Ann Intern Med 2008 Aug 5;149(3):177-84. Epub 2008 Jun 30.

Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update.

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BACKGROUND: Interferon-gamma-release assays (IGRAs) are alternatives to the tuberculin skin test (TST). A recent meta-analysis showed that IGRAs have high specificity, even among populations that have received bacille Calmette-Guérin (BCG) vaccination. Sensitivity was suboptimal for TST and IGRAs. PURPOSE: To incorporate newly reported evidence from 20 studies into an updated meta-analysis on the sensitivity and specificity of IGRAs. DATA SOURCES: PubMed was searched through 31 March 2008, and citations of all original articles, guidelines, and reviews for studies published in English were reviewed. STUDY SELECTION: Studies that evaluated QuantiFERON-TB Gold, QuantiFERON-TB Gold In-Tube (both from Cellestis, Victoria, Australia), and T-SPOT.TB (Oxford Immunotec, Oxford, United Kingdom) or its precommercial ELISpot version, when data on the commercial version were lacking. For assessing sensitivity, the study sample had to have microbiologically confirmed active tuberculosis. For assessing specificity, the sample had to comprise healthy, low-risk individuals without known exposure to tuberculosis. Studies with fewer than 10 participants and those that included only immunocompromised participants were excluded. DATA EXTRACTION: One reviewer abstracted data on participant characteristics, test characteristics, and test performance from 38 studies; these data were double-checked by a second reviewer. The original investigators were contacted for additional information when necessary. DATA SYNTHESIS: A fixed-effects meta-analysis with correction for overdispersion was done to pool data within prespecified subgroups. The pooled sensitivity was 78% (95% CI, 73% to 82%) for QuantiFERON-TB Gold, 70% (CI, 63% to 78%) for QuantiFERON-TB Gold In-Tube, and 90% (CI, 86% to 93%) for T-SPOT.TB. The pooled specificity for both QuantiFERON tests was 99% among non-BCG-vaccinated participants (CI, 98% to 100%) and 96% (CI, 94% to 98%) among BCG-vaccinated participants. The pooled specificity of T-SPOT.TB (including its precommercial ELISpot version) was 93% (CI, 86% to 100%). Tuberculin skin test results were heterogeneous, but specificity in non-BCG-vaccinated participants was consistently high (97% [CI, 95% to 99%]). LIMITATIONS: Most studies were small and had limitations, including no gold standard for diagnosing latent tuberculosis and variable TST methods and cutoff values. Data on the specificity of the commercial T-SPOT.TB assay were limited. CONCLUSION: The IGRAs, especially QuantiFERON-TB Gold and QuantiFERON-TB Gold In-Tube, have excellent specificity that is unaffected by BCG vaccination. Tuberculin skin test specificity is high in non-BCG-vaccinated populations but low and variable in BCG-vaccinated populations. Sensitivity of IGRAs and TST is not consistent across tests and populations, but T-SPOT.TB appears to be more sensitive than both QuantiFERON tests and TST.

PMID: 18593687 [PubMed - indexed for MEDLINE]