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Published in:
Environmental Health Perspectives

Publication date:
1994

Document version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Mercury in the Umbilical Cord: Implications for Risk Assessment for Minamata Disease

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Umbilical cord tissue was obtained from 50 births in the Faroe Islands, where high mercury intake is due to ingestion of pilot whale meat. The mercury concentration correlated significantly with the frequency of maternal whale meat dinners during pregnancy and with mercury concentrations in umbilical cord blood and in maternal hair. The results were compared with published values for mercury in umbilical cord tissue from 12 infants diagnosed with congenital methylmercury poisoning in Minamata, Japan. From the regression coefficients obtained in the Faroese samples, the median umbilical cord mercury concentration of 4.95 nmol/g dry weight in Minamata would correspond to 668 nmol/l cord blood and 114 nmol/g maternal hair. These levels agree well with other evidence of susceptibility of the fetus to increased exposure to methylmercury. Key words: blood analysis, hair, mercury, methylmercury, Minamata disease, pregnancy, seafood. Environ Health Perspect 102:548–550 (1994)

We have therefore examined the relation between the mercury concentrations in umbilical cord tissue (UC-Hg) with that in maternal hair and in umbilical cord blood. The samples were obtained in connection with a cohort study in the Faroe Islands where mercury exposures from seafood may approach those that occurred in Minamata (2).

Materials and Methods

Umbilical cords were collected at consecutive births from 1 March 1986 until the end of 1987 at the three Faroese hospitals (2). Maternal hair and umbilical cord blood were also obtained for mercury analysis. A questionnaire was administered by the midwife to obtain basic information on the general course of the pregnancy and nutritional habits, including frequencies of dinners based on pilot whale meat or fish, use of alcohol, and tobacco smoking. A total of 1023 births were included in the cohort, representing 75% of all births during the sampling period (2). Obstetric data indicate that limited selection bias took place (5).

About 10 cm of the umbilical cord was collected close to the umbilicus and kept frozen at -20°C until analysis. On the basis of the mercury concentrations in maternal hair and umbilical cord blood (2), a selection of 50 samples was made to obtain a maximal range and a relatively even distribution of expected mercury concentrations, i.e., with an overrepresentation of high levels of mercury.

From each cord sample, a specimen of 0.5–1 cm was excised. The specimen was freeze-dried for at least 24 h and then stored in a desiccator. To determine mercury concentrations in umbilical cord blood, we placed an accurately weighed, freeze-dried sample of at least 0.05 g with 3 ml of 8 M ultrapure HNO3 (Merck, Darmstadt, Germany) in a PTFE-lined digestion vessel (CEM, Indian Trail, North Carolina). The closed vessel was heated for 10 min in a microwave oven (CEM 80) at 100% power. Under these digestion conditions, all organic compounds except for aromatics are decomposed (4), thereby removing all major sources of interference with the detection method. The digest was transferred to a Minisorp tube (NUNC, Roskilde, Denmark) and kept closed until analysis within 48 hr. As documented by Pineau et al. (5), storage of the digested sample for a maximum of 1 week does not cause any change in the mercury concentration. A volume of 250 µl of digested sample was transferred to another Minisorp tube, and 2 ml of saturated KMnO4 (Merck) in 3% H2SO4 (Merck) was added. The tubes were sealed with perforated parafilm (American Can Company, Greenwich, Connecticut) and agitated before incubation in a 75°C warm water bath for 30 min. After cooling, we reduced excess potassium permanganate by carefully adding 250 µl saturated hydroxylamine hydrochloride (Merck). The solution was agitated carefully until clear. Each digested sample was prepared and analyzed in duplicate.

The mercury analysis was performed by flow-injection cold-vapor atomic absorption spectrometry (Perkin-Elmer model 5100 with FIAS-200 and AS-90; Perkin-Elmer, Norwalk, Connecticut). The mercury results were read against a standard curve prepared from a mercury stock solution of 1 g/l by dilution 10-fold the first time and thereafter two times at 100-fold with 1% HCl (Merck), containing a few drops of 5% KMnO4 per 50 ml of solution, until a 10 µg Hg/l solution was obtained. From this standard solution, dilutions to 1, 2, and 4 µg Hg/l were made and used for a standard curve, including a blank consisting of 1% HCl with 5% KMnO4. The total analytical imprecision was estimated to be 8.7% at a mercury concentration of 72.3 nmol/l. The accuracy of the mercury determination was assessed by the use of Seronorm Trace Element batch 906 (Nycomed, Oslo, Norway) as quality control material. The average mercury concentration measured in seven determinations was 72.3 nmol/l (assigned value 73 nmol/l). The detection limit estimated from a blank solution (mean ± 3 SD) was 0.75 nmol/l. All analyses were conducted without any information available on mercury concentrations previously found in cord blood and maternal hair.

Results

Determination of the mercury concentrations in duplicate samples of umbilical cord showed a variation that averaged 3.65% (coefficient of variation; CV). This variation is similar to the average imprecision (CV) of 4.03% seen in split samples from the 50 individuals. The overall medi-
an UC-Hg concentration was 1.53
nmol/g, with a maximum of 6.38 nmol/g.

