Reviewer's report

Title: Association between the plasma/whole blood lead ratio and history of spontaneous abortion: a nested cross-sectional study

Version: 1 Date: 19 April 2007

Reviewer: Victor H Borja-Aburto

Reviewer's report:

General

This is an original study that evaluates for the first time the plasma/whole blood lead ratio as a marker of susceptibility for the toxic effects of lead exposure. This hypothesis is based on the fact that the plasmatic fraction is the toxicologically active fraction of lead. Therefore, women with higher plasma/whole blood lead ratio would have an higher risk of miscarriage due to higher plasma lead crossing the placental barrier for a given whole blood lead.

Since the risk of spontaneous abortion was evaluated retrospectively and plasma lead has a large inter-individual variability the authors suggest that this variability makes it difficult to find associations with current plasma lead measurements. In contrast plasma/whole blood lead ratio could be influenced by polymorphic alleles of genes coding for proteins involved in the partitioning of circulating lead and would be stable over time.

The authors analyzed data from two cohorts with up to date methods for blood and plasma lead measurements. There are no major concerns of selection or information bias.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors based their conclusions on the direct evaluation of the effect of the mentioned ratio; however, there is no mention of any assessment of the effect of whole plasma or bone lead on spontaneous abortion stratified by the ratio of plasma/whole blood lead. The statistical advantage of the simultaneous consideration of the susceptibility marker and the current lead exposure as an interaction term in the model would add to the evaluation of the postulated hypothesis that the partitioning modulates the effect of lead exposure. If there is a problem with the statistical power to identify the ratio-current exposure interaction, this could be mentioned in the discussion.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

The description of the Poisson model used could be shortened.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

Level of interest: An article of outstanding merit and interest in its field.

Quality of written English: Acceptable.

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests