

Temporal variation of blood and hair mercury levels in pregnancy in relation to fish consumption history in a population living along the St. Lawrence River[☆]

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Abstract

Fish consumption from the Great Lakes and the St. Lawrence River has been decreasing over the last years due to advisories and increased awareness of the presence of several contaminants. Methylmercury (MeHg), a well-established neurotoxicant even at low levels of exposure, bioaccumulates to differing degrees in various fish species and can have serious adverse effects on the development and functioning of the human central nervous system, especially during prenatal exposure. Most studies on MeHg exposure have focussed on high-level consumers from local fish sources, although mercury (Hg) is also present in fresh, frozen, and canned market fish. Moreover, little information exists on the temporal variation of blood and hair Hg in pregnant women, particularly in populations with low levels of Hg. The aim of the present study was to characterize the temporal variation of Hg during pregnancy and to investigate the relation between fish consumption from various sources prior to and during pregnancy and maternal cord blood and mother's hair Hg levels. We recruited 159 pregnant women from Southwest Quebec through two prenatal clinics of the Quebec Public Health System. All women completed two detailed questionnaires concerning their fish consumption (species and frequency) prior to and during pregnancy. The women also provided blood samples for all three trimesters of pregnancy and hair samples after delivery of up to 9 cm in length. Blood and hair Hg levels were analyzed by cold-vapor atomic-absorption and -fluorescence spectrometry methods, respectively. Results showed that maternal blood and hair Hg levels decreased significantly between the second and third trimesters of pregnancy. However, cord blood Hg was significantly higher than maternal blood at birth. Maternal hair was correlated with Hg blood concentration and was highly predictive of the organic fraction in cord blood. A strong dose relation was observed between the frequency of fish consumption before and during pregnancy and Hg exposure in mothers and newborns. Fish consumption prior to and during pregnancy explained 26% and 20% of cord blood Hg variance, respectively. For this population, detailed multivariate analyses showed that during pregnancy market fish (fresh, canned, and frozen) were more important sources of Hg exposure than were fish from the St. Lawrence River. These results should be taken into account for future advisories and intervention strategies, which should consider Hg levels in different species from all sources in order to maximize the nutritional input from fish and minimize the toxic risk.

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1. Introduction

Methylmercury (MeHg) neurotoxicity was well established following the serious poisoning epidemics in Japan and Iraq, in which there were many cases of congenital poisoning involving neurological abnormalities and severe developmental retardation (Marsh et al., 1987; Harada, 1995). Data from these disasters showed

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that infants exposed in utero to MeHg developed marked neurological developmental delays, even when their mothers experienced little or no overt signs of toxicity (Takeuchi, 1977). More recent longitudinal cohort studies have shown that even at much lower levels of in utero MeHg exposure, levels insufficient to produce overt neurological disorders, MeHg bioaccumulated in fish may present important risks for growing children (Grandjean et al., 1992, 1998, 2003), even with the benefits of essential amino acids, vitamins, minerals and trace elements, and omega-3 polyunsaturated fatty acids. The susceptibility of the fetus is believed to be due, in part, to the high vulnerability of developmental processes (i.e., cellular division, differentiation, and migration) to disruption by mercury (Hg) (Choi et al., 1978; Sager et al., 1982; Choi, 1989; Castoldi et al., 2001). In addition, the presence of an incomplete blood–brain barrier, the possible lack of MeHg excretion by the fetus, and the high levels of red blood cells are factors contributing to prenatal MeHg toxicity (Grandjean et al., 1994; Rodier, 1995; Oliveira et al., 2001; Sakamoto et al., 2002).

In 1990, the World Health Organization (WHO) gave a prudent interpretation of the Iraqi data by implying that a 5% risk of developing psychomotor retardation in offspring may be associated with a peak Hg level of 10–20 µg/g in maternal hair. However, a discernible and insidious prenatal effect seems to be present below a limit of 10 µg/g Hg in maternal hair (Grandjean et al., 1997, 2003). Prospective longitudinal studies in the Faroe Islands and in New Zealand found poorer performance in fine motor function and language in relation to prenatal MeHg exposure (Kjellstrom et al., 1986, 1989; Grandjean et al., 1999, 2003). In addition, increased blood pressure (Sorensen et al., 1999) and a slowing of auditory evoked potentials (Murata et al., 1999) were reported in children from the Faroe Islands with prenatal exposure to MeHg. In contrast, no effect on neurological function has been observed with similar prenatal Hg exposure in children from the Seychelles Islands (Davidson et al., 1995, 2001; Myers et al., 2003). Several hypotheses have been put forward to explain these differences, including diet (Grandjean, 1999; Passos et al., 2003).

Epidemiological studies on prenatal MeHg exposure have been carried out on populations with moderate or high fish consumption. However, no study has examined the possible neurofunctional effects of Hg in a general population in which the Hg exposure level is below the US Environmental Protection Agency (EPA) and Health Canada recommendations (1.5 and 6 µg/g in hair, respectively). Furthermore, little information exists on the temporal variation of blood and hair Hg in pregnant women, especially in populations with low levels of Hg exposure. Previous studies carried out on the temporal variation of Hg in hair characterized it

only by trimester of pregnancy or on two sampling times but not monthly (Oskarsson et al., 1994; Cernichiari et al., 1995; Boischio and Cernichiari, 1998; Vahter et al., 2000). Mean concentrations of MeHg in newly grown head hair are directly proportional to concentrations in whole blood (Al-Shahristani et al., 1976). Segmental analysis of hair provides the opportunity to reconstitute past exposure history. Since hair growth rate is approximately 1 cm per month, a segmental analysis of 9 cm collected at the time of delivery generates a temporal profile of maternal Hg exposure for the entire pregnancy and also provides an index of fetal exposure (WHO, 1990; Cernichiari et al., 1995).

