Reviewer's report

**Title:** Effect of praziquantel treatment of Schistosoma mansoni during pregnancy on immune responses to schistosome antigens among the offspring: results of a randomised, placebo-controlled trial.

**Version:** 2  **Date:** 20 May 2011

**Reviewer:** Daniel Colley

**Reviewer's report:**

This is a generally well-organized and written manuscript that describes a challenging, but important study of the impact of praziquantel treatment of Schistosoma mansoni-infected women during pregnancy on the immune responses of the child of that pregnancy at birth and one year later. It is difficult to overstate the logistical challenges and difficulties of doing such a study in an area endemic for schistosomiasis over this period of time. The findings are not dramatic, but that does not make them any less important. This is information that is needed and the study is soundly based on questions raised in the literature in this field.

Discretionary Revisions

1. Methods, Whole blood culture and….., last line. It would be useful to some readers if the authors would provide at least the range of control cytokine levels that were subtracted from the antigen-stimulated levels. Were they highly variable? Were they substantial? If so, were there differences between groups?

2. The actual levels of eggs/gram of stool would be of considerable interest to some readers, and while it is impossible to give them all, at least a median and a range might be useful.

3. The Journal may not wish to do so, but for me the “Additional Files” contain valuable information that adds to an understanding of the manuscript. If possible I would recommend their inclusion in the manuscript proper.

Minor Essential Revisions

1. Results – cord blood cytokine responses. The responsiveness of the cells of 29% to 33% of the cord bloods to make IFNg and IL-2 and 58% to make IL-10 seems significant, but the authors rather dismiss this antigen-stimulated responsiveness. This seems odd to me. The IL-10 responsiveness is dismissed as being due to non-lymphoid cells, but as I understand the Methods section this is the level of IL-10 produced by stimulation with either SWA or SEA – with the levels produced without SWA or SEA subtracted out, i.e., representing the antigen-specific responsiveness. This confuses me, and I think the authors should reconsider their explanation and think in terms of what these presumably antigen-specific responses mean. A more trivial explanation which they might be able to address, is that there are traces of LPS in the antigen preparations – then
the non-lymphoid source of IL-10 would make more sense.

2. Abstract, Results; Results, 2nd paragraph; Results, last paragraph; Discussion, 5th paragraph. The authors state, in several places, that there is no evidence that any of the 1 year olds are infected with S. mansoni. I would submit that their own data argue against that conclusion. What would be correct would be to say that all the stool examinations by Kato-Katz (and they do not say in the manuscript how many were done) were negative for S. mansoni eggs. It is well known and has been documented many times that egg-positivity can often be a matter of how many stools and slides are examined. The IgG1 and IgE antibody responses to SEA, which the authors find “surprising” (last paragraph/Results), are not at all surprising to me. In fact, based on other literature from Ugandan lakeside villages, they are rather expected in a proportion (the authors only state “a number” but Figure 3D makes the IgG1 look like at least several) of 1 year olds in a such a setting. Early infections in this setting are much more common than previously thought, and a paper from Kenya indicates that anti-schistosome (in this case anti-worm) antibodies are detected before eggs are numerous enough to detect in the stool. If I might conjecture further, if a 6 or 8 month-old infant is exposed to S. mansoni cercariae their worm burdens by 1 year of age may still be quite low, although their one or two worm pairs might have been producing eggs for 4 or 5 months, which would fit nicely with the authors observations that anti-SEA levels are greater than anti-SWA levels. I strongly suggest that the authors reconsider their conclusions that none of their 1 year-olds are infected, and if possible it would be of interest to re-examine those who are anti-SEA+ (for IgG1 and IgE) in terms of their mother’s status (intensity), etc. It is quite likely that there is nothing more there than they already report, but this subgroup that I believe did get infected during their first year of life (based on their responsiveness) might be worth a second look.

3. Results, paragraph 14. The authors refer to Tables 4 and 5, but I can only find Table 1 and Additional File 1. This needs to be sorted out.

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

**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.