Reviewer's report

Title: Differential Diagnosis of Tuberculous meningitis from partially treated cases of pyogenic meningitis by Cell ELISA.

Version: 2 Date: 26 May 2004

Reviewer: Guy Thwaites

Reviewer's report:

General
This manuscript describes an assessment of the diagnostic performance of a cell ELISA to a 30Kd protein in the CSF of 24 patients: 12 with tuberculous meningitis, and 12 with presumed partially treated pyogenic meningitis. The diagnosis of tuberculous meningitis is difficult and new methods, such as that described by the authors, are urgently required. However, without revisions it is difficult or impossible to conclude whether this method may be a useful future diagnostic test.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The methods section requires substantial revision. More details regarding the Hospital setting (primary, secondary, or tertiary referral centre) and the methods for recruiting patients are required. Were patients selected prospectively and consecutively, or were they selected retrospectively? Were all the CSF specimens from the TBM patients taken before the start of anti-tuberculosis treatment? The diagnostic criteria are extremely loose, such that it may be difficult to be sure patients with TBM are truly being compared with PTPM. More clinical data (duration of history, peripheral white cell counts, and radiological evidence from both chest and brain) than given in table 1 and 2 would be helpful. The concentration of glucose in the CSF should be compared with that in the plasma, but the plasma values are not given. All the clinical data could be presented in one table. It is unclear whether the 30 Kda was prepared from the CSF of patients in this study, or another group. I assume the later, but if it were the former it would have major implications for the interpretation of the results. Please clarify how the antigen was prepared.
The results section and the figures are very confusing, particularly as Figure 1 is not referred to in the text, and the reference to Figure 2 in the text appears incorrect. Figure 1 seems to come from a different manuscript and the legend contains inexplicable reference to 92 patients. The confusion continues to table 3, which is headed, 'prevalence of Anti CFP IgG antibodies', and plainly does not give the ELISA absorbance values as suggested in the text. The authors conclusions regarding the diagnostic utility of this assay are dependent upon the absorbance cut-off they use for the detection of 30Kda IgG, but how they arrived at the cut-off, and the value they used, are not given. This should be explained. The authors have also calculated specificity incorrectly: it should be 11/12 (92%), not 93%.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The mislabelling of figures and tables must be corrected, as stated above.

Discretionary Revisions (which the author can choose to ignore)
Please give absolute numbers in the abstract and elsewhere, not just percentages. The citation of reference 4 in the first paragraph does not appear to relate to the text. Expand on why (background, para 2) the performance of ELISA for the diagnosis of TBM 'is sometimes debatable'. Cut para 3 from the background to make room for this discussion. The conclusions should be far more cautious. There are limited data in this manuscript to suggest...
the assay, 'is very useful in the differential diagnosis of TBM from PTPM.' The assay represents an interesting new approach to the diagnosis, but needs a much larger and more rigorously designed clinical study before these bold conclusions can be made.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**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:** No

**Declaration of competing interests:**

None