The St. Lawrence River system flows northeastward from the North American Great Lakes into the Atlantic Ocean. Upstream of Montréal, the St. Lawrence River widens into two lakes, Lake St. Louis and Lake St. François, where commercial, sport, and subsistence fishing are practiced. There are extensive environmental data available on the contaminants present in the various compartments of the ecosystem of these lakes, including Hg and PCBs (Environment Canada, 1996). From 1984 to 1989, mean concentrations of Hg surpassed the recommended levels for walleye (*Stizostedion vitreum*) and pike (*Exox lucius*) in both of these lakes (Blaney et al., 1996; Duchesne et al., 1996), although recent reports suggest that the levels of Hg may have decreased (Lucotte, unpublished data). A previous study on these upper St. Lawrence River lakes found higher concentrations of MeHg and a diminished capacity for information processing among fish eaters compared to non-fish eaters (Mahaffey and Mergler, 1998; Mergler et al., 1998). A recent report on women of childbearing age from the Montreal area who consumed sport fish frequently or for extended periods revealed blood Hg concentrations approaching levels of concern for fetal protection (Nadon et al., 2002).

Fish consumption studies among populations from the St. Lawrence River Basin have focused solely on local fish-eating habits (Mahaffey and Mergler, 1998; Kosatsky et al., 1999, 2000; Nadon et al., 2002), and little attention has been paid to possible Hg exposure from market sources. Canned tuna, for example, which is consumed to a great degree in many communities, can contain Hg level above the Health Canada recommended level of 0.5 ppm (Morrisette et al., unpublished data); fresh market fish, such as tuna, swordfish, and shark, may also contain high Hg levels (Health Canada, 2002; CFIA, 2002). Overall dietary habits during pregnancy in relation to Hg exposure have never been examined.

The present study sought to examine the following in a sample of pregnant women from a population with low levels of Hg exposure: (i) the temporal variation of Hg during pregnancy; (ii) the relation between different sources of fish (local and market fish) eaten prior to

and during pregnancy and maternal/cord blood and mother's hair Hg levels; and (iii) the relation between these biological indicators.

2. Materials and methods

2.1. Study design

Pregnant women living in the region of St. Lawrence lakes St. François and St. Louis were recruited in collaboration with the prenatal programs of the Local Community Services Centres of the Public Health System in Southwest Québec. Inclusion criteria for recruitment were no history of workplace exposure to toxic chemicals and no history of previous neurological illness. Following acceptance into the study, the women signed a consent form, responded to a questionnaire on socio-demographics and fish-eating habits (sources and frequency), and provided samples of blood prior to the 13th week for those who were recruited in the first trimester and between the 14th and 24th gestational weeks for those who were recruited in the second trimester.

When recruitment took place in the first trimester before the first ultrasound examination, gestational age at sampling was self-reported; it was later corrected a posteriori. Thus, 20 women recruited in the first trimester were initially sampled in the early second trimester (>13 weeks) and had two samples taken during the second trimester. Dated data from the first sample from these women were included in longitudinal analyses only.

For those who gave birth at the regional hospital, maternal and cord blood samples were taken. Two weeks following birth, a second questionnaire on medical and obstetrical history, birth data, smoking drinking, and fish-eating practices during pregnancy was administered. At this time a hair sample was taken.

2.2. Population

A total of 176 women were recruited into the study at either the first or second trimester and answered the first questionnaire; 159 (90.3%) continued in the study until birth and completed the second questionnaire. The drop-outs were due to miscarriages, moving, or a decision to leave the study. Since not all women entered the study during the first 3 months of pregnancy, most blood Hg data were obtained for the second trimester ($n = 147$). Of the 60 women who entered the study at the first trimester, 43 were reclassified a posteriori since their first blood samples were from early in the second trimester (blood Hg levels were available for 39 of these women). At delivery, we were able to collect 101 mothers' and 92 cord blood samples.

2.3. Biological sampling and Hg determination

Blood samples for the first and second pregnancy trimesters were collected at the women's residence, while the third-trimester sample was taken at the hospital at delivery. Whole blood samples were refrigerated at -20°C until analysis for Hg concentration. Laboratory analyses using cold-vapor atomic-absorption spectrometry were carried out at the Centre de Toxicologie du Québec for total Hg (THg) and inorganic Hg (IHg); organic mercury (OHg) was calculated as the difference between THg and IHg. Laboratory analyses were performed using standardized quality-control procedures. An internal control was used for each series of analyses. The detection limits were $0.2\ \mu\text{g/L}$ for blood Hg analysis. For non-detected values of Hg, half the detection limit was used for statistical analyses.

Hair samples were collected from the mothers at the time of the administration of the second questionnaire at the women's residence. Hair strands from the root were cut from the occipital region of the head and placed in plastic bags, with the root end stapled on a paper sheet. Analyses for Hg determination were conducted in the GEOTOP Laboratory of the University of Québec in Montréal, using cold-vapor atomic-fluorescence spectrometry. Hair strands were cut in 1-cm segments, with a maximum of 9 cm, and each segment was analyzed for THg according to the procedure described by Bloom and Fitzgerald (1988). The detection limit for hair THg analysis was 5 ng/g. Precision and accuracy of Hg determination were ensured by the use of internal hair standards, which were provided by the Hair Mercury Inter-laboratory Comparison Program, Health Canada, Ottawa, Canada (Gill et al., 2002).

