From the authors:

We thank K. Shah and Z. Udwadia for their comment on the joint systematic review and meta-analysis of the role of interferon-γ release assays (IGRAs) for the diagnosis of active tuberculosis (TB) by the Tuberculosis Network European Trials Group (TBNET) and the European Centre for Disease Prevention and Control [1]. It was demonstrated that immunodiagnosis by tuberculin skin testing and conventional IGRAs performed on cells from the peripheral blood, *i.e.* the QuantiFERON®-TB Gold In-Tube (Cellestis, Carnegie, Victoria, Australia) and the T-SPOT®.*TB* (Oxford Immunotec, Abingdon, UK) assays, has a limited role in the diagnosis of active TB. Although the sensitivities of both IGRAs in detecting active TB are higher than that of the tuberculin skin test, their sensitivities are not high enough to be used as rule-out tests for TB and their specificities are insufficient to distinguish active TB from latent infection with *Mycobacterium tuberculosis*. This standpoint is also expressed in the new European Union guidance on the use of IGRAs in support of the diagnosis of TB [2].

In contrast, immunodiagnosis using mononuclear cells from bronchoalveolar lavage either by IGRA in the ELISPOT format [3–6] or by fluorescence-activated cell sorting analysis [7] is a promising method with a high sensitivity and specificity for the rapid discrimination of active TB *versus* latent infection with *M. tuberculosis*, particularly in cases of acid-fast bacteria sputum smear-negative pulmonary TB in countries with low TB incidence. However, more evidence is needed to further validate these findings.

Local immunodiagnosis from extrasanguinous fluids by IGRAs has also been explored in extrapulmonary TB, *e.g.* in meningitis [8], pericarditis [9], peritonitis [10] and pleuritis [11]. Although the method is very sensitive, it was, using strict criteria for active infection, deemed not specific enough for the correct diagnosis of active pleural TB to be routinely recommended. Measurement of unstimulated interferon-γ in pleural effusions could be more accurate to distinguish TB from non-TB aetiologies in regions of high TB incidence [12].

It was not a subject of our systematic review and meta-analysis to evaluate other methods for the diagnosis of active TB than IGRAs. However, we agree with K. Shah and Z. Udwadia that measurement of adenosine deaminase (ADA) in pleural effusion could be considered as an inexpensive method for the diagnosis of tuberculous pleurisy. A recent meta-analysis including 63 studies aimed at estimating the diagnostic accuracy of ADA measurement in pleural effusion identified a sensitivity of 0.92 (95% CI 0.90–0.93) and a specificity of 0.90 (95% CI 0.89–0.91), demonstrating that it is a reliable alternative method for the rapid diagnosis of tuberculous pleurisy, especially when the pre-test probability for TB is high and healthcare resources are limited [13].

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