

Bangladesh (ICDDR,B)—had no role in the study design, data interpretation or writing of this manuscript.

Competing interests RR and DS are the inventors of the antibodies in lymphocyte supernatant assay which is patented; however, the ICDDR,B is the patent holder. Any potential financial gain will be for the Centre if/when this assay is commercialised. There are no other potential conflicts of interest related to the work presented.

Ethics approval This study was conducted with the approval of the Ethics Review Committee of the ICDDR,B.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 7 December 2010
Published Online First 12 January 2011

Thorax 2011;**66**:727–729.
doi:10.1136/thx.2010.147363

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A comparison between interferon gamma release assays and the tuberculin skin test in the contact tracing of patients with chronic kidney disease

We welcome the recent guidelines from the British Thoracic Society on the management of *Mycobacterium tuberculosis* infection and disease in patients with chronic kidney disease (CKD).¹ We note the paucity of evidence (particularly from the UK) in this population regarding the use of interferon gamma release assays (IGRA) in screening patients for latent tuberculosis infection (LTBI).

We present data to show the first UK-based cohort comparing the tuberculin skin test (TST) and the two commercially available IGRA—T-SPOT.TB (Oxford Immunotec, Abingdon, UK) and Quantiferon-Gold-in-Tube (Cellestis, Carnegie, Australia)—in a population of inpatients with CKD. It involves the follow-up of 61 patients from a renal inpatient ward who were screened for LTBI following exposure to a staff member with smear-negative, culture-positive pulmonary tuberculosis in 2008.

Overall Results

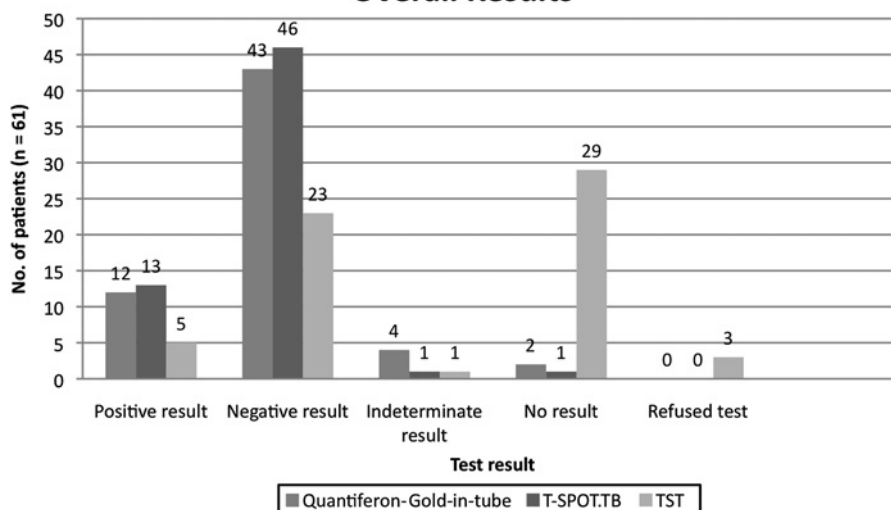


Figure 1 Overall results comparing TST, T.SPOT.TB and Quantiferon-Gold-in-tube across the whole cohort.

The mean age of the cohort was 62 years (range 28–88). Thirty patients were male. Eight patients were of Afro-Caribbean ethnicity, three middle eastern, one south-east Asian, 31 Caucasian and 18 from the Indian subcontinent. Forty-five patients were receiving haemodialysis; three patients had CKD stages II–IV; one patient had acute kidney injury; 12 patients were post-renal transplant; 29.5% were positive for at least one of the three tests; none of these had evidence of active disease. The results of each test are shown diagrammatically in figure 1. Of note, 48% of patients did not receive a completed TST despite standard follow-up by experienced tuberculosis nurses; 19.6% of the cohort had a positive Quantiferon-Gold-in-Tube test, 21.3% of the cohort had a positive T-SPOT.TB test and 8.1% of the cohort had a positive TST (≥ 15 mm if *Bacillus Calmette–Guérin* vaccinated; ≥ 5 mm if not). There were no significant associations between age, gender, diagnosis, or ethnicity and the likelihood of TST completion.

Twenty-five patients had all three tests performed. Of this group, four patients had a positive TST, five patients had a positive Quantiferon-Gold-In-Tube and eight patients had a positive T-SPOT.TB (see supplementary table 1 and supplementary figure 2, available online only). χ^2 tests (using Fisher's exact methods) were used to calculate associations between test modalities in this group: (1) T-SPOT.TB/Quantiferon-Gold-in-Tube: $\kappa=0.694$; $p<0.002$; (2) T-SPOT.TB/TST: $\kappa=0.364$; $p=0.08$; (3) Quantiferon-Gold-in-Tube/TST: $\kappa=0.324$; $p=0.17$.

