Mercury concentrations in pregnant women in circumpolar Sweden (Kiruna)

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Summary

High exposure to mercury have been found in populations living in circumpolar areas, due to high consumption of sea food and accumulation of mercury closer to the north pole. The developing fetus is especially sensitive to effects of mercury. Exposure to mercury has previously been examined in pregnant women in Sweden, but not in pregnant women residing in Sweden north of the polar circle.

In the years 2015-2016, mercury was measured in whole blood from 51 pregnant women living in the city of Kiruna in circumpolar Sweden, taking part in an international comparison between eight circumpolar countries. This report presents the Swedish results on mercury concentrations and associations with some exposure determinants. Also, compliance to dietary advice on fish consumption, appointed to fertile women, was examined.

The median concentration of total-Hg in whole blood was 0.40 µg/L (min, max; <0.40, 1.88) among the 51 pregnant women in Kiruna. This is similar or lower compared to concentrations of mercury in pregnant women in other parts of Sweden. None of the women in the study had concentrations of mercury that are considered as dangerous.

Mercury concentrations were associated with total fish consumption but not to consumption of predatory fish, known to be higher in mercury. All of the women in the study had knowledge about dietary advice on fish consumption. One woman exceeded the recommended consumption of predatory fish, limited due to risk of high mercury content, but this woman did not have high concentrations of mercury. While the vast majority of women thus followed the recommendations of not eating too much polluted fish, only 15 % of the women reported sufficient fish consumption to comply with the dietary advice (2-3 times/week).

In conclusion, pregnant women in circumpolar Sweden have low exposure to mercury, and do not deviant from pregnant women in other parts of Sweden. Knowledge about dietary advice on fish consumption appointed to fertile women is very good. The public health concern though, is that pregnant women in circumpolar Sweden do not eat enough fish.
Introduction

Mercury has been recognized as one of the most dangerous chemicals to public health by the World Health Organization. The organic form, methylmercury is the most detrimental form to humans with neurological effects in high doses, but also with effects on the immune system, the cardiovascular system and the kidneys [1]. Humans are mainly exposed to methylmercury through consumption of sea food. Emissions of mercury are mainly in the metallic or inorganic forms, but transformation to methylmercury occurs in the aquatic environment.

The unborn fetus is especially sensitive to methylmercury, passing both the placenta and the blood brain barrier, and neurological defects can occur already at relatively low levels [2]. There are recommendations on concentrations of mercury in tissues as well as in food items, based on risk assessments [3]. In Sweden, as well as in some other countries, there are specific dietary recommendations on fish consumption for pregnant women, women of fertile age, and children, with the aim to limit exposure of methylmercury without missing out on the beneficial nutrients in fish [4]. Total mercury in whole blood includes methylmercury and metallic mercury, the latter mainly originating from amalgam fillings. Young women in Sweden have generally none or few amalgam fillings, and therefore total mercury in whole blood can be assumed to mainly reflect exposure to methylmercury.

Previous studies have found that humans living in some circumpolar areas are more exposed to mercury, because of a diet containing wale and seal, but also due to accumulation of mercury closer to the north pole [5]. Several studies have found higher concentrations of mercury in native populations compared to other residents in the same geographical area, but this has not been examined in Sweden.

In Sweden, mercury concentrations in pregnant have been previously reported [6]. Mercury concentrations above the recommended have been found, yet below concentrations known to cause negative health effects. No data have previously been presented on pregnant women in Sweden residing above the polar circle.

Emission of mercury has decreased over time in Sweden, but internationally emissions have continued mainly through burning of coal, extraction of gold and mercury mines. Mercury vapor from emission may be spread long distances making this a global issue [7].
The Minamata convention was developed as an attempt to limit negative effects caused by mercury on human health and on the environment. The convention was signed by a majority of the countries of the world (n=128) in 2013 [8]. To enable evaluation of the effect of the Minamata convention, the international project MERCU-NORTH was performed, measuring mercury concentration in blood from pregnant women living in eight countries with circumpolar areas, including women in the municipality Kiruna in circumpolar Sweden.

The aim of this study is to present data on mercury concentrations in pregnant women living in circumpolar Sweden. We also aim to compare the Hg concentration with those previously reported for pregnant women in other parts of Sweden, and to examine exposure determinants.

Materials and Methods

In the international project MERCU-NORTH mercury concentrations in blood were measured in 2015-2016 in pregnant women in eight countries with circumpolar areas, including Sweden. The Swedish women were enrolled in maternal health care in the city Kiruna.

The study was approved by the Ethical Review Board in Umeå (Dnr 2014/400-31).

