Highlights from this issue

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The Triumvirate

REMAIN AT THORAX

On 22 June this year, 52% of those taking part in the UK referendum voted to leave the European Union. In the preceding weeks, the economic and political consequences of Brexit were discussed in a debate that rarely allowed thoughtful discussion of complex issues. In the sphere of medicine and science, there are close links between the UK and EU institutions through the funding of health research, the regulation of medicines and through professional societies such as the European Respiratory Society. *Thorax* is an international journal that has been enriched by many key papers from academics based in EU countries and participating in EU collaborations. We want more of these and we encourage colleagues engaged in respiratory research throughout the EU, and indeed from around the world, to continue to send us their best work. As the UK looks set to leave the EU, on a wave of populist sentiment, *Thorax* will continue to reach out to European colleagues. Never has it been more important for those of us who understand the importance of collaboration and co-operation to demonstrate our commitment to working together. At *Thorax*, we are fully aware that within Europe there is more that we have in common than divides us and there will be no Brexit on the pages of our journal.

…SEPARATED BY A COMMON LANGUAGE

Clinical research in the field of acute bronchiolitis has long been hampered by differences in diagnostic terminology between North America and Europe. In this issue of *Thorax*, Dumas and colleagues tackle this problem with latent class analysis of bronchiolitis phenotypes in two cohorts of young children – one from the US and a second from Finland (***see page 712***). They describe distinct subgroups: rhinovirus with previous wheeze or eczema; RSV with new onset wheeze; and severe or moderate illness phenotypes. In an accompanying editorial, Cunningham and colleagues propose that the term "viral lower respiratory tract infection" should replace "bronchiolitis" – in clinical trials of new drugs and perhaps more widely (***see page 679***). In young infants, bronchiolitis can be life threatening (18% of the US cohort were admitted to intensive care) and yet we can still only offer supportive therapy. A common terminology is essential if we are to accurately describe disease mechanisms, develop new therapies and give these therapies to the children who need them most.

TB CASE FINDING IN THE GENOMICS ERA

Around one third of the world's population have latent TB and 10% of those will develop TB disease. Annually, there are approximately 8000 cases of active TB diagnosed in the UK. For decades public health teams have relied on contact tracing to identify TB clusters and prevent the spread of TB. Recently typing techniques such as "mycobacterial interspersed repetitive units – variable number tandem repeats" (MIRU-VNTR) have been available to public health teams. In this issue, Saavedra-Campos *et al* describe how they used this highly discriminatory genotyping data to identify TB clusters and risk factors for localised transmission in a large population from the North of England for the period 2010–2012 (***see page 742***). Risk factors include homelessness, prison and pulmonary disease. Individuals born in the UK and those from a non-white ethnic group were also at increased risk. Similar risk factors were seen in a study from London, conducted over the same three year period (***see page 749***). Both papers suggest prioritising those with identifiable risk factors in case finding.

SPOIL THE SHIP FOR A HA'PWORTH OF TAR…

The use of genotyping data to enhance TB case finding is further explored in a linked article by Mears and colleagues (***see page 734***). In a national evaluation of the TB strain typing service in England, this group question the value of new technologies for TB control. They found that the TB strain typing service (using MIRU-VNTR) had no significant effect on contact tracing yield or diagnostic delay and was not likely to be cost effective over the next 20 years. In their mixed methods study they cite delayed development of clustering software and limited resources for public health action as factors contributing to this failure. Strain typing itself was well resourced.

A MISMATCH BETWEEN PATIENT AND CLINICIAN…

Health-related quality of life (HRQL) and outcome is important to both patients and clinicians. Spinou and colleagues report a systematic review of the questionnaires used to assess HRQL in patients with bronchiectasis and investigate the relationship between subjective and objective clinical outcome measures (***see page 683***). 38 studies were included in the meta-analysis with nine validated questionnaires identified. The interesting finding was that there was a stronger relationship with subjective outcome measures thanobjective clinical measures. Indeed, the current HRQL questionnaires for bronchiectasis assess aspects of health that are not captured by the objective measures. This diversity between the patient symptoms and clinical outcome needs to be addressed.

A PATHOMECHANISTIC MATCH BETWEEN CANCER AND IDIOPATHIC PULMONARY FIBROSIS (IPF)

Common pathomechanisms between IPF and cancer include the dysfunctional pan-PI3 kinase (PI3K) signalling pathway. Mercer and colleagues report a dosing framework for a PI3K/mammalian target of rapamycin (mTOR) inhibitor, GSK2126458, in fibroblast functional assays, from IPF lung tissue, and IPF patient-derived bronchoalveolar lavage (BAL) cells (***see page 701***, Editors' choice). In addition to PI3K pathway activation in fibrotic foci, GSK2126458 inhibited PI3K signalling and functional responses in IPF-derived lung fibroblasts, inhibiting Akt phosphorylation lung tissue and BAL derived cells. PI3K is a potential therapeutic target in IPF requiring a proof-of-mechanism trial, which is discussed in the accompanying editorial (***see page 675***).

KEEPING THE PRESSURE DOWN….

Pépin and colleagues report the results of a double-blind, randomised clinical trial of the treatment of blood pressure (BP) with either fixed-level CPAP or auto-titrating CPAP in obstructive sleep apnoea (OSA) patients (***see page 726***). The primary endpoint was the change in office systolic BP after 4 months. 161 patients were randomised to fixed level CPAP and 161 patients to auto-titrating CPAP but no difference was observed in office BP between the groups. Although the authors report that the fixed level CPAP was more effective in reducing 24 hour diastolic blood pressure, as a secondary outcome, perhaps we need not focus on the type of CPAP treatment but its effects in the treatment of REM and non-REM OSA, as discussed in the editorial (***see page 677***).

SLEEPING MOTHERS…DON'T ASK

Pamidi and colleagues report the effect of maternal sleep-disordered breathing (SDB) on fetal outcomes in the third trimester of pregnancy with a focus on the delivery of small for gestational age (SGA) infants (***see page 719***). 234 pregnant women were studied with SGA infants delivered in 12% of the mothers. Although symptoms of SDB had poor overall sensitivity and specificity for diagnosing polysomnography identified SDB, an apnoea-hypopnoea index above 10 events/hour increased the likelihood of delivering an SGA infant. So, don't ask the mother…