Author's response to reviews

Title: Immune cell counts and risks of respiratory infections among infants exposed pre- and post-natally to organochlorine compounds: a prospective study

Authors:
Anders Glynn (anders.glynn@slv.se)
Ann Thuvander (ann.thuvander@socialstyrelsen.se)
Marie Aune (marie.aune@slv.se)
Anders Johannisson (anders.johannisson@afys.slu.se)
Per Ola Dårnerud (poda@slv.se)
Gunnar Ronquist (gunnar.ronquist@akademiska.se)
Sven Cnattingius (sven.cnattingius@ki.se)

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Author's response to reviews: see over
Dear Editor-in-Chief

We resubmit the manuscript “Immune cell counts and risks of respiratory infections among infants exposed pre- and post-natally to organochlorine compounds: a prospective study” to EH after revision. Below are the answers to the comments included in the e-mail from the Editorial Team.

1. In regard to items 3 and 12, it seems that you have information on the time of infections. You should therefore be able to exclude subjects with a current infection, which would seem appropriate. Please clarify.

We have now reanalysed the immune cell results. We excluded the 6 infants who had an ongoing infection or had an infection within 7 days before sampling. The tables and figures have been revised with the new results and the information about this exclusion is now present in the Calculations and statistics section on page 10, beginning of 2nd paragraph. The Abstract, Results and Discussion sections have been revised in light of the new results.

2. In regard to item 6, it is unclear how you calculated the participation rate (49%) from the number of participants (86) and the total number eligible (149). Moreover, you also explain that not all subjects could be examined due to lack of funds. So it seems that some of the eligible subjects were not contacted. Please explain.

We have now gone back to our files and corrected the numbers regarding the participation rate (see page 6, last paragraph).

3. On item 7, the exclusion of subjects with less than 3 days of infection should be mentioned in the Methods as well. You did not address our concern that the interval since last infection might be a confounder. Should these children be excluded? In none had had an infection within the last several days, please state that.

On page 12, 1st paragraph in the Methods this use of a stricter definition of infection is mentioned. We do not understand the comment that the interval since last infection could be a confounder in the analysis of associations between OC exposure and infections. We think that in the infection part of the study the infants with ongoing infection at the end of the observation period should not be excluded. The exclusion of infants with an ongoing or recent infection in the immune cell part is understandable since recent or ongoing infection could affect the immune cell results.

4. In regard to postnatal exposure (item 8), the lipid content would seem an important factor in determining the milk intake.
of an infant. If you have reasons to rely on volume as the determining factor, please provide a reference.

When doing an OC intake calculation from mothers’ milk the infants’ cumulative OC intake is the product of the OC concentration of the mothersmilk (per gram fresh weight), the amount of milk consumed per day (in grams), and the number of days of nursing. We did not have information about the amount consumed, instead we had information about the degree of nursing each week (full, partial or none). Consequently, the degree of nursing was used instead of the amount of mothers’ milk consumed in the intake calculation. We included this explanation in the Calculations and statistics section on top of page 9. Some references about this have also been included.

5. This journal does not, in principle, have any space limitations. We consider it important that all methods are described in the Methods section. Please insert information how the TEQ were calculated and provide a reference to the TEFs used (item 9).

We have included information about this, and a reference, on page 10, 1st paragraph.

6. Thank you for inserting the information on the covariates on p 10 (item 11). Please clarify what you mean by “infections during the period before sampling”. Do you mean a past history of infection? We need a similar explanation on the covariates for the infection analyses (subsequent paragraph), perhaps just by saying that you used the same covariates, except for a past history of infection.

We have clarified that we mean history of infection up to 7 days before sampling on page 11, end 1st paragraph. On page 11, end of last paragraph, and page 12, beginning of first paragraph, explanation of the covariates for the infection analyses have been included.

7. On item 13, we prefer exact p values, if possible.
We have changed it to the exact p values (page 13, last paragraph).

8. In regard to item 16, because your study is small, it is very important that the results are presented so that comparisons and combined analyses with other studies becomes possible. You note this possibility and that previous studies have used measures of “total PCB and CBV-153 as exposure biomarkers. We urge you to present the results using comparable exposure indicators, either in the text or in the tables. This information could also be included in the Abstract.

We have included results for CB-153 in Tables 2 and 4, and in the additional files in Tables A-E. Information about the results are presented in the Abstract, Results and Discussion sections.
9. In regard to formatting requirements previously communicated, please shorten the heading to "Abbreviations". Please follow the instructions in regard to the requested short titles for the figure legends. We discourage the use of bold types for numbers in the tables, the asterisk should be sufficient.

We now have short titles for the figures of maximum 15 words and detailed legends of maximum 300 words. Bold types for numbers have been omitted.

Best regards

Anders Glynn