Highlights from this issue

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Whatever we may have once optimistically thought, TB remains with death, taxes and political chicanery as being inevitable, unavoidable and deeply unpleasant. It shows every sign of weathering the storm of potent anti-tuberculous medications and superb randomised controlled trials to emerge in ever-increasingly drug-resistant forms, potentially turning the clock back to the 1930s. This edition of *Thorax*, coinciding with world TB day, is themed to recognise the ongoing sinister successes of *Mycobacterium tuberculosis*, unarguably the most successful human pathogen of all time.

IGRA TESTING AND HIGH RISK POPULATIONS

We, being simple minded airway doctors, have struggled to keep ourselves updated on the nuances of interferon-gamma release assays (IGRA) testing. For those similarly afflicted, we have commissioned a brief review (***see page 288***). This would be an excellent place to start before tackling two papers from very fine institutions in London and Leicester investigating the role of IGRA testing in high risk populations. Manish Pareek and colleagues from Imperial (***page 230***; hot topic) show that a selective, single step IGRA testing strategy in immigrants from high risk countries is more cost effective and only marginally less sensitive than current practice, which is much less selective and includes CXR screening. Pranabashis Haldar and colleagues (***page 240***; hot topic) clarify the role of IGRA testing in screening of contacts. One in seven untreated individuals with a positive test developed active TB over 2 years. IGRA testing was 5 times less likely to be positive in contacts of smear negative compared to smear positive cases, although the proportion of patients with a positive test who went on to develop active disease was similar. Chemoprophylaxis seemed to be highly effective in the young but the situation was less clear in older contacts, many of whom may have been infected remotely. Ormerod (***page 201***) reminds us that TB rates are rising more quickly in the UK than in other developed countries with similar immigration. Perhaps one way to reverse this trend without breaking the bank is to adopt better screening practices using IGRA testing.

TO INFINITY AND BEYOND! IGRA PLUS: THE NEXT GENERATION OF IMMUNODIAGNOSTICS

IGRA tests are not without their problems: they are unable to distinguish latent from active disease; and they are significantly less sensitive in patients with deficient T-cell responses due to immunodeficiency (most usually patients with HIV infection). Ashenafi and colleagues (***page 269***; editors' choice) describe a new approach to TB diagnosis which assesses antibody production in lymphocyte supernatants. These antibodies are newly produced and therefore indicate current infection rather than past exposure. Raised BCG specific IgG and plasmablasts look like a promising immunodiagnostic, as they discriminate patients with active and latent disease moderately successfully and the response is, if anything, enhanced in patients with HIV. However, as Ajit Lalvani and David Connell (***page 204***) point out, a great deal more work is needed to address the validity and feasibility of this test in the field. Ajit has been kept very busy this month, reflecting his world class and pioneering work in this field, which we applaud. We are delighted to have a podcast recording of Ajit describing the development of IGRAs and discussing some of the manuscripts published this month. Please do take the time to visit the Thorax website and listen to this.

HUSH! HUSH! WHISPER WHO DARES, THE MAKERS OF STEROIDS ARE SAYING THEIR PRAYERS

We all know that when the very first inhaled corticosteroids (ICS) first came on the scene, they transformed the management of asthma, with minimal side-effects at low doses. Over the years, mission creep has led to them being seen as the panacea for all airway diseases and more and more potent variants being developed, with the twin aims of improving the ratio of local activity to systemic toxicity, and the more discreditable one of further bloating the coffers of big Pharma. Discredit to us clinicians too—potent systemic corticosteroids are immunosuppressive, so why should not potent topical steroids affect mucosal barriers? And of course, they do affect local immunity—the increased risk of pneumonia in COPD patients is well known, a real DOH! moment for us all! Now, Andrejak et al report COPD patients never treated with ICS have a 7.6-fold increased risk of non-tuberculous mycobacterial disease, and this rises to a staggering 29.1-fold increased risk for those currently ICS-treated (***see page 256***). Increasing the likelihood that this is a real finding, there was a dose effect, and also a greater effect with the most potent ICS studied, fluticasone. With the increasing appreciation of the diversity and importance of the airway microbiome, and its interactions with epithelial cells and the innate and adaptive immune systems should come the realisation that we should think carefully and critically about how we meddle with these complex systems. *Primum non nocere* rather than *primum make money*!

AND THEN THERE WERE THREE (!)

The most ignorant student knows that the left lung comprises upper and lower lobes—so what is this third structure confronting the Thoracic Surgeon who opened this patient's chest? ***See page 308***.