor | p,p′-DDE | p,p′-DDT | Mirex | HBC | Oxychlorodane | trans-Nonachlor | PCB 153 |
|-------------------|-------|---------------|----------|----------|-------|-----|----------------|-----------------|---------|
| Cord blood (n = 98)|       |               |          |          |       |     |               |                 |         |
| cis-Nonachlor      | 0.73* | 0.73*         | 0.76*    | 0.69*    | 0.83* | 0.65*|               |                 |         |
| p,p′-DDE           | 0.71* |               | 0.76*    | 0.79*    | 0.86* | 0.89*|               |                 |         |
| p,p′-DDT           |       |               |          |          | 0.56* | 0.71*| 0.55*          |                 |         |
| HCB                |       |               |          |          | 0.79* |     |               | 0.98*           | 0.72*   |
| Oxychlorodane      |       |               |          |          | 0.79* |     |               |                 |         |
| trans-Nonachlor     |       |               |          |          | 0.91* |     |               |                 | 0.87*   |         |
| Breast milk (n = 116)| 0.74* | 0.85*         | 0.65*    | 0.45*    | 0.78* | 0.82*|               |                 |         |
| cis-Nonachlor      | 0.82* |               | 0.79*    | 0.55*    | 0.90* | 0.86*|               |                 |         |
| p,p′-DDE           | 0.81* |               | 0.76*    | 0.85*    | 0.89* | 0.88*|               |                 |         |
| p,p′-DDT           | 0.74* |               | 0.70*    | 0.76*    | 0.63* |     |               |                 |         |
| Mirex              |       |               | 0.54*    | 0.62*    | 0.62* | 0.79*|               |                 |         |
| HCB                |       |               | 0.86*    | 0.91*    | 0.95* | 0.86*|               |                 |         |
| Oxychlorodane      |       |               | 0.95*    | 0.86*    | 0.80* |     |               |                 |         |
| trans-Nonachlor     |       |               | 0.95*    | 0.86*    | 0.80* |     |               |                 |         |

Values shown are Pearson r. *p < 0.000.
antineurotoxic and only moderate intercorrelations with Hg. The strength of the cord Se–cord Hg association observed in the Nunavik cohort underscores the importance of measuring and controlling Se in further analysis examining the developmental effects of Hg. A significant but somewhat weaker cord Se–cord Hg association ($r = 0.35$) was observed in the Faroe Islands cohort by Grandjean et al. (56).

With regard to OC exposure, it is difficult to compare the data in the present study with those from early PCB neurobehavioral studies conducted in Michigan (29) and North Carolina (57), which used packed column gas chromatography for OC determination. In Table 11, OC concentrations observed in the present sample are compared with those from the general Canadian and American populations and with more recent cohort studies using contemporary analytic methods for PCB determination (congener specific analysis). For each comparison, we recalculated the Nunavik OC concentrations according to the method used in the comparison study. For example, to compare our data with those of the Faroe cohort, where total PCB exposure was calculated as two times the sum of congeners 138, 153, and 180, we performed a similar calculation using the Nunavik data. Comparison of breast milk and cord plasma PCB and pesticides concentrations show that the prenatal OC exposure among the Nunavik Inuit is two to three times higher than that observed in general populations in southern Quebec and in New Bedford, Massachusetts (58–60). PCB concentrations in Nunavik are similar to those found in cord and maternal plasma samples of the Netherlands study (61); the Nunavik breast milk PCB concentrations, however, are somewhat lower. Concentrations of OCs in cord plasma and breast milk samples from Nunavik are about two to three times lower than those found in the groups of marine mammal consumers from the Greenland and Faroe Islands cohorts (9,48). This result suggests that marine mammal consumption may be less frequent in Nunavik women than in those Arctic groups.

PCB concentrations in plasma and milk are highly correlated, but levels in milk are somewhat higher than those in plasma. The difference in PCB accumulation between plasma and breast milk lipids could be caused by a difference in lipid polarity between plasma and milk. Alternatively, this discrepancy may result from differences in the analytic methods used to quantify lipids (gravimetric in milk vs. enzymatic in plasma). The lower concentrations in cord plasma relative to maternal plasma are more difficult to explain because these contaminants are believed to partition between fat compartment on a 1:1 ratio; however, a similar cord–maternal plasma ratio (0.87) has been reported by Bjertnæs and Hansen (9).

