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*Title* **A Systematic Review of Rapid Diagnostic Tests for the Detection of Tuberculosis Infection**

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## Aim

To evaluate the effectiveness of available rapid diagnostic tests to identify tuberculosis infection.

## Conclusions and results

*Tests for active tuberculosis (TB):* The review included 212 studies providing 368 datasets, plus 19 studies assessing fully automated liquid culture. Nucleic acid amplification test (NAAT) accuracy was far superior when applied to respiratory samples vs other body fluids. For pulmonary TB, although better-quality, in-house studies, were better at ruling out TB than the commercial tests, they were less good at ruling it in, but it is not possible to recommend any one over another.

NAAT specificity was high when applied to body fluids, eg, for TB meningitis and pleural TB, but sensitivity was poor, indicating that these tests cannot reliably rule out TB. High specificity estimates suggest that NAATs should be the first-line test to rule in TB meningitis, but they need to be combined with other tests to rule out disease.

No evidence supports adenosine deaminase tests in diagnosing pulmonary TB, but considerable evidence supports their use to diagnose pleural TB and TB meningitis. Anti-TB antibody tests performed poorly, regardless of TB type. More research is needed to establish the accuracy of these tests in other forms of TB and for tests such as phage tests. Speed and precision of fully automated liquid culture methods were superior to culture on solid media.

*Tests for latent TB infection (LTBI):* The review included 13 studies. Assays based on RD1-specific antigens, ESAT-6 or CFP-10, correlate better with intensity of exposure and are more likely to accurately detect LTBI, than TST/PPD based assays. They are also more likely to be independent of BCG vaccination status and HIV status.

## Recommendations

NAATs are a reliable way to increase specificity in diagnosing pulmonary TB, but sensitivity is too poor to rule out disease especially in smear-negative disease where clinical diagnosis is equivocal and clinical need greatest.

For pleural TB and TB meningitis, adenosine deaminase tests have high sensitivity, but limited specificity. NAATs have high specificity and could be used alongside ADA to increase overall sensitivity and specificity.

RD1 antigen based assays are more accurate than TST and PPD based assays in diagnosing LTBI in low prevalence countries.

## Methods

Literature was identified from electronic databases and other sources. All databases were searched from 1975 to August 2003 for tests for active TB and to March 2004 for tests for LTBI. Reference lists of studies and relevant review articles were also scanned. (For more details see Executive Summary link above.)

## Further research/reviews required

*For active TB,* large, prospective, well-designed studies are needed to assess the incremental value of test combinations, particularly for samples of biological fluids. For pulmonary TB, NAAT tests should be evaluated in clinically equivocal smear-negative patients. The place of ADA, IFN-gamma, and lysozyme in diagnosing pleural TB needs further investigation. The place of ADA in diagnosing TB meningitis needs to be established. *For latent TB infection,* research is needed in different settings, including countries with a high prevalence of TB, of NTM, in populations with high BCG coverage, and in immunosuppressed populations. Head-to-head comparisons of the main existing commercial assays are needed.

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