

been described by other authors as the 'reversed halo sign'.

Zompatori *et al*<sup>2</sup> first used the term 'atoll sign' in 1999 to describe the imaging finding of a focal rounded area of ground-glass opacity surrounded by a more or less complete ring of consolidation.<sup>3</sup> Although the abnormality frequently resembles an atoll, the Fleischner Society<sup>4</sup> prefers the term 'reversed halo sign', as initially proposed by Kim *et al*.<sup>3</sup> Although both terms adequately describe the imaging characteristics of the lesion, the term 'reversed halo sign' should be used to avoid confusion and to standardise the keywords used in literature searches. A review of the US National Institutes of Health digital archive of biomedical and life sciences journal literature (PubMed) found only three occurrences of the term 'atoll sign', whereas the term 'reversed halo sign' was found in 22 articles. The uniform use of descriptors is critical when reporting on lesions, to avoid the overlooking of otherwise important articles, such as the one presented by Walsh and Robertson, in literature reviews.

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## UK immigrant screening is inversely related to regional tuberculosis burden

We read with interest the editorial by Moore-Gillon *et al*,<sup>1</sup> which advocated a more comprehensive system of immigrant screening/treatment for latent tuberculosis

infection (LTBI) as a means of augmenting tuberculosis (TB) control in the UK.

A recent comprehensive, national evaluation of local TB services/primary care organisations (PCOs) in the UK, which provides key insights into UK screening practices,<sup>2</sup> found that the existing National Institute for Health and Clinical Excellence (NICE) guidance from 2006 was often not followed. While all TB services would follow-up new entrants referred to them with suspected active TB, only just over half attempt to screen migrants with normal chest x-rays for LTBI; more pertinently it was those local TB services/PCOs that served the highest TB burden areas that were four times less likely to undertake LTBI screening. There was also deviation from NICE guidance in the LTBI screening methods employed (tuberculin skin test vs interferon gamma release assays). Therefore, there is a need for effective national coordination if a new strategy is to be effective in controlling TB.

Furthermore, while we agree with Moore-Gillon *et al* on the need to change policy, we believe that there needs to be an expanded evidence base to determine which specific immigrants we should screen, where we should screen them and what tools we should use as well as a change in attitude about the importance of tackling LTBI in migrants to drive down the UK's TB burden. Crucially, in an increasingly cost-constrained environment, comprehensive health-economic analyses will be required to determine which changes in policy are justified.

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**Competing interests** AL is inventor of patents underpinning T cell-based diagnosis. The IFN-gamma ESAT-6/CFP-10 ELISpot was commercialised by an Oxford University spin-out company (T.SPOT-TB, Oxford Immunotec Ltd, Abingdon, UK) in which Oxford University and AJ have minority shares of equity and royalty entitlements.

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## Rethinking TB screening: politics, practicalities and the press

In support of the urgent need for improvements to new entrant TB screening,<sup>1</sup> which must encourage the diagnosis of both active and latent forms of TB, we would like to offer two audits of new entrant screening from an area with a low TB incidence (4.3/100 000).<sup>2</sup>

In 2006, we audited 29 new entrant referrals, all of whom had a chest x-ray reported by the Port Health Control Unit at Heathrow Airport as 'abnormal' (predominantly hilar calcification).<sup>3</sup> Of the 29 referrals, 22 attended for local screening. Each received a tuberculin skin test (TST) and a repeat chest x-ray that was reported by a respiratory consultant and then by a consultant radiologist. Sixteen (73%) were subsequently reported as having a normal chest x-ray (and negative TST).

While the practical difficulties of screening large numbers of new entrants at the point of entry (in a short space of time) are high, inaccurate reporting of chest x-rays results in wasted resource and a financial burden that is passed on to both the new entrant and local TB services through the need for repeated screening.

Further, the NICE new entrant TB screening guidelines (2006)<sup>4</sup> allow certain groups of new entrants to be screened solely via chest x-ray (CXR), limiting a TST to all those aged 0–15 and those aged 16–34 from sub-Saharan Africa. As the authors highlight, this potentially under-diagnoses the latent TB infection (LTBI).

To investigate this, we undertook a retrospective case-note analysis of 547 new entrants over a 44-month period (2006–2009).<sup>5</sup> All patients were invited for screening using a locally adapted 'Dorset' algorithm that combined CXR and TST unless contraindicated. Each case was then re-evaluated using the NICE algorithm. This allowed direct comparison of each algorithm's ability to detect LTBI. Results: 397 (72%) new entrants attended screening, 41 (10.3%) patients were diagnosed with LTBI (all HIV negative). Comparison of the algorithms showed that only 27/41 cases (65.8%) were detected when using the NICE algorithm. This represents a 34.1% shortfall in LTBI detection when following NICE guidance (95% CI 19.63% to 48.67%, 99% CI 15.04% to 53.26%).