OC contaminants are detected more easily in breast milk because it provides a larger quantity of fat for analysis; therefore, we measured certain lower chlorinated congeners that could not be detected in the other two media. However, these low chlorinated congeners constitute a very small proportion (only 4%) of the total PCB body burden as indicated in maternal milk. Similarly, $p,p^\prime$-DDT, which breaks down relatively rapidly in the environment, constitutes a very small proportion (only 4%) of the total DDT body burden ($p,p^\prime$-DDE + $p,p^\prime$-DDE), indicating that the Arctic exposure consists primarily of the more persistent forms of these pesticides. By contrast, half the total DDT (52%) exposure in the Michigan cohort in the early 1980s consisted of $p,p^\prime$-DDE, indicating that the source of that exposure was more recent pesticide use and/or that there was a local source of DDT (62).

The high intercorrelations of PCB congeners 153 with all of the moderate-to-heavyy chlorinated congeners and with most pesticides except $p,p^\prime$-DDT suggest that congener 153 can be considered a marker for exposure to most OCs in the Arctic region. Although several different OC mixtures were introduced into the environment in industrial countries between the 1930s and 1970s, most of the lower chlorinated congeners have biodegraded. These data show that, generally speaking, the mixture of OC contaminants persisting in the Arctic today is quite homogeneous, so much so that it seems unlikely that the neurobehavioral effects associated with

### Table 9. Intercorrelations between contaminants and nutrients.

| Contaminants | Cord blood Se | Cord blood DHA |
|--------------|---------------|---------------|
| Cord blood PCB 153 | 0.19 | 0.27** |
| (µg/kg lipid basis) | (92) | (96) |
| Cord blood mercury | 0.51** | 0.34** |
| (µg/L) | (92) | (93) |
| Hair mercury, averaged | 0.37* | 0.51** |
| (µg/g) | (69) | (72) |
| Hair mercury, third trimester | 0.45** | 0.45** |
| (µg/g) | (70) | (72) |
| Cord blood lead | 0.08 | 0.15 |
| (µg/L) | (92) | (93) |

DHA, docosahexaenoic acid. Values shown are Pearson r values. *Average of the total mercury concentrations found at first, second, and third trimesters of pregnancy. **p ≤ 0.05. ***p ≤ 0.001.

### Table 10. Comparison of mercury concentrations in Nunavik with those observed in other cohorts.

| Cohort | Medium | Years | No. | Geometric mean | Range | IQR |
|--------|--------|-------|-----|----------------|-------|-----|
| Canada | Nunavik Inuit | Cord blood (µg/L) | 1996–2000 | 95 | 18.5 | 2.8–97.0 | 12.0–27.2 |
| &nbsp; &nbsp; | &nbsp; | Maternal blood (µg/L) | | 130 | 10.4 | 2.6–44.2 | 6.6–17.0 |
| &nbsp; &nbsp; | &nbsp; | Maternal hair (µg/g) | | 123 | 3.7 | 0.3–14.0 | 2.5–6.2 |
| Southern Québec (41) | Cord blood (µg/L) | 1993–1995 | 1,108 | 1.0 | 0.9–1.0 |
| James Bay Cree (30) | Women’s hair, not pregnant (µg/g) | 1992 | 70 | 2.5 | Maximum = 19.0 |
| Northern Québec Cree (49) | Maternal hair (µg/g) | 1977–1978 | 215 | 6.0** | 5.2** |
| United States (47) | Women’s hair, not pregnant (µg/g) | 1981 | 1,274 | 0.38* | 0.14–0.90 |
| Faroe Islands | First cohort (18) | Cord blood (µg/L) | 1986–1987 | 894 | 22.9 | 13.4–41.3 |
| &nbsp; | &nbsp; | Maternal hair (µg/g) | | 914 | 4.3 | 2.6–7.7 |
| Second cohort (48) | Cord blood (µg/L) | 1994–1995 | 163 | 20.4 | 1.9–102.0 | 11.8–40.0 |
| Seychelles Island | Maternal hair (µg/g) | 1994–1995 | 160 | 4.1 | 0.4–16.3 | 2.5–7.4 |
| Main study (20) | Maternal hair (µg/g) | 1989–1990 | 740 | 5.9* | 0.25 |
| Pilot study (17) | Maternal hair (µg/g) | 1988–1990 | 789 | 6.9* | 0.6–36.4 |
| New Zealand (14) | Maternal hair (µg/g) | 1978–1984 | 935 | 8.5* | 6.0–86.0 |
| Greenland, Disko Bay (8) | Cord blood (µg/L) | 1994–1996 | 178 | 25.3 | 2.4–181.0 |
| &nbsp; | &nbsp; | Maternal blood (µg/L) | | 180 | 12.8 | 1.3–75.6 |

