Reviewer’s report

Title: Para-occupational exposure to pesticides, PON1 polymorphisms and hypothyroxinemia during the first half of pregnancy in women living in a Mexican floricultural area.

Version: 0 Date: 22 Dec 2018

Reviewer: Robert Barouki

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The study shows that paraoccupational exposure to pesticides does not appear to be significantly correlated with hypoparathyroxinemia. However, the authors observed that certain PON1 polymorphisms are correlated to hypothyroxinemia. The topic (role of the maternal thyroid function in early pregnancy) is highly relevant, but the study is essentially observational.

Comments:

- There are two different investigations in this study: one attempting to correlate paraoccupational exposure to pesticides (in a highly exposed region) to thyroid toxicity, the other assessing the possible interaction between PON1 polymorphisms and thyroid function. The link is that PON1 is involved in the metabolism of organophosphates (OP). But it should be stressed that PON1 has many other functions and the effects of the genetic polymorphisms of PON1 may be correlated to cardiovascular outcomes and possibly to differences in pesticide metabolism.

- I am puzzled by the frequency of hypothyroxinemia in pregnant women in this study. More women have low T4 than normal levels. How does this compare to other studies?

- The evidence for a role of OPs in this study is not sufficiently supported. The authors did not assay OPs through biomonitoring for budgetary reasons. They do not have evidence for the actual pesticides that are used by the workers. Maybe they do not all use OPs (?) and this could make a difference in statistical analysis.

- Because of the number of studied individuals, the number of actual hypothyroidism is low. The clinical characterization of the individuals with high TSH is lacking.

- The observed correlation between PON1 polymorphisms and hypothyroxinemia is interesting although it is quite descriptive at this stage. There could be some biases as mentioned by the authors since the hypothyroxinemia group differs from the control group in many respects.

This study addresses some important questions. There are some interesting observations but none has been explored sufficiently. Assessing OP levels at least in a subgroup of individuals would
improve the study as well as a better characterization of the type of pesticide used if this information is available.

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