2.4. Statistical analysis

Only 159 participants (women who completed two questionnaires) were retained for analyses. The Wilcoxon paired test was used to determine the changes in fish consumption before and during pregnancy as well as for mother–cord comparisons. Blood and hair Hg concentrations were log-normally distributed and were log-transformed when necessary. For each trimester, the relation between Hg and other factors was examined using cross-sectional analysis of variance (ANOVA), general linear model, and correlation procedures. In addition, longitudinal analyses (mixed model (PROC MIXED) for repeated time measures considering the within-subject Hg level change) were used to examine the overall relation between fish consumption and Hg levels throughout pregnancy. The blood Hg levels from women recruited during the first trimester and reclassified a posteriori were excluded from cross-sectional analyses but were included in a mixed model in which

the gestational age at sampling was included as a continuous variable. All statistical analyses were performed using SAS version 8.12 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Population and fish-eating characteristics

Characteristics of the mothers and newborns are presented in Table 1. Fifty-three percent of the mothers had at least 12 years of schooling. Almost half of the participants (43%) smoked prior to pregnancy, and 31% continued smoking during pregnancy. The mean daily cigarette consumption during pregnancy was 13 cigarettes/day (range of 2–37 cigarettes/day). At birth, six newborns (4%) weighed less than 2500 g, and for eight (5%) the gestational age was less than 37 weeks. The sex ratio of girls to boys was 0.94.

Table 1
Characteristics of participants and newborns ($n = 159$)

Characteristics	Mean	SD	Range	Percentage
<i>Mother</i>				
Maternal age (years)	26.7	5	15–39	
Weight (kg)	66.4	16.0	42–124	
Education (years)	12.3	2.6	6–19	
Income \$ <25,000				29.7
Smoking (prior to pregnancy)				42.1
Smoking (during pregnancy)				30.6
Primiparous				42.7
<i>Newborn</i>				
Gestational age (weeks)	39.0	1.5	34–42	
Birth weight (kg)	3.3	0.5	1.9–5.0	
Length (cm)	50.6	2.9	31–59	
Head circumference (cm)	34.4	1.5	30–39	
Girls				48.0

The survey of fish-eating habits showed that prior to and during pregnancy, over 80% ate at least one fish meal/month. Table 2 presents the distribution of fish-eating habits prior to and during pregnancy with respect to reported fish-eating sources. Although the large majority of pregnant women continued to eat at least one fish meal/month, there was a reduction within all categories. Among the fish eaters, more women reduced or maintained their fish consumption during pregnancy ($n = 106$) than increased it ($n = 25$). Paired analyses showed a significant decrease in the number of fish meals/month during pregnancy compared to those prior to pregnancy (Wilcoxon signed rank, $P < 0.001$). The most significant decrease was for fluvial fish.

For the 25 women who increased their fish consumption during pregnancy, the difference was significantly due to all sources of fish. Canned fish consumption increased from less than 1 meal/month to almost 1 meal/week; the maximum consumption for canned tuna during pregnancy was 1 meal/day. Those who increased their consumption of fish during pregnancy had a tendency to weigh more at the onset of pregnancy (mean of 74.5 ± 23.9 kg vs. 65.9 ± 15.9 kg).

Yellow perch was the most commonly eaten fluvial fish and was consumed by 95% of the 43 women who reported eating St. Lawrence fish prior to pregnancy. The next most commonly eaten was walleye (33%), followed by smallmouth bass (19%) and pike (16%). During pregnancy, of the 35 women who ate fish from the St. Lawrence River lakes, 86% reported eating yellow perch, while only 14% ate smallmouth bass, 9% walleye, and 6% pike. For fresh market fish (including seafood), shrimp were the most popular prior to pregnancy, reported by 74% of the 77 women, followed by sole (35%), scallops (37%), lobster (34%), and salmon (32%). For the 66 women who ate fish during pregnancy, 75% reported having eaten fresh shrimp, 28% sole, 28% scallops, and 28% salmon. For the 93 women who ate market canned fish, the most consumed

Table 2
Distribution of fish-eating habits prior to and during pregnancy with respect to reported fish-eating sources ($n = 159$)

	All sources	St. Lawrence fish	Fresh market fish	Canned market fish	Frozen market fish
<i>Prior to pregnancy</i>					
Mean/median (meals/month)	3.6/3.0	0.5/0.0	0.8/0.0	1.6/1.0	1.6/1.0
Range (meals/month) ^a	0–19.5	0–8.5	0–6.0	0–12.0	0–8.0
n (%) of consumers	142 (89)	43 (27)	77 (48)	93 (58)	113 (71)
<i>During pregnancy</i>					
Frequency	3.2/2.0	0.3/0.0	0.6/0.0	1.2/0.0	1.4/0.5
Range	0–31.5	0–4.5	0–8.0	0–30	0–12.0
n (%) of consumers	132 (83)	35 (22)	60 (38)	78 (49)	94 (59)
Wilcoxon signed rank (P value)	0.0007	0.001	0.01	0.01	0.07

^aMinimum–maximum.

were tuna (85%), salmon (39%), and shrimp (25%), while for the 78 who ate canned fish during pregnancy, 77% reported eating canned tuna, 32% canned salmon, and 17% canned shrimp. For those who consumed frozen fish prior to pregnancy ($n = 113$), 72% reported having eaten fish sticks, 42% frozen shrimp, and 41% frozen sole, during pregnancy ($n = 94$), 72% reported having eaten frozen fish sticks, while 37% reported having eaten frozen shrimp and 31% frozen sole.

3.2. Temporal variation of blood and hair Hg levels in pregnancy

Descriptive statistics for maternal and umbilical cord blood Hg analyses for each trimester are presented in Table 3. The distribution was log-normal. Median values for THg were 0.60 µg/L for all trimesters and cord blood, while for OHg, median values were 0.2 µg/L for the second trimester and delivery and 0.3 µg/L for cord blood. For IHg, 24%, 39% and 49% were below the level of detection for maternal blood at the second trimester and at delivery and for cord blood. For all forms of Hg, there was a decrease in maternal blood concentrations over time, but cord blood levels were higher than maternal levels at birth for both total and organic Hg, while for IHg cord blood levels were lower. For total and organic Hg, paired analyses (Wilcoxon signed rank) revealed significant decreases between the second trimester and delivery ($P < 0.01$ and $P = 0.02$, respectively) and significant increases between maternal blood at delivery and cord blood ($P = 0.03$ and $P < 0.001$, respectively). For IHg, there were significant

decreases between the second trimester and delivery ($P = 0.01$) and between maternal blood at delivery and cord blood ($P < 0.0001$).