Study population
Women in gestation week 25 visiting the maternal health care in Kiruna were asked to participate in the study. Inclusion criterias were an essentially uncomplicated pregnancy, residing above the polar circle at least the last year and sufficient language and intellectual skills to be able to understand the information about the study. Recruitment continued until 52 women were included in the study. All pregnant women during the recruitment fulfilled the inclusion criteria and they all consented to participate in the study. Recruitment took place from October 2015 until February 2016.

Sampling of blood
Blood samples were drawn at a visit in week 28-29. Two tubes with 7 ml blood each were sampled. Of this, 2 ml whole blood was refrigerated in polypropylene tubes to -20°C at a local
laboratory. The rest of the blood was centrifuged in 3000 rpm during 15 minutes, and thereafter plasma was filled in glass tubes and refrigerated. The samples were kept refrigerated until transportation to Canada where chemical analyses were performed.

Samples from eight participants were destroyed because of incorrect storage. Seven of these participants could leave new samples but the eighth participant was no longer pregnant and therefore no new sample was drawn, leaving 51 women with mercury measurements in the study.

Chemical analysis
Total mercury was analysed in whole blood with inductively coupled mass spectrometry (ICP-MS) at the Institut national de santé publique du Québec (INSPQ), Canada. The blood samples were diluted 20 fold with a solution containing 0.5 % ammonium hydroxide and 0.1 % octylphenol ethoxylate. A calibration curve was prepared by diluting 20 fold the corresponding volume of blood from volunteers with the same diluent and thereafter spiking with different volumes of 1 mg/L multi-elements standard solution. $^{195}$Pt was used as internal standard for both calibration curve and samples analysis.

For quality control, 5 different reference materials (QM-B-Q1108, QM-B-Q1201, QM-B-Q1302, QM-B-Q1505 and QM-B-Q1512) were used. These were included in Québec Multielement External Quality Assessment Scheme (QMEQAS) (Tabell 1).

Mercury in whole blood was measured in nmol/L and recalculated to $\mu$g/L with the formula $\mu$g/L = 0.20059 x nmol/L. Before recalculation concentrations below 1 nmol/L were changed to 1 nmol/L and other concentrations were changed to the closest whole number.

In the analysis, 16 out of the 51 samples were below the detection limit (2 nmol/L ≈ 0.4 $\mu$g/L). These results were included in calculations of medians and in the regression.

Accuracy
The quality and accuracy of the analytical methods employed in these studies were assessed by participating in various interlaboratory comparison programs such as PCI Comparison Program for Metals in Biological Matrices (Canada), QMEQAS Quebec Multielement External Quality Assessment Scheme (Canada), PMQAS Priority Metals Quality Assessment
Scheme (Canada), LAMP Lead and Multielement Proficiency Program (USA), State of New-York Department of Health (USA) as well as G-EQUAS External Quality Assessment Scheme (Germany).

The internal quality control (QC) of the analyses was ensured by analyzing non certified reference after calibration, after every 10th sample as well as at the end of each analytical sequence. The internal QC was within 1σ of the expected values.

**Anthropometric data and questionnaire**

Weight, height and number of amalgam fillings were noted by the midwife at gestation week 28-29. A questionnaire was filled out under guidance of the midwife at the same visit. Consumption of fish during pregnancy, including changes in fish consumption and knowledge of dietary advice on fish consumption, family situation, educational level, previous child birth and nursing, income and if the participant had been living abroad during the last years were asked for in a questionnaire. Also, consumption of reindeer meat was asked for in the questionnaire, as a proxy for a traditional Sami diet.

**Statistical analyses**

Associations between mercury concentrations and possible determinants were examined with linear regression analysis. Mercury concentrations between groups were compared non-parametrically using Mann-Whitney U-test. SPSS for Windows (versions 23 and 24, SPSS inc., Chicago, IL, USA) was used for statistical analyses.

Results

The median concentration of total-Hg in whole blood was 0.40 µg/L (min, max; <0.40, 1.88) among the 51 pregnant women in Kiruna. Mean age of the women was 29 years (min, max; 20, 42) and median body mass index before the pregnancy was 24.3 kg/m² (min, max; 18.6, 41.3). All women, except one, had finished high school (“gymnasiet”) and 28.8 % of the women had completed a university degree (Table 2).

**Determinants of mercury concentrations**
Mercury concentration was associated with total fish consumption (p<0.001), but not with consumption of predatory fish, fatty fish from the Baltic Sea or consumption of reindeer meat (proxy for traditional Sami diet) (Table 2). Higher education was associated with higher concentrations of mercury; median concentration was 0.40 µg/L for those with high school education or lower and 0.80 µg/L for those with completed or on-going academic education. Those with higher education had higher fish consumption (median fish consumption was once a week for those with completed or on-going academic education compared to 0.5 times/week among those with lower education). Those with amalgam fillings (n=6) had higher median mercury concentration, 0.80 µg/L compared to 0.40 µg/L in those with no amalgam fillings, but the association between having amalgam fillings and mercury concentration was not statistically significant (Table 2).

