Author's response to reviews

Title: Mercury in human brain, blood, muscle and toenails in relation to exposure

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Author's response to reviews: see over
To the Editorial Team

We are grateful for the comments from the Editorial Team and the reviewers. Below, please find a point-by-point response.

**A. Response to comments from the Editorial Team**

There is no material left for analysis of hemoglobin in blood. Thus, we can not adjust for hemoglobin concentration in blood.

In the Discussion section (p. 13) we have included “Although the number of amalgam surfaces at the time of death do not reflect lifetime cumulative exposure to Hg0 or dental amalgam restorations, there was a significant correlation between amalgam surfaces at the time of death and concentration of I-Hg in brain at the time of death. This suggests that the biological half-time in the brain of the main fraction of Hg stored in brain after low level Hg0 exposure from dental amalgam restorations and other low level environmental sources is relatively short and that other environmental sources have limited importance at a group level.”

Language/grammar check: Appropriate revisions are made (pg 4, pg 6).

The references are checked according to the instructions to authors.

Table titles appear above the tables and all rows and columns are visibly distinct.

A list of abbreviations is now included.

**B. Response to comments from the reviewers**

**Reviewer 1 (Alan Stern)**

*Major Compulsory Revisions:*

In the new version of the manuscript we have included a statement both in the Methods section and in the Results section that mercury content was related to the wet weight of the sample.

In the Methods section we have included details on sampling of toenail: “Generally, nails were clipped prior to the autopsy, and only small samples with a length of about
1 mm were available for collection. Clippings were collected from all toenails using a stainless steel scissors. Samples between 7.6 to 68 mg were used for analysis.” In the section with details on the analyses of mercury by ICP-SFMS we have added “The toenails were not cleansed before analysis.”

Some aspects of the MeHg/total-Hg ratio are now discussed in the Discussion section and a new reference is included (Passos et al, 2007).

The correlation coefficient between total-Hg in toenails and MeHg in blood is now included in the text.

Pg. 15, last line: We have added “addition to the differences in toxicokinetics of I-Hg in blood and brain”

Pg. 18, par. 1: We have added “---low total capacity, ---“ and “Alternatively, there is a mercury induced selenium dependent mechanism resulting in a formation of highly insoluble mercury selenide which could explain the observations.”

Pg. 20, par. 2: The discussion on the interpretation of mercury in toenail clippings is extended (pg. 13-14 and pg. 19) in the revised manuscript.

**Minor Essential Revisions:**

Results from the correlation analysis is now included as an ordinary table (Table 3) in the manuscript.

Pg. 7, par. 2: “Calculated” is changed to “estimated”

Pg. 11: In the Correlation Coefficients Table data are given for correlations between a number of variables including concentration of I-Hg in blood and number of surfaces filled with amalgam. The upper part of the table (above the diagonal) shows the correlations using all cases (n=30) and the lower part (below the diagonal) shows the correlations after exclusion of case #28.

Pg. 12, par. 3: Results from a regression model for Total-Hg in toenails are now included in Table 4.

Pg. 14, par. 2, sentence 2: The sentence is removed.

Pg. 16, par. 1: Case number is given.

Pg. 16, par. 2: A possible effect from variations in selenium status on I-Hg in brain needs further analyses.

Pg. 19: “as well as fish consumption” is added in the Conclusions
Reviewer 2 (Pál Weihe)

Discretionary Revisions:

Detailed information on dietary habits (seafood consumption) was not available in the hospital record.

The study was initially designed to focus on biomarkers of inorganic mercury exposure. Analyses of organic mercury in blood were included in the study as being the main biomarker for MeHg exposure. Because MeHg was not the primary focus, analyses of hair was included in the study.

Historical hospital records were not checked for the other cases. This is now mentioned in the new version of the manuscript.

Pg 10, par. 2: We have added “Contrary to blood from vena femoralis, samples from heart blood were highly inhomogeneous due to extensive coagulation and we did not consider the concentrations obtained in those samples as reliable. Thus, no data are presented for heart blood.” In the Methods section we have described the treatment of the samples which includes solubilization (homogenization) of samples due to technical requirements.

The wording of the aim of the study in the abstract and in the section “Background” is brought in accordance.

In the revised manuscript we have included more discussion on total mercury in toenails as a biomarker for MeHg stored in the body.

Sincerely,
Lars Björkman