Evidence-based Tuberculosis Diagnosis

One-page plain language summaries of systematic reviews - #13

Title: Antigen detection tests for the diagnosis of tuberculosis

This *systematic review* presents *evidence* from a collection of studies evaluating tests or strategies for the diagnosis of tuberculosis (TB). Terms in *italics* are defined in the TB Evidence Glossary.

Why this review is important: Tests that detect TB antigens in clinical specimens, if accurate, could provide direct evidence of active TB, thus allowing for the immediate start of TB treatment. In comparison with conventional diagnostics, antigen detection tests appear to offer several advantages: immunochromatographic tests (dipsticks are an example), are rapid (results may be available within minutes) and easy to operate. If developed into a point-of-care test, an antigen detection test could extend TB diagnosis to remote community health facilities. An antigen detection test using a specimen such as urine would be particularly attractive in children, who may have difficulty providing sputum. Finally, in patients suspected of extrapulmonary TB, an antigen detection test might prevent the use of more invasive tests.

Objective: To determine the *sensitivity* and *specificity* of antigen detection tests performed using different clinical specimens for the diagnosis of pulmonary and extrapulmonary TB in adults and children. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for sensitivity and specificity.

Main findings: 68 studies were included in the review. No studies provided results for children. For pulmonary TB (47 studies, 5036 participants), sensitivity ranged from 2% to 100% and specificity from 33% to 100%. Of the 47 studies, lipoarabinomannan (LAM) was the antigen most frequently targeted (23 studies), either as a single antigen or one of several antigens. Among the 20 studies targeting LAM alone, urine was the specimen most often evaluated (14 studies). Pooled sensitivity of urine LAM was higher in HIV-infected than HIV-uninfected individuals [47% (95% CI, 26, 68) versus 14% (95% CI, 4, 38)]; pooled specificity was similar, 96% and 97%, respectively. For extrapulmonary TB (21 studies, 1616 participants), sensitivity ranged from 0% to 100% and specificity from 62% to 100%. Five studies targeting LAM, ESAT-6, Ag85 complex, and 65 kDa antigens in cerebrospinal fluid, when pooled, yielded the highest sensitivity (87%; 95% CI, 61, 98), but low specificity (84%; 95% CI, 60, 95).

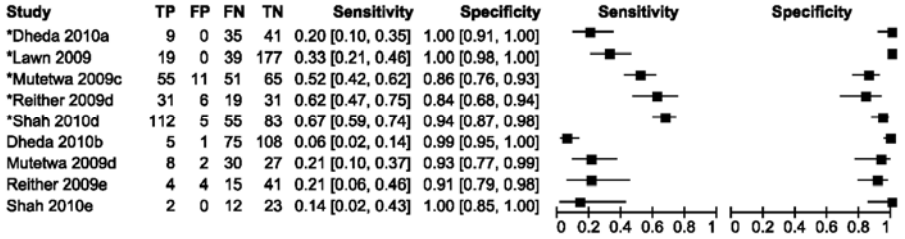

Figure. Forest plots of urine LAM sensitivity and specificity; studies in HIV-infected patients are identified with '*'. TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative. Squares show point estimates of sensitivity from each study; 95% CIs are shown by the horizontals lines**.**

Authors' conclusions: There were few studies targeting any specific antigen other than LAM; therefore no firm conclusions could be drawn about the overall clinical usefulness of these tests. Further studies are needed to determine the value of LAM detection for TB meningitis in high HIV prevalence settings. Since antigen detection tests could be transformed into point-of-care tests, research to improve their performance is urgently needed.

Policy implications: WHO has not issued a policy recommendation about antigen detection tests for active TB.

Comments: A point-of-care version of a LAM detection test for TB meningitis might be good to explore, especially if the test combined detection of LAM and other promising biomarkers,[a] such as interferon-gamma and adenosine deaminase.

Systematic review: Flores LL and Steingart KR et al. Antigen detection tests for the diagnosis of tuberculosis: A systematic review and meta-analysis. Clin Vaccine Immunol 2011, in press.

Publications and other resources of related interest

1. Minion J, Leung E, Talbot E, Dheda K, Pai M, Menzies D. Diagnosing tuberculosis with urine lipoarabinomannan: systematic review and meta-analysis. Eur Respir J. 2011 Jul 4

2. Peter J, Green C, Hoelscher M, et al. Urine for the diagnosis of tuberculosis: current approaches, clinical applicability, and new developments. Curr Opin Pulm Med. 2010 May;16(3):262-70.

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[a] "Biomarker can be defined as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention." US National Institutes of Health Working Group, 2001