



doi:10.1136/thoraxjnl-2015-208129

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MICROBIAL MUSE

It is rare to find a poet inspired by bacteria. However, one such rarity was Hilaire Belloc who penned the following cautionary verse:

*"The microbe is so very small
You cannot make him out at all
But many sanguine people hope
To see him through a microscope."*

These sanguine people will be disappointed in the case of latent tuberculosis, where affected individuals are, by definition, smear and culture negative. Detecting latent TB is an important part of the prevention of active TB because up to 10% of people with latent TB will progress, with immune deficient and immunosuppressed patients at particular risk. In this issue of the journal, Sunny Wong and colleagues explore the use of the interferon gamma release assay (IGRA) in one at risk group, patients with autoimmune disorders (primarily rheumatoid arthritis and inflammatory bowel disease) who may receive immunosuppressive therapy (see page 64). They conclude that the IGRA test should be done before the patient starts immunosuppressive therapy. In a linked editorial, Martina Sester and Beate Kampmann argue that both IGRA and the tuberculin skin test have a role in the diagnosis of latent TB (see page 3). Ultimately new and better biomarkers of TB infection are needed.

MICROBIAL VIEWS

Non tuberculous mycobacteria (NTM) have preoccupied the cystic fibrosis world in recent years, with the rise of *Mycobacterium abscessus* and other NTM. There is little evidence to guide prolonged multi-agent therapy and the outcome may be disappointing. However, guidance is at hand. On page 88 of this month's *Thorax*, Andres Floto summarises the recent Cystic Fibrosis Foundation and European Cystic Fibrosis Society Consensus Recommendations on the management of NTM. The full guideline is published as a supplement to *Thorax*.

BACK TO BLACK

In 1988 James Black was awarded the Nobel Prize in Physiology or Medicine, for his work in developing beta blockers (amongst other things). Since propranolol was synthesized in 1962 (and the cardioselective beta blockers a few years later), beta blockers have steadily acquired new

indications. In this month's *Thorax*, Bhatt and colleagues report observational data from over three thousand patients with COPD which show that the use of beta blockers is associated with significantly fewer exacerbations (see page 8). Despite correcting for confounding factors, the authors propose randomised controlled trial(s) are needed to test this hypothesis. Clinicaltrials.gov lists more than half a dozen trials of this intervention which are in set up or recruiting.

FROM BETA BLOCKERS TO BETA AGONISTS

Head to head comparisons of two popular drugs for the same indication are not popular with Pharma. If a competitor's product comes out on top it does not help sales figures. It is therefore often difficult for clinical researchers to recommend one treatment over another. Enter network meta-analysis. If one trial compares treatment A with treatment B and another compares treatment B with treatment C, then a network meta-analysis allow us to compare treatment A with treatment C. Got that? On page 15 of the journal, Oba and colleagues publish a network meta-analysis of long-acting beta agonist (LABA) and long-acting muscarinic antagonist (LAMA) combinations in COPD. They conclude that combination therapy is associated with improvements in lung function and quality of life. There were fewer severe exacerbations and no increase in safety concerns. The next challenge will to be to explain how beta agonists and beta blockers both help prevent COPD exacerbations!

BEAUTIFUL IMAGES OF ALLERGIC INFLAMMATION

Allergic bronchopulmonary aspergillosis (ABPA) is commonly treated with a combination of steroids and azole antifungals. This approach has changed little in the last few decades and yet clinical response is often disappointing, with repeated or prolonged courses of steroids often needed. On page 52 of the journal, Lee and colleagues explore the action of Phosphoinositide 3-kinase- δ inhibitors in an experimental model of ABPA. The response to steroids (dexamethasone) was disappointing but a PI3K- δ inhibitor reduced allergic inflammation and airway hyperresponsiveness in mice. The authors speculate that PI3K- δ inhibitors may be

useful in the treatment of steroid-resistant eosinophil-dominant allergic lung disorders. The elegant images in figures 2 and 6 could be from the Hubble space telescope but are in fact confocal laser immunofluorescence photomicrographs.

MENTAL HEALTH IN SHAKESPEARE AND IN CYSTIC FIBROSIS

"I have of late – but wherefore I know not – lost all my mirth, foregone all custom of exercises. And indeed it goes so heavily with my disposition that this goodly frame the earth seems to me a sterile promontory."

In Act II, scene 2, Hamlet makes this morose speech to his former childhood friends, Rosencrantz and Guildenstern. Had they been equipped with PHQ-9 and GAD-7 questionnaires, they might well have diagnosed Hamlet as suffering from depression and intervened with supportive care. Ophelia, on the other hand, would have required urgent intervention to prevent her impending suicide. In this issue of *Thorax* (see page 26), we publish the recommendations of an International Committee on Mental Health in Cystic Fibrosis. This important consensus document emphasises the high prevalence of mental health problems in people with CF and their families. The document makes lists fifteen practical recommendations for screening, diagnosis and treatment and should allow quality improvement and leverage more funding for mental health in this group of patients.

MISLEADING CASEATION

Where histology shows caseating granulomata, most of us would feel we were on the right track with anti-tuberculous chemotherapy. But supposing further histology revealed not acid and alcohol fast bacilli but osteoid matrix? *Images in Thorax* describes pulmonary lesions which were not what they seemed (see page 96).