Maternal hair THg levels for each month are presented in Fig. 1. Only one woman had THg concentration in hair higher than 1000 ng/g, but only during two months. Maternal blood and hair Hg levels decreased significantly between the second and third trimesters of pregnancy (ANOVA repeated measures; $P < 0.0001$ for hair THg; $P = 0.04$ and $P < 0.01$ for blood OHg and IHg, respectively). The hair THg curve during pregnancy can be described by a quadratic equation ($\text{THg}_{\text{hair}} \text{ (ppb)} = 169.3 - 0.6 \times (\text{gestational month})^2$; $P < 0.0001$). Also, the decrease of hair THg was more pronounced during the last 3 months of pregnancy. The average OHg concentration was 1.7-fold higher (range of 0–5 µg/L) in cord blood than in maternal blood for the third trimester (Wilcoxon signed-rank test; $P < 0.001$). Inversely, the inorganic fraction was significantly higher in maternal blood than in cord blood (Wilcoxon signed-rank test; $P < 0.001$). The maternal hair-to-blood ratio was 190, 203, and 213 for the first to third trimester of pregnancy.

Strong correlations between maternal hair and blood Hg levels (i.e., total, organic, and IHg) were observed (Table 4). In addition, maternal hair was strongly correlated with all three forms of Hg in cord blood and is highly predictive for the organic fraction, explaining 41% of the variance. Maternal blood concentrations were highly correlated ($P < 0.0001$) with cord blood (Spearman's $\rho = 0.74, 0.67,$ and 0.82 for THg for the first, second, and third trimesters, respectively, and $0.58, 0.58,$ and 0.72 for MeHg for the first, second, and third trimesters, respectively).

Table 3
Distribution of blood total, organic, and inorganic Hg during pregnancy

	Mother's blood			Cord blood ($n = 92$)
	First trimester ($n = 39$)	Second trimester ($n = 147$)	At delivery ($n = 101$)	
Total Hg (µg/L)				
GM	0.85	0.56	0.48	0.52
AM	0.99	0.74	0.61	0.69
5th–95th percentiles	0.40–2.20	nd–2.00	nd–1.20	nd–1.60
Organic Hg (µg/L)				
GM	0.36	0.30	0.23	0.39
AM	0.48	0.34	0.26	0.45
5th–95th percentiles	nd–1.20	nd–1.20	nd–0.80	nd–1.30
Inorganic Hg (µg/L)				
GM	0.45	0.30	0.24	0.19
AM	0.51	0.40	0.35	0.24
5th–95th percentiles	nd–1.80	nd–1.00	nd–0.80	nd–0.60

Abbreviations used: GM, geometric mean; AM, arithmetic mean; nd, non-detectable.

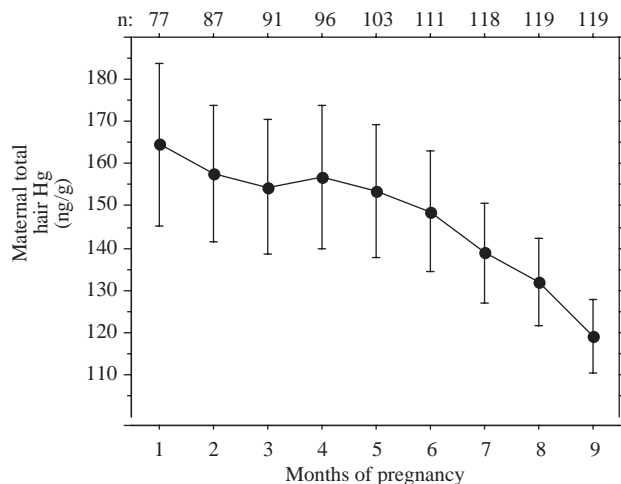


Fig. 1. Longitudinal, sequential maternal hair THg concentrations (ng/g) during the entire pregnancy. Each month corresponds to 1 cm of hair. Means and standard errors are presented. n , the number of samples for each centimeter.

Table 4
Spearman rank correlation coefficients (ρ) for total Hg in maternal hair with respect to maternal and cord blood Hg levels

	Maternal hair		
	First trimester	Second trimester (Spearman's ρ)	Third trimester
<i>Maternal blood</i>	(<i>n</i> = 20)	(<i>n</i> = 106)	(<i>n</i> = 93)
OHg	0.39	0.57****	0.52****
IHg	0.10	0.35***	0.21*
<i>Cord blood</i>	(<i>n</i> = 65)	(<i>n</i> = 81)	(<i>n</i> = 84)
OHg	0.56****	0.57****	0.68****
IHg	0.31*	0.31**	0.30**

* $P > 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

Alcohol consumption, mother's weight gain and age, education, income, hair treatment, and child's sex were not significantly associated with mother's hair and blood Hg and cord blood Hg concentrations. The mixed model showed that cigarette smoking during pregnancy was associated with lower blood inorganic and organic Hg levels throughout pregnancy ($P < 0.05$ for both, $F_i = 4.5$ and $F_o = 4.0$). A similar association was found between cord blood Hg levels and smoking during pregnancy; for women who smoked, the levels of cord blood inorganic and organic Hg were lower ($P = 0.003$ and $P = 0.009$, respectively) than for those who did not smoke. However, those who smoked during pregnancy did not have lower maternal hair Hg concentrations.

