**AUTHOR REPLY**

# Reply to "A Word of Caution in Considering the Use of the Lipoarabinomannan Lateral Flow Assay on Cerebrospinal Fluid for Detection of Tuberculous Meningitis"

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In their letter, Bahr and colleagues report their inability to detect lipoarabinomannan (LAM) in the cerebrospinal fluid (CSF) of patients with tuberculous meningitis (TBM) by using a lateral flow assay (Determine TB LAM; Alere, Waltham, MA, USA). Several studies have shown LAM positivity in the CSF of patients with TBM by using an enzyme-linked immunosorbent assay for antigen detection (1, 2). The lateral flow assay (LFA) that was used in our study and in the study by Bahr et al. for LAM detection is an immunochromatographic assay that attaches colloidal gold-labeled antibodies to LAM (3, 4). These complexes are captured by immobilized LAM antibodies further along the test strip and form a visual band. A number of test and sample properties determine the accuracy of a lateral flow assay, including the composition of the sample fluid and the concentration of the analyte (5). The use of LAM LFA with CSF is off label. Therefore, the test and sample properties of the LAM LFA with CSF have not been systematically determined.

There is a large difference in LFA performance between the study of Bahr et al. and our study. We used a histopathological diagnosis as the gold standard for TBM, while Bahr et al. used culture and PCR positivity as the gold standard. We performed the LFA in a controlled laboratory setting with stored frozen and thawed CSF samples that were obtained postmortem from the fourth ventricle of HIV-infected, deceased adults irrespective of clinical symptoms of meningitis. This setting is very different from the bedside testing of fresh CSF samples obtained through lumbar puncture from HIV-positive or -negative patients with presumed meningitis. Moreover, the influence of freezing and thawing of the analyte on the performance of the LAM LFA is unclear (6). Bahr et al. do not mention the cutoff point (CU) they used for test positivity. We reported our findings for both the CU + 1 and the CU + 2, with lower sensitivity when the CU is higher. In the current version of the Determine TB LAM, the CU + 1 has been deleted. Samples that were positive in our study at the CU + 1 would be missed by the newer version. Lastly, differences in the visual interpretation of faint bands and batch-to-batch variability may have occurred.

We think our results should be viewed as proof of the concept that LAM can be detected by the LFA in the CSF of HIV-infected adults with TBM. However, its clinical applicability has to be tested in a clinical setting. As we concluded in our paper, further evaluation of the LAM LFA in a clinical setting is warranted to evaluate its diagnostic potential in a population with a high rate of tuberculosis-HIV coinfection.

## REFERENCES

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