

Reviewer's report

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

Version: 1 **Date:** 10 September 2008

Reviewer: B. Paige Lawrence

Reviewer's report:

* Comments and Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

This manuscript presents an exploratory study aimed at refining our understanding of the association between exposure to environmental contaminants and children's health. This is an important and timely question. For this study, 10 organochlorines were selected and divided into 4 broad categories: two separate groups of non-dioxin-like PCBs, dioxin-like PCBs, and p,p'-DDE (a metabolite of DDT). A clear rationale for these groupings is provided. Levels of each of these compounds were measured in breast milk (to estimate post-natal exposure) and maternal serum during late pregnancy (which was used to estimate pre-natal exposure).

Based on the findings presented, the authors suggest that prenatal exposure to tri- to pentachlorinated PCBs may be associated with immune suppression, whereas exposure to mono- and di-ortho PCBs may cause "immunoactivation." Given that the only read-outs were the percent and number of different leukocyte subsets in the infant's serum and the incidence of reported respiratory illness, the data do not strongly support these conclusions. To the authors' credit, they candidly point out many caveats in the interpretation and utility of their findings. Indeed, they frankly note that the small size of this study, further attrition of samples due to technical and financial constraints, and possible reporting errors by the mothers are concerns. An additional weakness that the authors are encouraged to incorporate into their thinking is that the study was not designed to assess immune enhancement (i.e., Reduced incidence of respiratory infection doesn't necessarily mean that the immune system is more stimulated. Indeed, there are many other factors that could account for this--especially when examined only at a single point in time). Another concern is that disease diagnosis was not confirmed using medical records (as an aside, perhaps using the term influenza is therefore misleading as no confirmation of this specific illness was included). Despite these concerns, these findings are intriguing and clearly warrant more in-depth study.

To clarify their findings and make them a bit easier for readers to appreciate, 3 suggestions on data presentation follow:

- In Figures 1 and 2, it is not clear why mean lipid concentrations (ng/g lipid) are divided up into <3, 3.1-5.7 and #5.8. The middle group represents a rather small

range while the upper group reflects a rather large range. An explanation of this division would be welcome (perhaps this relates to the next comment?)

- Table 2 is somewhat confusing. In particular, the sub-division of mean organochlorine concentrations in serum and breast milk into the 3 columns "Infections," "white blood cells" and "lymphocytes" is not clear.
- It is a bit difficult to reconcile the data in Figures 1 and 2. In Figure 1, the number of lymphocytes is elevated in serum from subjects in the highest PCB level group; however, when the different lymphocyte subsets are analyzed, none of the subsets account for this increase (nor is there a slight increase in all subsets).

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

There are two minor essential revisions:

(1) All of the figures and tables present findings from "3 month-old infants exposed to organochlorines post-natally." It is not clear to me how prenatal exposure is removed from these data. Were not all infants exposed both pre- and post-natally? Explanation of this could be more explicit.

(2) Overall the paper is well written; however, there are some minor grammatical errors throughout the paper.

* Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

While the authors' candor about the limitations of this study is a strength of this manuscript, they may want to consider revising the way in which this is presented. For instance, on page 14, the statement that these results do not allow for firm conclusions (which I agree with) comes across so strongly that it dampens enthusiasm for the study all together. In its current form, the Discussion runs the convincing the reader that this report is too premature to be informative.

The idea that in utero exposure can enhance some aspects of immune function while impairing others is supported from work in animals, but this work is not cited here. For example, see Vorderstrasse et al (2004) Journal of Immunotoxicology (vol 1(2): 103-112) and Vorderstrasse et al (2006) Journal of Toxicology and Environmental Health, part A (vol. 69: 1-19). These findings may bolster observations reported here because, although in mice, they directly examine respiratory immune responses to influenza virus infection.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.