3.3. Fish consumption and Hg levels in pregnancy and at birth

As expected, blood IHg levels were not related to fish consumption prior to and during pregnancy, and analyses of the relation between fish consumption and blood Hg levels were performed only with regard to blood OHg levels.

A dose–response relationship between fish consumption during pregnancy from all sources and hair THg levels is presented in Fig. 2. Figs. 3a and b show the relation between fish consumption dose from all sources prior to (Fig. 3a) and during (Fig. 3b) pregnancy with respect to blood organic Hg levels throughout pregnancy. All significant findings were adjusted for cigarette smoking to verify any possible difference between adjusted and unadjusted results. The frequency of fish consumption during pregnancy (meals/month) was significantly and positively related to maternal and cord blood OHg levels during pregnancy (Tables 5 and 6). Furthermore, only consumption of canned and fresh market fish during pregnancy was significantly related to both blood and hair Hg concentrations during pregnancy. Multiple regression analysis showed that OHg in cord blood was explained by total fish meals/month

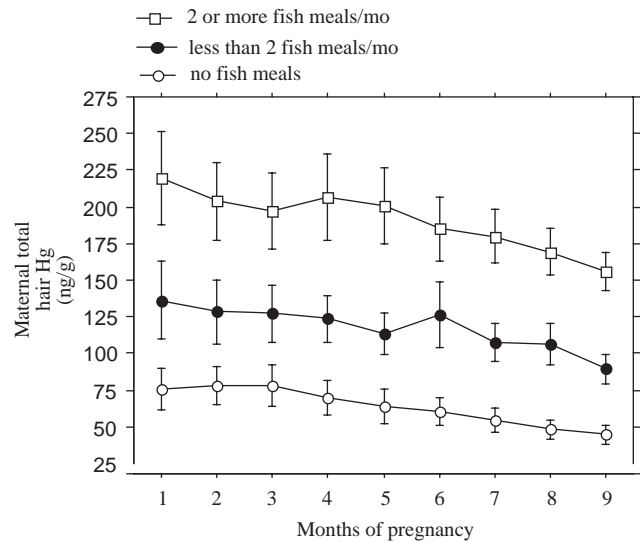


Fig. 2. Longitudinal sequential maternal hair THg (ng/g) during pregnancy in relation to fish consumption during pregnancy. Each month corresponds to 1 cm of hair. Means and standard errors are presented.

during pregnancy ($r^2 = 0.21$), as well as total fish meals/month prior to pregnancy ($r^2 = 0.22$).

The time trend of blood and hair Hg levels during pregnancy was similar in both fish consumers and non-fish eaters. In general, there was a tendency toward a decrease in hair Hg over the entire pregnancy.

Fig. 4 presents the blood OHg concentrations of women who did not consume fish during pregnancy and those who increased or decreased their fish consumption. For these three groups, cord blood Hg levels were significantly higher than maternal blood Hg at delivery, with the highest difference for women who increased their consumption.

4. Discussion

Most studies on Hg and fish consumption target populations with high consumption of local fish (Kjellstrom et al., 1989; Davidson et al., 2001; Muckle et al., 2001a, b; Grandjean et al., 2003; Myers et al., 2003; Lebel et al., 1998; Dolbec et al., 2001). In the present study, only 27% reported eating fish from the local source, the St. Lawrence fluvial lakes; most persons ate fish from the market. These pregnant women do not represent a high-fish-consumer population; they ate, on average, 3.5 fish meals/month during pregnancy. But even with this low consumption, a dose–response relationship was found between fish consumption from all sources and maternal blood and hair Hg levels prior to and during pregnancy.

Fish consumption, prior to pregnancy, with the exception of frozen market fish, contributed to maternal

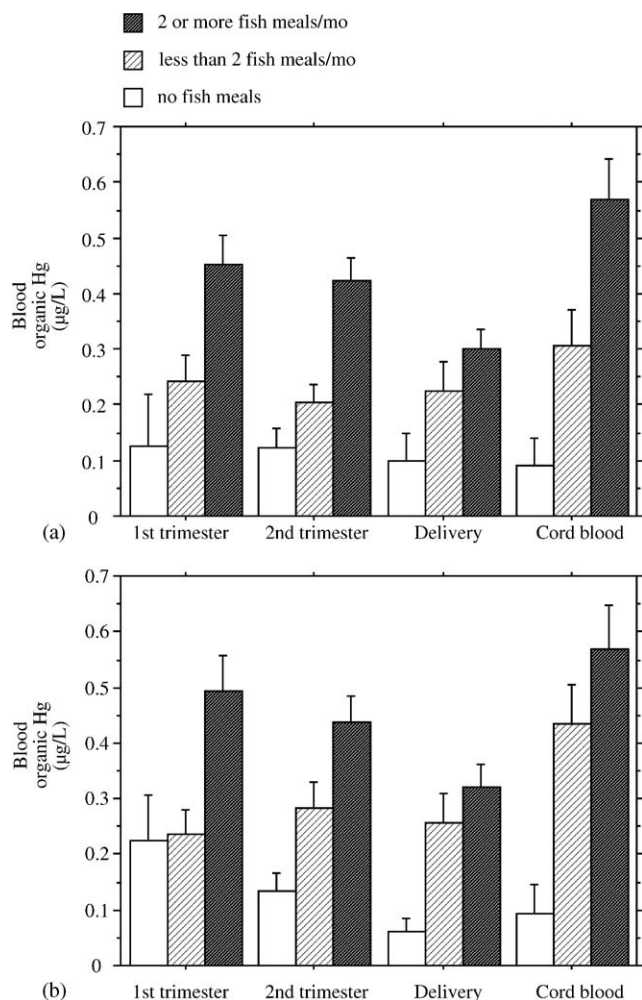


Fig. 3. (a) Blood OHg concentrations ($\mu\text{g/L}$) for maternal and cord blood in relation to fish consumption (meals/month) prior to pregnancy. (b) Blood OHg concentrations ($\mu\text{g/L}$) for maternal and cord blood in relation to fish consumption (meals/month) during pregnancy.