The results from these two audits lend strength to the authors' argument that over-reliance on CXR alone is inadequate;

combination screening with TST or IGRA should be considered. There remains a need for a robust national screening strategy that promotes the detection of latent as well as active tuberculosis.

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## Authors' response

We welcome the correspondence<sup>1 2</sup> relating to our recent editorial<sup>3</sup> and thank the authors for their interest.

Mr Thomas from the Royal Bournemouth Hospital presents two interesting local audits. The first highlights the possibility of wasted resources in screening individuals identified by the Port Health Control Unit as having an abnormal chest x-ray. The second demonstrates the potential shortcoming in the NICE guidelines, which can lead to an underidentification of latent tuberculosis (TB) infection. We share Mr Thomas's concerns, particularly on this latter point.

Dr Pareek and colleagues from Imperial College and the Health Protection Agency show that the NICE guidance is often not followed and that it is TB services which serve the areas with the highest TB burden which appear least likely to undertake screening for latent TB infection. This latter finding is, we would argue, unsurprising when resources are as scarce as they are in TB services. Those in high burden areas will be concentrating on 'fire fighting'—treating those cases of actual disease which actually do arise, with little or

no time left for detecting latent infection and preventing the emergence of new active cases. This is likely to be a funding issue. Even in 2001, only one in six of high TB burden districts met minimum staffing recommendations.<sup>4</sup> Despite the DH funding template produced in 2007, this is widely ignored by primary care trusts as 'not applying to them', continuing the under-resourcing of TB services in many high (and some low) burden districts.

These authors also highlight the deviation from the NICE guidance in the latent TB infection screening methods employed, and we agree that there is a need for effective national coordination. They agree with our arguments regarding the need to change policy and we too feel that there is a need for an expanded evidence base to determine the most effective structure for the future. We also agree on the need for health economic analysis in these cost-constrained times. We understand that this will be provided in the updated economic appraisal of this area, which should be part of the revised NICE TB guidelines in January 2011, and believe it will be fully supportive of our case.

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## Sarcoidosis is a Th1/Th17 multisystem disorder: wider implications

Facco *et al* demonstrated elevated levels of T helper 17 (Th17) cells in the peripheral blood and in the bronchoalveolar lavage of patients

with active sarcoidosis; increased expression of interleukin 17 (IL-17) and *IL-23R* in lung and lymph node specimens was also noted.<sup>1</sup> These results suggest a role for the IL-23/Th17 inflammatory axis in the pathogenesis of sarcoidosis.

Crohn's disease (CD) is a severe inflammatory bowel disease (IBD). Many components of the IL-23 pathway (*IL23R*, *IL12B*, *STAT3*, *JAK2*, *TYK2*) are true IBD susceptibility genes, suggesting a crucial role for this pathway in maintaining intestinal immune homeostasis.<sup>2</sup>

We recently reported the development of multisystem sarcoidosis in two CD patients who had received maintenance therapy with natalizumab, a selective adhesion molecule inhibitor that prevents lymphocyte migration to the gut.<sup>3</sup> We hypothesised that natalizumab may have contributed to the development of the disease by allowing dysregulated lymphocyte trafficking to the respiratory mucosa and other extraintestinal mucosal surfaces in genetically predisposed individuals.

Complex disease genetics has been revolutionised by the advent of genome-wide association (GWA) studies. Shared susceptibility genes between IBD and other immune mediated/inflammatory disorders (ankylosing spondylitis, psoriasis, systemic lupus erythematosus, rheumatoid arthritis, asthma, atopic dermatitis, coeliac disease, multiple sclerosis, type 1 and type 2 diabetes mellitus, mycobacterial disease) have already emerged, paralleling the reported epidemiological evidence.<sup>4</sup> A combined analysis of a limited (100 kb) GWA study in CD and sarcoidosis identified a common susceptibility locus on 10p12.2 (but not at GWA levels of significance).<sup>5</sup>

We feel that this recent publication provides further intriguing evidence of common immunopathogenic pathways between CD and sarcoidosis. Ongoing research into common pathways and susceptibility regions between these two granulomatous conditions is essential, with further exploration of the IL-23/Th17 axis looking increasingly like a good starting point.

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