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). 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.

The mean age of the cohort was 62 years (range 28–85). 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; 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). χ² 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: χ²=0.694; p=0.402; (2) T-SPOT.TB/TST: χ²=0.364; p=0.08; (3) Quantiferon-Gold-in-Tube/TST: χ²=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. 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.

D W Connell, A Singanayagam, R Charif, P M George, P L Molyneaux, C McCrudden, M Magtoto, E Harden, S L Seneviratne, N D Duncan, G M Kon

1TB Service, Imperial College Healthcare NHS Trust, London, UK; 2West London Renal and Transplant Centre, Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, UK; 3Department of Immunology, St Mary’s Hospital, Imperial College Healthcare NHS Trust, London, UK

Correspondence to Dr David W Connell, Department of Chest and Allergy, St. Mary’s Hospital, Imperial College Healthcare NHS Trust, Praed Street, London, W2 1NY, UK; d.connell@imperial.ac.uk

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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 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 (FeNO) 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 FeNO 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.2

Neil Martin,1 Chris E Brightling,1 Ian D Pavord2
1Institute for Lung Health, Glenfield Hospital, Leicester, UK; 2Glenfield Hospital, Leicester, UK

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Authors’ response
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