Reviewer's report

Title: Association between congenital toxoplasmosis and parent-reported developmental outcomes, concerns, and impairments, in 3 year old children.

Version: 1 Date: 4 January 2005

Reviewer: Gary Holland

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Minor Essential Revisions

1. Is it possible that the results reflect perceptions on the part of the parents more than true disease findings? There should be a clearer explanation of the extent to which this questionnaire has been validated. That is, is it truly known that parents’ answers provide the same information that would be found on a clinical examination by a child’s physician? The authors suggest this questionnaire has been validated against clinician examinations, but a review of the reference cited on page 7 (their reference 11; Salt, et al.) indicates that while the concept and components of parental questionnaires has been validated, this specific questionnaire has not. Furthermore, in the cited reference (page 3 of the draft manuscript of Salt, et al), it is stated that the validity across different countries is not known. These issues should be clarified in this manuscript.

2. The measures used for assessing vision loss are probably not sensitive enough or specific enough for this purpose. The need for glasses and the presence of strabismus are common in children whether or not they have retinal infection. The results might differ if they assess loss of vision despite glasses or loss of vision despite strabismus surgery. The investigators probably do not have that information, but it would be appropriate to discuss this limitation of their data.

3. In the authors’ reference 11, questions about vision had among the lowest response rates. That also should be mentioned among the factors that possibly affected results.

4. The authors should provide additional discussion of the issue of age at questionnaire completion. The questionnaire was only sent to subjects who were 3 years of age. From the texts and tables, the variation being analyzed appears to be related to the delay in returning the questionnaire after receiving it at 36 months of age. Is there a clinical explanation for a different results based on different ages, or is it somehow a reflection of parental motivation or thoroughness (i.e. results would differ whether or not parents returned the questionnaire immediately)?

5. On page 10, why would maternal age be expected to have a significant effect on parental reports of developmental outcome? (The authors state this fact as being expected).

6. On page 10, why would outcomes vary by site? Is it a real difference in disease or is it an artifact?

7. Although the information may be available in the references cited, it would help readers of this paper if the authors would provide at least brief definitions of key terms like behavior abnormalities.

8. On page 13, the authors discuss issue of bias based on the child’s condition before 4 months of age, and conclude a lack of bias. Why would that information not affect results? If serious problems were present before 4 months of age, would not there be developmental or visual problems later? The lack of relationship might be surprising to some readers and should be a
subject included in their discussion.

9. On page 7, there is a probable typographical error in the first sentence under Analyses. The words “Women suspected to have acquired” were probably meant to be deleted.

10. On page 6, the authors discuss the fact that 21 infected children were lost to follow-up, and thus were not included in these analyses. In view of the low rates of adverse events reported, these 21 cases might have had a significant affect on results, had they been available for inclusion. The authors may wish to discuss that potential problem as well. Also, in a review of their reference 11, I found mention of 17 patients (not 21) lost to follow-up in Figure 1 of that manuscript. Clarification is warranted.

11. The authors need to review the references carefully. There are many duplications of references in their reference list. For example, references 7, 9 and 12 are duplications of reference 5, while reference 23 is a duplication of reference 15 (these are examples, I did not compare exhaustively). It is possible that there is some problem with their referencing software; in addition to the duplications, some of the references do not appear to be appropriate. On page 10, line 5-7, they cite reference 7 when discussing details of the questionnaire, but reference 11 would seem to be the correct citation. As another example, they cite reference 17 when discussing validation of their questionnaire on page 8, but that manuscript is about eye disease.

Discretionary Revisions

1. It would be interesting to know whether the investigators compared known lesions found during infancy to questionnaire results. For example, was there a good relationship between eye lesions present at less than 4 months of age and vision impairment at 3 years of age? Was there a relationship between intracranial calcifications and behavioral or developmental problems? The manuscript does not provide analysis at that level of detail.