Fish consumption and compliance to dietary advice on fish consumption
All women responded that they were aware of the dietary advice on fish consumption. Median total fish consumption was once per week (25th and 75th percentile; 0.5, 1.0 times/week). Eight of the women (15.4 %) followed the dietary advice of total fish consumption (2-3 times/week) and none reported a higher consumption. Only one woman reported eating predatory fish 1-3 times/month (limited in the dietary advice to a couple of times a year for pregnant due to risk of high content of methylmercury) and five women reported eating fatty fish from the Baltic sea 1-3 times/month (limited in the dietary advice to a couple of times a year for pregnant due to risk of high content of persistent organic pollutants) (Figure 1).

Of the women, 9 (17.3 %) reported consumption of reindeer meet at least once a week (Figure 1).

Of the women, 46.2 % had changed their fish consumption due to the dietary advice appointed to pregnant women and this percentage was higher in the highest quartile of Hg-concentration. For those in the highest quartile of Hg-concentration it was common with decrease of intake of fish species limited in the dietary advice (Table 3).

Comparisons with other Swedish studies on mercury in pregnant women
The median concentration of total mercury was similar to concentrations previously found in pregnant women in Sweden. Concentrations have been found to decrease during the 1990ties
in the general population [9], and this is also the case in pregnant women with somewhat higher median concentrations found in the older studies (Figure 2).

Discussion

Main findings
Pregnant women in circumpolar Sweden have low concentrations of mercury in blood, even somewhat lower compared to other previous studies of pregnant in Sweden. None of the women in this study had a mercury concentration that can be considered detrimental.

Mercury concentration was associated with total consumption of fish, but not to predatory fish, known to be especially high in methylmercury. The reason is likely that consumption of predatory fish was very low among the pregnant women and that methylmercury is present in all fish, although often in low concentrations.

Reindeer meat, here used as a proxy for a traditional Sami diet, could not be associated with mercury concentrations, indicating that people with a traditional Sami diet are not more exposed to mercury compared to the rest of the population.

Dietary advice on fish consumption
All women in this study were familiar with the dietary advice on fish consumption appointed to pregnant women and very few exceeded the limits; only one woman for predatory fish high in mercury and this was not reflected in the mercury concentration. One woman had increased the consumption of fatty fish from the Baltic Sea to 1-3 times per month, which is above the recommended a couple a times a year for women in fertile age. This woman had a low mercury concentration, but persistent organic pollutants, which is the reason for a dietary advice on fatty fish from the Baltic Sea, were not measured in this study. It was found that those with the highest mercury concentration had limited their consumption of polluted fish the most, indicating that the dietary advice on fish consumption to pregnant are well communicated. However, it cannot be ruled out, that the midwifes working in this study was especially careful to communicate the dietary advice on fish consumption, knowing that they participated in a study on mercury, and thus the compliance to dietary advice may not be
representative to pregnant women in Sweden or not even to pregnant women in circumpolar Sweden.

A majority (85 %) of the women did not reach the recommendation of eating fish 2-3 times/week. This is of concern for public health, because fish is an important source of several nutrients of importance to the developing fetus [10].

Mercury concentrations in relation to other studies on pregnant women
Mercury concentrations were similar as in previous studies on Swedish pregnant women. Concentrations decreased during the 1990ties but have not evidently decreased further after that. In relation to women from the other circumpolar countries, the Swedish women had the lowest concentration, and there were other populations with concentrations above recommended (Vachon J et al. manuscript under preparation) indicating that mercury is still a problem in these populations.

Limitations
In this study, total-mercury was measured in whole-blood. Thus, it cannot be ruled out that some of the mercury have other exposure sources than fish, such as inorganic mercury from amalgam fillings. Few women (n=6) in his study had amalgam fillings and therefore this limitation can be considered as minor.

Strengths
The participation rate was 100 percent, that is, the participants must be considered as representative of pregnant women in Kiruna. The risk of pregnant women in Sweden not enrolling in maternal care must be considered very low, but can of course not be completely ruled out.

Conclusions
Dietary recommendations on fish consumption are well known and mercury exposure is not of concern in pregnant in circumpolar Sweden, where concentrations are similar as in the rest of the country. Low fish consumption during pregnancy is of public health concern.

