Reviewer's report

Title: Early life microbial exposure and fractional exhaled nitric oxide in school-age children: a prospective birth cohort study.

Version: 1 Date: 2 July 2013

Reviewer: Elisabet Johansson

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This manuscript communicates an interesting and topical study on the effects of early-life indoor microbial exposure on FeNO levels later in childhood. FeNO is considered a marker of eosinophilic airway inflammation, and is increasingly used in the diagnosis and management of asthma, but so far there have been few studies of how FeNO is influenced by microbial exposures, especially of indoor origin, that have been shown to be associated with allergic airway diseases. The manuscript is well-written and well organized, and the methodology appears to be appropriate. As discussed by the authors, the main limitation of the study is the heterogeneity of the three cohorts included.

SPECIFIC COMMENTS

Minor essential revisions:

1. Although the authors refer to the ATS guidelines in the methods section, a brief description of the FeNO measurements should be included. Were the FeNO values based on a single measurement, or the mean of several? Were children prescribed asthma medications excluded from the study?

2. Were any of the measurements below the LOD for the NIOX MINO device? If so, how were those measurements treated statistically?

3. The combined random-effects adjusted coefficient for endotoxin and its 95% CI given in table 3 do not agree with the text in the abstract and in the results section (p. 13).

Discretionary revisions:

4. On p. 15 the authors state that FeNO was higher in asthmatic and allergic children, but the data are not shown. Since this is a key finding that validates the measurements in any study of eNO levels, I suggest adding these data to the results section, e. g. in Table 2.

5. For the sake of clarity, the authors may want to rephrase the last sentence on p.14 (Similarly, no statistically significant associations……..). E. g. “ In this study, no statistically significant associations were found…..”. As the authors mention in the introduction, some recent studies have found associations between early exposure to mold and later asthma development. What could be the reason for the conflicting results of the various studies including this one? The authors might want to add some discussion about that.
6. The authors state on p. 15 that there were no differences in the associations between endotoxin and dog exposure and FeNO according to the report of asthma or allergy. In the manuscript, the results for all study subjects are compared to the results for the non-asthmatic subjects as shown in Table E3. However, since only a small number of the study subjects were asthmatic, it is to be expected that the results for the all study subjects and the results for non-asthmatics would be very similar. Were coefficients obtained for the group of asthmatic children alone? If not, was this due to limited power?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.