Highlights from this issue

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Andrew Bush, Ian Pavord, *Editors*

FIREFIGHTERS, HANG UP YOUR HOSES (NOT THE ARTICLES OF FEMALE ATTIRE!)?

These are heady days in the world of cystic fibrosis (CF). Diagnosis is for the most part early by newborn screening (NBS); designer, mutation specific treatments (Ivacaftor, Lumacaftor) are becoming available, and the first ever Gene Therapy trial (does it *help*, rather than can it be made to happen) will report later this year (***see page 962***). The treatment paradigm is changing from firefighting the downstream complications of the disease in sick patients to correction of the fundamental molecular defect in the virtually asymptomatic. But are we victims of our own success? Yes, say the London Poms, lung function (***see page 910***, **Hot topic**) and CT scans are so good a year after NBS CF diagnosis that huge studies will be needed to demonstrate any improvement over standard care. No, say the AREST-CF group in Australia, both function and structure are so rubbish that new treatments are urgently needed. Piggy in the middle, editorialist Peter Merkus tries to make sense of these disparate results (***see page 888***) without much success. CF genotypes do not differ between the groups, but modifier genes might. Are there treatments or environmental factors which differ between the hemispheres? Clearly optimal treatments are mandated for all CF NBS infants before busting the budgets and exposing the growing lung to experimental treatments; can we find an early marker of doing badly in the very long term and target this group only? Or an early marker of impending imminent deterioration, which seems a more achievable goal? More work needed and preferably published in *Thorax*.

YOU SAY TOMADO, I SAY TOMATO

Tomado may sound like a particularly powerful wind blast, or a mutant tomato (or both!) with destructive potential but it is, in fact, the acronym for a cross-over randomised controlled trial published in this issue of *Thorax* (***see page 938***, **Editors' choice**). The trial compares three oral mandibular advancement devices (SleepPro 1, SleepPro 2 and a bespoke locally produced device) and no treatment in patients with mild to moderate obstructive sleep apnoea-hypopnoea syndrome. The SleepPro 1 is a thermoplastic 'boil and bite' self-moulded device whilst the others are semi- or fully-bespoke. All devices reduced the apnoea/hypopnoea index and daytime sleepiness significantly when compared to no treatment. Patient preference and costs per QALY were marginally in favour of the SleepPro 2 semi-bespoke device. We suggest that tomatoes are better placed raw in a salad, rather than boiled and bitten—fresh is best. But, keep your heads down if the Met Office issues a TOMADO warning! Joking apart, does TOMADO, TOMATO or CPAP get the adherence vote from the patients?

INTERFERING WITH INTERFERONS?

Received truth in adult asthma is that defective interferon (IFN) -β and –λ responses are key players in viral-induced asthma lung attacks, hence a recent Phase 2 trial of nebulised IFN-β in this context. Next stop children? In a really important study, Spann *et al*., (***see page 918***) could not demonstrate any difference in IFN responses in any respiratory epithelial cells from wheezy/atopic children exposed *in vitro* to human metapneumovirus, but did show greater viral shedding, implying a hitherto undescribed mechanism. However, IFN-β but not –λ responses to respiratory syncytial virus were reduced in these children, only in nasal but not tracheal cells, but IFN regulated factors and pro-inflammatory cytokines were not differentially regulated. In an accompanying editorial (***see page 887***), Sejal Saglani restores Anglo-Australian diplomatic relations by pointing out key important methodological strengths this study highlights. These include demonstrating that upper and lower airway epithelial cells may respond differently to viruses and that small children are not miniature adults, and hence adult studies cannot answer paediatric questions. A call to action, paediatricians; we cannot wait around to be told what to do as a result of adult studies; we need to get out there and do the work in children. One size clearly does not fit all ages and all viruses.

FIBULIN-3, MESOTHELIN-4

The medical literature is littered with reports of promising biomarkers crashing on the rocks of independent validation. Is this the case for fibulin-3, recently identified as a promising biomarker of malignant mesothelioma? Jeanette Creaney and colleagues (***see pages 895***) compare plasma and pleural fluid fibulin-3 with the more established biomarker mesothelin in 82 patients with malignant mesothelioma and 71 with other malignant and non-malignant pleural diseases. The result was a narrow victory for mesothelin but neither biomarker measured in pleural fluid or plasma achieved the high sensitivity required for a rule-out test or the high specificity necessary for a positive diagnosis. Elevated pleural effusion fibulin-3 was associated with worse survival and, in the sub-group of patients with complete data, was an independent prognostic predictor. However, on the basis of all the findings, it would be difficult to make a strong case for either biomarker to be used in clinical practice. X factor-5 anyone?

DON'T BE SHEEPISH!

This 42-year-old man from Afghanistan had a non-resolving pneumonia; what was this gelatinous membrane occluding the anterior segment of the left upper lobe? If you can't work it out, turn to the *Pulmonary Puzzle* (***see page 965***).