Acknowledgment
We thank the Swedish Environmental Protection Agency for financing this project. We also thank Julien Vachon, Mélanie Lemire, Catherine Pirkle and Pierre Ayotte in the collaboration Arctic Monitoring and Assessment Programme (AMAP) for coordinating the international report.
References

3. (EFSA) EFSA: Scientific opinion on the risk for public health related to the presence of mercury and methylmercury in food. *EFSA Journal* 2012, **10**:2985.
Table 1. Quality control by Québec Multielement External Quality Assessment Scheme

<table>
<thead>
<tr>
<th>Reference material</th>
<th>QM-B-Q1108</th>
<th>QM-B-Q1201</th>
<th>QM-B-Q1302</th>
<th>QM-B-Q1505</th>
<th>QM-B-Q1512</th>
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</thead>
<tbody>
<tr>
<td>Expected value ± 1σ (nmol/L)</td>
<td>66.2 ± 4.4</td>
<td>27.4 ± 1.4</td>
<td>7.68 ± 0.51</td>
<td>28.3 ± 2.5</td>
<td>65.2 ± 6.5</td>
</tr>
<tr>
<td>Measured value</td>
<td>63.3 ± 3.9</td>
<td>26.4 ± 1.42</td>
<td>7.15 ± 0.78</td>
<td>28.4 ± 0.85</td>
<td>59.6 ± 2.12</td>
</tr>
<tr>
<td>Number of samples</td>
<td>15</td>
<td>26</td>
<td>7</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
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Table 2. Baseline characteristics and associations between potential sources of Hg-exposure or other factors and mercury concentrations in blood in pregnant women in Kiruna

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Low Hg (Q 1-3)</th>
<th>Higher Hg (Q 4)</th>
<th>p-value All</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Potential sources of Hg-exposure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fish, intakes/wk</td>
<td>52</td>
<td>1.0 (0.50, 1.0)</td>
<td>0.50 (0.50, 1.0)</td>
<td>1.0 (0.62, 2.13)</td>
</tr>
<tr>
<td>Predatory fish, intakes/wk</td>
<td>52</td>
<td>0 (0, 0.05)</td>
<td>0 (0, 0.05)</td>
<td>0 (0, 0.04)</td>
</tr>
<tr>
<td>Fatty fish from the Baltic Sea, intakes/wk</td>
<td>52</td>
<td>0 (0, 0.05)</td>
<td>0 (0, 0.05)</td>
<td>0.05 (0, 0.05)</td>
</tr>
<tr>
<td>Reindeer meat, intakes/wk</td>
<td>52</td>
<td>0.05 (0.05, 0.50)</td>
<td>0.05 (0.05, 0.50)</td>
<td>0.05 (0.05, 0.50)</td>
</tr>
<tr>
<td>Amalgam fillings, %</td>
<td>52</td>
<td>11.5</td>
<td>7.69</td>
<td>25.0</td>
</tr>
<tr>
<td><strong>Other factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y (SD)</td>
<td>52</td>
<td>28.7 (4.53)</td>
<td>27.9 (4.01)</td>
<td>31.1 (5.53)</td>
</tr>
<tr>
<td>BMI, kg/m³</td>
<td>52</td>
<td>24.3 (22.4, 27.9)</td>
<td>25.6 (23.0, 28.3)</td>
<td>24.4 (21.7, 27.4)</td>
</tr>
<tr>
<td>Academic education, %*</td>
<td>52</td>
<td>44.2</td>
<td>35.9</td>
<td>75.0</td>
</tr>
<tr>
<td>Income &gt; 24 000 SEK, %</td>
<td>51</td>
<td>56.9</td>
<td>53.8</td>
<td>63.6</td>
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<tr>
<td>Household income &gt;35000 SEK, %</td>
<td>48</td>
<td>83.3</td>
<td>80.6</td>
<td>90.9</td>
</tr>
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</table>

*Finished or on-going academic education
Table 3. Proportions with varying change in fish consumption during pregnancy in all participants and in those with low and higher mercury concentrations separately.

<table>
<thead>
<tr>
<th>Change in fish consumption</th>
<th>All</th>
<th>Low Hg (Q 1-3)</th>
<th>Higher Hg (Q 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>51</td>
<td>27.4</td>
<td>21.1</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>51</td>
<td>21.1</td>
<td>50.0</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>50</td>
<td>15.7</td>
<td>25.0</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>51</td>
<td>13.2</td>
<td>11.8</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>51</td>
<td>7.89</td>
<td>25.0</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>50</td>
<td>24.0</td>
<td>45.5</td>
</tr>
<tr>
<td>Median (25th, 75th percentile)</td>
<td>52</td>
<td>20.5</td>
<td>58.3</td>
</tr>
</tbody>
</table>
Figure 1. Consumption frequencies of total fish, predatory fish, fatty fish from the Baltic Sea and reindeer meat.

Figure 2. Median mercury concentrations in blood (µg/L) in studies on pregnant women in Sweden [11-14].