Xpert MTB/RIF test may improve diagnosis of tuberculous meningitis in HIV-infected individuals

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Tuberculous meningitis is a serious and often fatal illness that is difficult to diagnose particularly in resource-poor areas and is especially common in individuals infected with HIV. In this week's *PLOS Medicine*, Vinod B. Patel and colleagues used Xpert MTB/RIF, a newly available DNA test that can be used in resource-poor settings and is generally used to detect TB in sputum, to detect TB DNA in cerebrospinal fluid.

Tuberculous meningitis (TBM) is a serious and often fatal illness that is difficult to diagnose particularly in resource-poor areas and is especially common in individuals infected with HIV. In this week's *PLOS Medicine*, Vinod B. Patel and colleagues from University of KwaZulu-Natal, Durban, South Africa, and University of Cape Town, South Africa, used Xpert MTB/RIF, a newly available DNA test that can be used in resource-poor settings and is generally used to detect TB in sputum, to detect TB DNA in cerebrospinal fluid. They performed the study in 204 South African patients with a meningeal-like illness, of whom 87% were HIV-infected. In this cohort, using a gold standard of positive culture or traditional polymerase chain reaction to determine who truly had TBM, 59 individuals had definite TBM, 64 had probable TBM, and 81 did not have TBM. Overall sensitivity of the Xpert MTB/RIF test (percentage of individuals correctly identified as having TBM) was 62% (95% confidence int ervals, 48%–75%) and specificity of the test (percentage of individuals correctly identified as not having TBM) was 95% (95% confidence intervals, 87%–99%). The sensitivity of Xpert MTB/RIF was

significantly better than that of smear microscopy (62% versus 12%; p = 0.001) and sensitivity improved to 82% (95% confidence intervals 62%–94%) when the test was performed after centrifuging the sample. The test did not perform well in the few individuals who were not HIV-infected. The authors conclude, "Xpert MTB/RIF may be a good rule-in test for the diagnosis of TBM in HIV-infected individuals from a tuberculosis-endemic setting, particularly when a centrifuged CSF pellet is used. Further studies are required to confirm these findings in different settings."

In a related Perspective, David Boulware (uninvolved in the study) of the Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota, Minneapolis, Minnesota, states "Tuberculous meningitis (TBM) is characterized by copious cerebrospinal fluid (CSF) inflammation and yet few Mycobacterium tuberculosis. This combination creates a disease that is notoriously difficult to definitively diagnose…Xpert MTB/RIF appears to be a highly useful test to "rule in" the diagnosis of TBM, yet the clinical acumen of physicians remains a necessity for the wise use of any new diagnostic test. Careful application of these new diagnostic tools should improve clinicians' ability to deliver timely, cost-effective care to patients with suspected TBM throughout the world, an approach that future studies should systematically evaluate."

More information: Patel VB, Theron G, Lenders L, Matinyena B, Connolly C, et al. (2013) Diagnostic Accuracy of Quantitative PCR (Xpert MTB/RIF) for Tuberculous Meningitis in a High Burden Setting: A Prospective Study. PLoS Med 10(10): e1001536. DOI: 10.1371/journal.pmed.1001536

Perspective Article: Boulware DR (2013) Utility of the Xpert MTB/RIF Assay for Diagnosis of Tuberculous Meningitis. PLoS Med 10(10): e1001537. DOI: 10.1371/journal.pmed.1001537