Hg exposure during pregnancy. However, only consumption of canned and fresh market fish during pregnancy was significantly related to blood and even more to hair Hg levels in pregnancy. The significant relation between lake fish consumption prior to pregnancy but not during pregnancy may have been caused by the reduction during pregnancy in the relative frequency of the consumption of predators with high levels of Hg. While 33% ate walleye prior to pregnancy, only 9% ate it during pregnancy. Pike consumption decreased from 16% to 6%. Walleye and pike from this region are known to have high levels of Hg (Blaney et al., 1996), and there are advisories regarding their consumption. Nadon et al. (2002) also observed that few Montreal-area women of childbearing age consumed local sport fish frequently or for extended periods. The levels observed in the present study among fluvial fish eaters are similar to those reported for women of

childbearing age by Nadon et al. (2002). In the present study, we observed a higher Hg level in cord blood among women who increased their fish consumption during pregnancy. Thus, increasing fish consumption during pregnancy did lead to higher fetal Hg accumulation.

In this population, canned tuna was one of the fish sources that contributed the most to Hg exposure. Frozen market fish, mostly fish sticks, did not contribute to Hg exposure risk for these women since no significant results were found between maternal Hg level and frozen fish consumption. However, there was a significant relation with cord blood, independent of the time of maternal consumption of frozen fish (prior to or during pregnancy). The constant ingestion of lower levels of MeHg from frozen fish sources and the active placental transfer of Hg to the fetus may possibly explain this fetal MeHg exposure from frozen fish.

Analyses of hair Hg levels during pregnancy confirmed that exposure of this population was very low. Pregnant women had blood and hair Hg levels below the 6- and 1.5- $\mu\text{g/g}$, recommendations for Hg exposure of Health Canada (Health Canada, 2000) and the EPA, respectively (Rice et al., 2003). Hair THg levels observed in the present study are very far below those reported in the Faroe Islands (geometric mean, 0.09 $\mu\text{g/g}$ compared to 4.27 $\mu\text{g/g}$), where neurobehavioral, neurophysiologic, and cardiovascular effects have been observed in relation to in utero exposure to Hg (Murata et al., 1999; Sorensen et al., 1999; Grandjean et al., 1997, 2003). In an earlier study on residents of the Upper St. Lawrence River Basin (Mahaffey and Mergler, 1998), blood Hg of the population of women of childbearing age (20–39 years) was similar to that found in this study 0.57 vs. 0.41 $\mu\text{g/L}$ MeHg for the first trimester in the present study. A recent study of 112 non-occupationally exposed pregnant women in Sweden with a low intake of freshwater fish reported median maternal blood MeHg at delivery of 0.73 $\mu\text{g/L}$ (Ask et al., 2002); this value is higher than the 0.2 $\mu\text{g/L}$ observed here. In the 2003 National Health and Nutrition Evaluation Examination Survey (NHANES) in the United States (CDC, 2003), blood THg was assessed for women of childbearing age (16–49 years). The reported median value and the 90th percentile were again higher: 0.9 and 4.9 $\mu\text{g/L}$ compared to 0.6 and 1.6 $\mu\text{g/L}$ (first trimester) for the women in the NHANES vs. the women within the present study, respectively. In addition, in the NHANES inorganic blood Hg was below the level of detection and all of the Hg was attributed to MeHg, which would further enlarge the observed differences between the two populations.

As expected, a temporal variation over pregnancy was observed for both maternal blood OHg and hair THg. This diminution may be due, in part, to the hemodilution that would be linear from the end of the first

Table 5

Relations between blood organic mercury (OHg) and hair total mercury (THg) and the frequency of fish consumption *during pregnancy*: results of cross-sectional (each trimester) and longitudinal (throughout-pregnancy) analyses

Fish consumption (meals/month)	Blood OHg ($\mu\text{g/L}$)					Hair THg (ng/g)				
	First trimester	Second trimester	At delivery	Throughout pregnancy	Cord blood	First trimester	Second trimester	At delivery	Throughout pregnancy	
Model parameters for fish consumption from all sources	$F(1;37) = 5.0$ $P < 0.05$ $r^2 = 0.12$	$F(1;145) = 20.0$ $P < 0.0001$ $r^2 = 0.12$	$F(1;99) = 17.1$ $P < 0.0001$ $r^2 = 0.15$	$P < 0.0001$	$F(1;90) = 24.0$ $P < 0.0001$ $r^2 = 0.21$	$F(1;89) = 6.9$ $P < 0.01$ $r^2 = 0.07$	$F(1;109) = 9.7$ $P < 0.01$ $r^2 = 0.08$	$F(1;117) = 23.4$ $P < 0.0001$ $r^2 = 0.17$	$P < 0.0001$	
Model parameters include the four fish sources	$F(4;34) = 2.4$ $P < 0.05$ $r^2 = 0.22$	$F(4;142) = 7.9$ $P < 0.0001$ $r^2 = 0.18$	$F(4;96) = 4.4$ $P < 0.01$ $r^2 = 0.15$		$F(4;87) = 6.0$ $P < 0.001$ $r^2 = 0.22$	$F(4;86) = 4.0$ $P < 0.01$ $r^2 = 0.16$	$F(4;106) = 5.6$ $P < 0.001$ $r^2 = 0.17$	$F(4;104) = 8.0$ $P < 0.0001$ $r^2 = 0.22$		
Fluvial fish	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
Fresh market	ns	ns	ns	$P < 0.05$	$P < 0.05$	$P < 0.05$	$P < 0.05$	$P < 0.01$	$P < 0.01$	$P < 0.01$
Canned market	ns	$P < 0.0001$	$P < 0.01$	$P < 0.0001$	$P < 0.05$	$P < 0.01$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.0001$
Frozen market	ns	ns	ns	ns	$P < 0.05$	ns	ns	ns	ns	ns

ns, not significant.