High mercury concentrations in the
cord tissue were clearly related to the fre-
quency of whale meat dinners during preg-
nancy, although considerable individual
variation occurred. The mercury concen-
trations in the umbilical cord correlated
well with those in cord blood ($r_e = 0.85$; $p$
< 0.001) and almost as well with mercury
in maternal hair ($r_e = 0.77$; $p < 0.001$; Figs.
1 and 2). The regression lines can be cal-
culated from these data (UC-Hg in nmol/g):

\[
\text{Cord blood-Hg (nmol/l)} = 139.42 \times (\text{UC-Hg}) - 21.86
\]

\[
\text{Hair-Hg (nmol/g)} = 19.49 \times (\text{UC-Hg}) + 17.86
\]

Using these equations, the results from
Harada et al. (1) can be translated into
more commonly used indicators of mer-
cury exposure (Table 1). In addition, the
approximate daily intake under chronic
exposure conditions can be estimated. This
calculation is based on the finding that the
steady-state concentration in blood (in
micrograms per liter) is approximately 0.8
times the daily methylmercury intake (in
micrograms) (6), and that the fetal cord
blood mercury concentration is about 20%
higher than that of maternal blood (7)
(Table 1).

**Discussion**

The high mercury exposures that occur in
the Faroe Islands are a result of frequent
intake of marine food items, and pilot
whale meat is the main source (2). The
mercury concentrations in whale meat vary,
depending on age and catch, for
example, but averages (8) are usually sev-
eral-fold above a limit of 0.5 mg/kg applied
in many countries for mercury in seafood.
As expected, the highest mercury concen-
trations in the cord tissue were associated
with frequent whale meat dinners.

Although we determined total mercury
only, we observed a highly significant cor-
relation between mercury concentrations
in umbilical cord versus blood and mater-
nal hair. The ratio of mercury concen-
trations in hair (nmol/g) versus blood
(nmol/l) seen in this study is in reasonable
accordance with the overall expected
average of about 250 (9). The relation to
cord mercury concentrations has not been
reported previously. Due to the wide range
of exposures in the Faroe Islands, the
regression equations for mercury concen-
trations in these different types of speci-
mens are particularly useful for interpret-
ing the data on cord mercury concentra-
tions obtained in Minamata.

The mercury contents in umbilical
cord tissue from Minamata may have
changed during desiccation and storage at
room temperature. Quite conceivably, the
mercury concentrations could decrease
with time, for example, due to reduction
by microorganisms and subsequent evap-
oration. The rate of this change is obviously
difficult to ascertain *a posteriori*. Also, the
desiccation process and prolonged storage
may have led to a final dry weight that is
lower than the one obtained in the labora-
tory by drying a tissue sample that has
been preserved by freezing. A loss in dry
weight would result in higher mercury
concentrations. Whether this process
might counterbalance a potential loss in
mercury from the tissue is unclear. In this
regard, the considerable variation in cord
mercury concentrations from Minamata
patients is noteworthy; some of the
patients had very low concentrations of
mercury that were similar to those seen in
the control groups. However, misclassifica-
tion of Minamata disease in patients with
spastic paresis of other etiology, for exam-
ple, may have played a role in this regard.
That misclassification occurred is indicated
by the fact that some mercury concen-
trations were very high in children with men-
tal development problems presumed differ-
ent from congenital Minamata disease.

Despite these limitations, the data for
Minamata disease obtained by Harada (1)
are of interest to calculate at least an order
of magnitude for the corresponding mer-
cury concentrations in maternal hair and
in cord blood. The data given in Table 1
illustrate the approximate levels of mercury
exposure that would be associated with
congenital Minamata disease. Somewhat
higher intakes were calculated by
Futatsuka (10), who reported a median
daily mercury intake around the Minamata
Bay of 3597.5 nmol (719.5 μg); this level
was based on a dietary survey among 80
female members of full-time fishermen’s
families residing at Minamata Bay, where
the highest prevalence rate for Minamata
disease was found.

From data obtained in Iraq where
methylmercury poisoning was due to con-
taminated flour, a maternal hair mercury
concentration of 50–100 nmol/g seemed
to imply a 5% risk of congenital Minamata
disease (9,11). The data given in Table 1
suggest that all but one of the Japanese
patients had exposures above this limit. Although the detailed dose–response relationship is by no means clear, a recent study by Kjellström et al. (12) suggested a risk of delayed mental development in children whose mothers had ingested shark meat during pregnancy and acquired a hair concentration above 65–75 nmol/g mercury, and similar but less marked effects seemed to occur down to 30–50 nmol/g. This study is of particular interest because the exposure was chronic and mediated by passage through the food chains. The Faroese cohort is now being examined in detail to disclose any neurobehavioral dysfunctions that can be attributed to prenatal methylmercury exposures.

REFERENCES


