

## Tuberculosis Screening Before Biologics — T-SPOT for All?

To the Editor:

There remains considerable uncertainty and widespread variation in practice throughout rheumatology departments in the UK of screening methods for latent tuberculosis (LTB) prior to anti-tumor necrosis factor- $\alpha$  (anti-TNF- $\alpha$ ) therapy. In recent articles, Pradeep, *et al*<sup>1</sup> used clinical history, chest radiograph, and Heaf testing, whereas Chikura and colleagues<sup>2</sup> routinely used T-SPOT. On an international level, there is also marked variation in practice. In the USA, the tuberculin skin test (TST) is routinely performed in all patients. In Switzerland, all patients have an interferon- $\gamma$ -release assay (IGRA), of which the T-SPOT is one example. The British Thoracic Society (BTS) guidelines<sup>3</sup> suggest use of risk stratification if a detailed history, examination, or chest radiograph raises suspicion. They state the Heaf test is unreliable in patients who are immunosuppressed, which most patients being considered for anti-TNF- $\alpha$  are. The British Society for Rheumatology<sup>4</sup> supports the latter — but with the advent of T-SPOT testing should we actually be changing our practice?

We conducted a retrospective audit of 90 patients who were screened for LTB prior to anti-TNF- $\alpha$  therapy at Gartnavel General Hospital, Glasgow. The study group consisted of patients started on anti-TNF- $\alpha$  between February 2007 and November 2009. All patients had a detailed clinical history and examination, along with a chest radiograph and a T-SPOT assay. We found only 4.5% (4 patients) had a positive T-SPOT result and received chemoprophylaxis. These patients had previously received vaccination for bacillus Calmette-Guerin (BCG), and had all been receiving methotrexate (MTX). Of these patients, only one had risk factors for TB. In 5.5% (5 patients) the T-SPOT was indeterminate. All these patients were subject to repeat testing. In 4 patients T-SPOT results remained inconclusive and subsequent Mantoux test was negative. These patients were all receiving MTX therapy and they all had a history of BCG vaccination. No patient in the cohort developed active TB.

It is well known that TST has poor sensitivity (particularly in immunocompromised groups) and poor specificity (due to cross-reaction with BCG and most mycobacteria). T-SPOT was licensed in the European Union in July 2004, and received US Food and Drug Administration premarket approval in July 2008<sup>5</sup>. Higher sensitivities of 96%<sup>6</sup> and specificities of 98%<sup>7</sup> to 99%<sup>6</sup> have been reported for the T-SPOT. The results are reportedly unaffected by previous BCG vaccination or in immunocompromised patients and requires a simple blood test.

However, should T-SPOT testing be used as a screening tool in all patients? Does it have sufficient superiority to warrant its expense? Is it diagnostic of LTB in the absence of risk factors? Our audit demonstrates a relatively low diagnostic yield with the T-SPOT in our population. It is an expensive test, costing approximately £140 per sample, which occasionally needs repeating with no further diagnostic gain. Unnecessary treatment of false-positives is relatively inexpensive (~£210), but delays early treatment with anti-TNF- $\alpha$  therapy. The risk of drug-induced hepatitis with chemoprophylaxis for TB is between 278 and 1766 per 100,000<sup>3</sup>.

Further studies are needed to determine whether T-SPOT testing is cost-effective as a screening tool in adding further diagnostic and management decisions over and above current recommendations of risk stratification by the BTS. Or should its place be confined to those who have risk factors? The health economics and risk-benefit analysis need to be addressed to provide guidelines for the rheumatology community that are clear and up to date.

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*J Rheumatol* 2011;38:1; doi:10.3899/jrheum.100628