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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 While not ideal, this has worked well for similar patients who live a considerable distance from a centre (H Milburn, unpublished data 2009).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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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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Authors' response

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

certain design limitations. The data were obtained during the run-in for another study (Cowan *et al*, *Thorax* Published Online First: 23 September 2010. doi:10.1136/thx.2010.144592). However, the principal finding remains: while we agree that the presence of airway eosinophilia is a reliable predictor of steroid responsiveness, the absence of eosinophilia does not accurately predict steroid unresponsiveness. Whether intentionally or not, these authors imply that only patients with demonstrable sputum eosinophilia are steroid responsive. This is not the case.

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Potential risk factors for recurrence of pulmonary tuberculosis

Among UK residents of South Asian descent potential risk factors for pulmonary tuberculosis (PTB) and, possibly, also for its recurrence, include vitamin D deficiency (as proposed by Crofts *et al*),[1] the population-attributable fraction (PAF) for PTB attributable to diabetes mellitus,[2] and end-stage chronic kidney disease(CKD).[3]. The PAF for PTB attributable to diabetes mellitus can be as high as 19.6% (95% CI 10.9% to 33.1%) and 14.2% (95% CI 7.1% to 26.5%) for UK Asian men and women, respectively, versus 6.9% (95% CI 3.1% to 12.4%) and 8.2% (95% CI 3.0% to 15.6%) for their white male and female counterparts, respectively.[2] Furthermore, in the presence of diabetes mellitus, recognition and treatment of PTB can be complicated by the fact that its radiographic stigmata can simulate those of lower lobe community-acquired pneumonia, and by the fact that median time to culture conversion may be significantly (p=0.03) longer in subjects with diabetes than in their counterparts without diabetes.[4] Relative to their white counterparts, UK Asians also have a 13.66-fold higher risk of end-stage diabetic nephropathy,[5] end-stage CKD itself being associated with an acquired immunodeficiency state characterised by a 10- to 25-fold increase in risk of PTB.[3] When vitamin D deficiency complicates CKD[6] this might, arguably, further compound the risk of PTB and its recurrence.

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Authors' reply

In response to Dr Jolobe, our understanding of the epidemiology of tuberculosis in South Asians in the UK is that extrapulmonary disease is more common in this group.[1] South Asians are therefore not necessarily predisposed only to pulmonary tuberculosis and its recurrence but to tuberculosis in general. What is likely is that being immunocompromised in this population, arising potentially from vitamin D deficiency[2] and type 2 diabetes,[3] is the important risk factor for tuberculosis and its recurrence. We therefore agree that diabetes could be another reason why South Asians appear to be at greater risk than other groups for recurrence of tuberculosis, but not necessarily just pulmonary forms of the disease. Although we have discussed potential factors associated with recurrence,[4] national surveillance does not collect information on diabetes precluding us from assessing its role.

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Mains-powered hypoxic gas generation: a cost-effective and safe method to evaluate patients at risk from hypoxia during air travel

For the evaluation of patients at risk of hypobaric hypoxia during air travel, the British Thoracic Society Recommendations describe the normobaric hypoxic challenge as a substitute for the use of hypobaric chambers, which are not widely available.[1]

In the normobaric hypoxic challenge, breathing 15% oxygen at sea level replicates the reduced P_{O_2} in ambient air at 8000 ft (2438 m), the maximum permissible cabin altitude during commercial flight. This method has been shown to produce results comparable with those obtained using hypobaric chambers and oxygen desaturation similar to that found in patients with chronic obstructive pulmonary disease (COPD) during flight.[2 3] The methods described in the British Thoracic Society Recommendations include using a cylinder of 15% oxygen in nitrogen, delivered by either a breathing circuit or a body box. Alternatively, a cylinder of nitrogen may be used to drive a 40% Venturi mask resulting in a fractional inspired oxygen (F_{IO_2}) of 15%. As pure nitrogen is an asphyxiant gas, F_{IO_2} can fall dangerously low if Venturi mask ports become blocked or the nitrogen concentration becomes too high in an enclosed space. Furthermore, these