Table 6

Relations between blood organic mercury (OHg) and hair total mercury (THg) and the frequency of fish consumption *prior to pregnancy*: results of cross-sectional (each trimester) and longitudinal (throughout-pregnancy) analyses

Fish consumption (meals/month)	Blood OHg ($\mu\text{g/L}$)					Hair THg (ng/g)				
	First trimester	Second trimester	At delivery	Throughout pregnancy	Cord blood	First trimester	Second trimester	At delivery	Throughout pregnancy	
Model parameters for all sources	$F(1;37) = 13.4$ $P < 0.001$ $r^2 = 0.27$	$F(1;145) = 55.6$ $P < 0.0001$ $r^2 = 0.28$	$F(1;99) = 10.5$ $P < 0.01$ $r^2 = 0.09$	$P < 0.0001$	$F(1;90) = 25.4$ $P < 0.0001$ $r^2 = 0.22$	$F(1;89) = 17.3$ $P < 0.0001$ $r^2 = 0.16$	$F(1;109) = 29.4$ $P < 0.0001$ $r^2 = 0.21$	$F(1;117) = 50.4$ $P < 0.0001$ $r^2 = 0.30$	$P < 0.0001$	
Model parameters include the four fish sources	$F(4;34) = 6.7$ $P < 0.001$ $r^2 = 0.44$	$F(4;141) = 21.3$ $P < 0.0001$ $r^2 = 0.38$	$F(4;95) = 3.4$ $P < 0.05$ $r^2 = 0.13$		$F(4;86) = 7.2$ $P < 0.0001$ $r^2 = 0.25$	$F(4;85) = 4.7$ $P < 0.01$ $r^2 = 0.18$	$F(4;105) = 8.3$ $P < 0.0001$ $r^2 = 0.24$	$F(4;113) = 13.0$ $P < 0.0001$ $r^2 = 0.31$		
Fluvial fish	$P < 0.05$	$P < 0.0001$	ns	$P < 0.01$	$P < 0.05$	ns	ns	ns	ns	ns
Fresh market	$P < 0.05$	$P < 0.01$	$P < 0.05$	$P < 0.001$	$P < 0.01$	ns	$P < 0.05$	$P < 0.01$	$P < 0.01$	$P < 0.05$
Canned market	$P < 0.01$	$P < 0.0001$	ns	$P < 0.0001$	ns	$P < 0.01$	$P < 0.001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
Frozen market	ns	ns	ns	ns	$P < 0.05$	ns	ns	ns	ns	ns

ns, not significant.

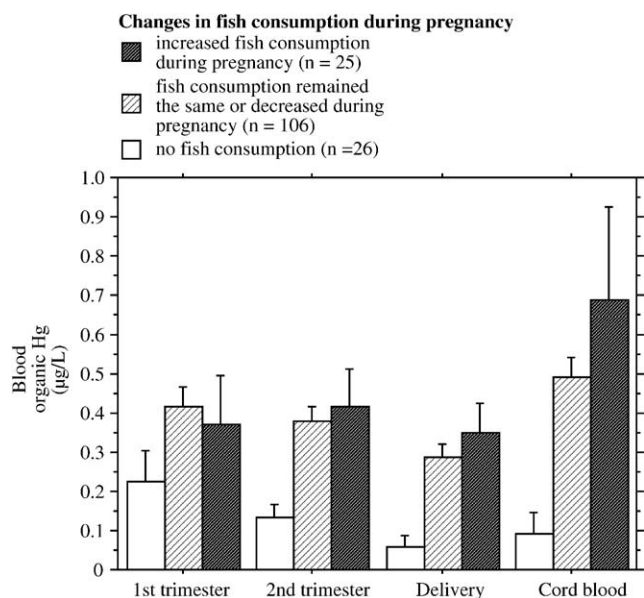


Fig. 4. Blood OHg concentrations during pregnancy in relation to changes in fish dietary habits during pregnancy.

trimester to term (Hyttén, 1985). Transplacental transfer of Hg could be another factor contributing to this decrease in maternal Hg. Although we did not have a month-to-month survey of fish consumption, and decreased fish consumption may have contributed to this decrease in hair Hg, this does not appear to be the case since the same tendency for a decrease in Hg level was observed among the non-fish eaters. The significant decrease of Hg levels between the last two trimesters is important because it suggests that there is a higher Hg placental transfer during the last three months of pregnancy (Fig. 1). Pregnant women do not have stable biokinetics with respect to Hg, as the fetus grows rapidly and has the capacity to retain a substantial amount of Hg (Bartell et al., 2000). Even if the nervous system seems to be particularly vulnerable to this neurotoxicant in early periods of neural tube formation (first month of pregnancy), the brain undergoes tremendous growth beginning early in gestation and continuing into the postnatal period (Rice and Barone, 2000). Various parts of the brain develop at different times and have different windows of vulnerability, both prenatally and postnatally, based on the temporal and regional maturation mediated through a multitude of developmental processes. Fetal exposure in the last trimester of pregnancy might affect neurogenesis in the cerebellum and hippocampus (brain areas of formation), as well as other processes like cell migration, myelination (ontological peak during the last trimester), and synaptogenesis in areas that have already undergone neurogenesis (Rice and Barone, 2000). Alterations in those developmental processes can cause developmental neurotoxicity, since the cerebellum subserves motor function and

motor learning as well as cognitive processes (Parkins, 1997; Thach, 1998).