When repeating the above analysis in the whole cohort ($n=61$), using positive test versus non-positive test as comparators, similarly significant associations were observed (see supplementary table 2, available online only).

On multivariate analysis, there were no significant associations with any of the three tests and gender, age, ethnic background or mode of renal replacement therapy. Length of exposure to the index case had no effect on the test results. (Mann–Whitney U test, $p>0.1$ for all three tests, comparing the median number of 'exposed' shifts for those with a positive test and those with a negative test).

In conclusion, these data support the growing body of evidence that IGRA appear more sensitive and accurate than the TST in detecting LTBI in this immunosuppressed group of patients.^{2–4} Importantly, they also provide evidence of the clinical utility of IGRA in contact tracing, and the difficulty of performing the TST, in large numbers of patients undergoing dialysis.

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Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.

Accepted 17 August 2010
Published Online First 14 October 2010

Thorax 2011;**66**:729–730.
doi:10.1136/thx.2010.149088

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CORRESPONDENCE

Authors' response

We thank Dr Connell and colleagues for their interesting letter in response to the 2010 British Thoracic Society guidelines for the management of tuberculosis infection and disease in patients with chronic kidney disease (CKD),¹ and for demonstrating their recent experience with both commercially available interferon- γ release assays (IGRA) and the Mantoux tuberculin skin test (TST) in a group of patients with CKD who had been exposed to tuberculosis. This is a welcome addition to the literature which currently remains sparse in this patient group, particularly in the UK.

We note the disappointingly poor completion of the TST (in only 48%) and subsequent reduction in positive TST responses. We can only assume that the patients, who were initially inpatients at the time of contact, subsequently dispersed to be managed in satellite clinics. In the past we have managed this problem by teaching patients and their carers to read the TST and have followed this up with a telephone call 48 h after administration of the Mantoux test. While not ideal, this has worked well for similar patients who live a considerable distance from a centre (H Milburn, unpublished data 2009).

It is interesting that Connell and colleagues did not find any association of any of the three tests with length of exposure to the index case, as suggested in other studies for the IGRA tests but not the TST.² It is possible that larger numbers would be needed to demonstrate such an association. This study also described the performance of the three tests in a contact tracing situation, so the numbers tested have depended on the numbers thought to have had significant contact with a particular index case.

We are only aware of two published studies on the relative use of all three of

these tests in screening^{3 4} (as opposed to contact with a known index case) in patients receiving haemodialysis, which is important for the management of patients with CKD, particularly before transplantation.¹ Both publications favoured the IGRA tests over the TST in this patient group, but also identified limitations with these tests. There is also one large multicentre study in immunocompromised patients currently underway across Europe, and this includes groups of patients with CKD as well as those with solid organ transplants (Tuberculosis Network European Clinical Trials Group). It is hoped that this study will report next year and will give us definitive data on the relative merits of each of the IGRA tests as well as the TST in this complex group of patients.

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Competing interests None declared.

Provenance and peer review Not commissioned; not externally peer reviewed.

Accepted 31 August 2010
Published Online First 14 October 2010

Thorax 2011;**66**:730.
doi:10.1136/thx.2010.150102

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Eosinophils best marker of steroid response

There are important aspects of the study design that cast doubt on the claim of Cowan *et al* that 'modified responses' to corticosteroids occur in patients with non-eosinophilic asthma.¹

First, the population recruited was more likely to include patients who experienced loss of control of their asthma after steroid withdrawal than those who remained stable or improved. This increases the potential for regression to the mean as well as identifying a particularly steroid-responsive population. Secondly, it is not possible to make any firm claims about the efficacy of inhaled corticosteroids in either population as the intervention was not placebo controlled. In the only placebo-controlled trial, Berry *et al*² showed no evidence of a response to inhaled corticosteroids in patients with non-eosinophilic asthma.

A more reasonable interpretation of the authors' findings is that there is a much greater response to re-introduction of inhaled corticosteroids in patients classified as eosinophilic compared with non-eosinophilic. This reinforces the view that the presence of sputum eosinophilia is a strong predictor of steroid responsiveness. The apparent relationship between the fraction of exhaled nitric oxide (FE_{NO}) and improvement in airway responsiveness after re-introduction of inhaled steroids in the non-eosinophilic patients is interesting. One possible explanation is that an increased FE_{NO} is an early marker of returning eosinophilic airway inflammation. The concept that non-eosinophilic asthma can be subclassified into a group that is non-eosinophilic as a result of treatment and a group where eosinophilic inflammation is not a component of the disease is supported by a recent study investigating the presence of eosinophilic proteins in airway macrophages.³

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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 17 July 2010
Published Online First 23 September 2010

Thorax 2011;**66**:730.
doi:10.1136/thx.2010.144592

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Authors' response

We are grateful to Dr Martin *et al* for their comments, and accept that our study had