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# Performance of immune-based and microbiological tests in children with tuberculosis meningitis in Europe: a multicentre Paediatric Tuberculosis Network European Trials Group (ptbnet) study

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All existing immunological and microbiological TB tests have suboptimal sensitivity in children with TBM. Combining immune-based tests with CSF culture and PCR results in far higher positive diagnostic yields, and should therefore be standard practice. <http://bit.ly/2TSAARl>

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#### ABSTRACT

**Introduction:** Tuberculous meningitis (TBM) is often diagnostically challenging. Only limited data exist on the performance of interferon- $\gamma$  release assays (IGRA) and molecular assays in children with TBM in routine clinical practice, particularly in the European setting.

**Methods:** Multicentre, retrospective study involving 27 healthcare institutions providing care for children with tuberculosis (TB) in nine European countries.

**Results:** Of 118 children included, 54 (45.8%) had definite, 38 (32.2%) probable and 26 (22.0%) possible TBM; 39 (33.1%) had TBM grade 1, 68 (57.6%) grade 2 and 11 (9.3%) grade 3. Of 108 patients who underwent cranial imaging 90 (83.3%) had at least one abnormal finding consistent with TBM. At the 5-mm cut-off the tuberculin skin test had a sensitivity of 61.9% (95% CI 51.2–71.6%) and at the 10-mm cut-off 50.0% (95% CI 40.0–60.0%). The test sensitivities of QuantiFERON-TB and T-SPOT.TB assays were 71.7% (95% CI 58.4–82.1%) and 82.5% (95% CI 58.2–94.6%), respectively ( $p=0.53$ ). Indeterminate results were common, occurring in 17.0% of QuantiFERON-TB assays performed. Cerebrospinal fluid (CSF) cultures were positive in 50.0% (95% CI 40.1–59.9%) of cases, and CSF PCR in 34.8% (95% CI 22.9–43.7%). In the subgroup of children who underwent tuberculin skin test, IGRA, CSF culture and CSF PCR simultaneously, 84.4% had at least one positive test result (95% CI 67.8%–93.6%).

**Conclusions:** Existing immunological and microbiological TB tests have suboptimal sensitivity in children with TBM, with each test producing false-negative results in a substantial proportion of patients. Combining immune-based tests with CSF culture and CSF PCR results in considerably higher positive diagnostic yields, and should therefore be standard clinical practice in high-resource settings.