*The average Hg concentration was reported in nmol/L; this concentration was divided by 5 to convert to µg/L. **95% confidence interval. *Women 15–38 years old. **Arithmetic mean. *SD. A% among seafood consumers. A% among nonseafood consumers. Median. *In the high Hg group.
individual congeners and pesticides can be evaluated in this population. Dietary fish oils are particularly high in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) acid, which are n3-PUFAs. High intake of marine mammals is also associated with Hg concentrations in Nunavik Inuit adults. These data suggest that we will be able to test hypotheses regarding protective effects of n3-PUFA.

The very high OC intercorrelations in the three media assessed in this data set indicate that the measurement of PCB and pesticide concentrations in these specimens are very reliable. These associations are lower on a wet weight basis (data not shown), which may explain the lower maternal plasma–breast milk correlations for individuals with incomplete data. Differences in laboratory procedures and quantification methods. When compared with data from the southern Quebec cohort analyzed in the same laboratory as those from Nunavik, because there are important measurement differences obtained in the present study contrast dramatically with the intercorrelations found in the Netherlands study (61). The very high correlations obtained in this data set indicate that the measurement of PCB and pesticide concentrations in these specimens are very reliable. These associations are lower on a wet weight basis (data not shown), which may explain the lower maternal plasma–breast milk correlations for individuals with incomplete data. Differences in laboratory procedures and quantification methods.

| Table 11. Comparison of OC concentrations in Nunavik with those observed in other cohorts. |
|---------------------------------------------------------------|
| **Comparison cohorts** | **Nunavik cohort (1996–2000)** |
| **Years** | **Comparison cohorts** | **Nunavik cohort (1996–2000)** |
| **Data suggest that we will be able to test hypotheses regarding protective effects of n3-PUFA.** | **Data suggest that we will be able to test hypotheses regarding protective effects of n3-PUFA.** |
| **Individual congeners and pesticides can be evaluated in this population.** | **Individual congeners and pesticides can be evaluated in this population.** |
| **Dietary fish oils are particularly high in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) acid, which are n3-PUFAs.** | **Dietary fish oils are particularly high in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) acid, which are n3-PUFAs.** |
| **High intake of marine mammals is also associated with Hg concentrations in Nunavik Inuit adults.** | **High intake of marine mammals is also associated with Hg concentrations in Nunavik Inuit adults.** |
| **These data suggest that we will be able to test hypotheses regarding protective effects of n3-PUFA.** | **These data suggest that we will be able to test hypotheses regarding protective effects of n3-PUFA.** |
| **The very high OC intercorrelations in the three media assessed in this data set indicate that the measurement of PCB and pesticide concentrations in these specimens are very reliable.** | **The very high OC intercorrelations in the three media assessed in this data set indicate that the measurement of PCB and pesticide concentrations in these specimens are very reliable.** |
| **These associations are lower on a wet weight basis (data not shown), which may explain the lower maternal plasma–breast milk correlations for individuals with incomplete data.** | **These associations are lower on a wet weight basis (data not shown), which may explain the lower maternal plasma–breast milk correlations for individuals with incomplete data.** |
| **Differences in laboratory procedures and quantification methods.** | **Differences in laboratory procedures and quantification methods.** |
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