A more direct bioindicator of prenatal Hg exposure is Hg in cord blood. Geometric mean cord THg concentrations in the present study ($0.52 \mu\text{g/L}$) (Table 3) were lower than the levels found in the Faroe Islands infants; median THg levels in the Faroes study were $24 \mu\text{g/L}$ compared to $0.3 \mu\text{g/L}$ for this study (Grandjean et al., 1992). Cord THg concentrations were also lower than the $0.96 \mu\text{g/L}$ reported by Rhainds et al. (1999) for 1109 newborns from hospitals in Southern Québec (data were collected between 1993 and 1995). In the Swedish study, in which the median MeHg cord blood level was $1.4 \mu\text{g/L}$ compared to $0.3 \mu\text{g/L}$ for this pregnant population, the authors reported almost a two-fold increase in the ratio of maternal to cord blood Hg. Earlier studies have also reported this two-fold tendency (Tsuchiya et al., 1984; Vahter et al., 2000; Ramirez et al., 2000; Sandborgh-Englund et al., 2001; Ask et al., 2002). It has been demonstrated that MeHg is actively transferred to the fetus across the placenta via a neutral amino acid carrier (Kajiwara et al., 1996). Indeed, several studies on humans and animals have demonstrated higher MeHg accumulation in the fetus than in the mother (Choi, 1989; WHO, 1990; Vahter et al., 2000; Sakamoto et al., 2002). The present study confirms that there is an approximate two-fold increase even for very low levels of Hg. These results are important, since the developing brain is more sensitive than that in adults (Choi, 1989; WHO, 1990; Castoldi et al., 2001).

In the present study, lower concentrations of IHg were found in cord blood compared to maternal blood at delivery (Table 3). This difference may be attributed to the placental barrier less permeable to IHg ions (Clarkson, 1997); however, other studies have not observed significant differences between cord and maternal blood (Sandborgh-Englund et al., 2001; Ask et al., 2002).

Strong correlations were observed between THg in hair and in organic blood Hg (Table 4). Other studies have also reported good relations between these exposure indicators in pregnant women (Muckle et al., 2001a, b; Grandjean et al., 1992). Indeed, it has been demonstrated that the concentration of MeHg in the active hair follicle is related to the blood concentration and total body burden and that the hair-to-blood ratio is a constant rate of approximately 250 (Al-Shahristani et al., 1976; WHO, 1990). In this study of low fish consumers, the hair-to-blood ratio for THg was lower than 250 and tended to increase during pregnancy from 190 in the first trimester to 213 in the third trimester. This may have been due to physiological factors during pregnancy, such as hemodilution. Correlations between cord blood Hg and maternal hair and blood Hg were very good. In fact, all three forms of Hg in cord blood were related to maternal hair Hg level. Hair was

predictive of the organic fraction in cord blood, explaining 41% of the variance. These results confirm the relatively strong association between Hg cord blood and maternal hair at delivery found in others studies (Grandjean et al., 1999; Muckle et al., 2001a, b).

The main source of exposure to IHg is dental amalgam filling, which releases metallic Hg vapor (Hg^0) (Clarkson et al., 1988). In the body, inhaled Hg^0 is oxidized to inorganic Hg^{2+} by catalase already within the blood. Whereas Hg^{2+} does not readily pass cellular membranes, some Hg^0 remains in the circulation long enough to cross the placental and blood–brain barrier (Denecker et al., 1983; Nylander et al., 1987; Dock et al., 1994). Maternal and fetal tissue concentrations of Hg have been found to be associated with the number and surface area of maternal dental amalgam fillings (Drasch et al., 1994; Lutz et al., 1996; Vahter et al., 2000; Ask et al., 2002; Becker et al., 2002; Lindow et al., 2003; Pizzichini et al., 2003). In the present study, in which Hg was measured in maternal hair and blood samples and fish consumption was low, dental sources possibly represented, for many pregnant women, a greater proportion of the total exposure. Indeed, in this population, mean maternal IHg levels were equal to or higher than maternal OHg levels during pregnancy. Our results for IHg were lower than those reported by Ask et al. (2002) for pregnant women (0.32 and 0.34 $\mu\text{g}/\text{L}$ for maternal and cord blood), while in the present study these values were both 0.2 $\mu\text{g}/\text{L}$. The authors of the Swedish study also showed a strong correlation between IHg levels and dental amalgam fillings. Unfortunately, dental amalgam fillings were not surveyed in the present study.

The association between cigarette smoking during pregnancy and the diminution of inorganic and organic maternal and cord blood Hg levels is difficult to understand and contradicts data obtained by various authors (Langworth et al., 1991; Visser et al., 1991; Akesson et al., 2000; Pizzichini et al., 2003). Cigarette smoking was not associated with lower levels of fish consumption. Moreover, cigarette smoking did not influence the relation between fish consumption and Hg levels. Income, education level, and maternal age were not associated with cigarette consumption. Since cigarette smoking was inversely associated with IHg, it seems possible that dental amalgams could have been involved. One possibility is that cigarette smokers had fewer dental amalgams than non-smokers. However, Sibling et al. (1993) evaluated the smoking habits of subjects with and without amalgam fillings and found more smokers in the amalgam group. Another possibility is that the accumulation of dust from cigarettes upon the metal surface prevents vaporization, thereby decreasing Hg release. It could also have been the result of metabolic changes (enzyme induction) produced by smoking. Finally, this could have been a chance finding.

Most guidelines recommend, for pregnant women, consumption limits for freshwater fish with high Hg levels. There are, however, few recommendations for Hg from other fish sources (store bought, canned, frozen). For the community study here, market-bought fish, and especially canned tuna, were the fish sources most consumed. It would be useful to have guidelines that include all fish. A more ecosystemic approach that involves identifying inter- and intraspecies differences within all of the sources and their effects would be useful for providing information that would allow pregnant women to eat fish, which are beneficial to their health and that of the developing fetus, while minimizing the risk of toxic exposure.

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