Highlights from this issue

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Andrew Bush, Ian Pavord, *Editors*

NOW IS THE WINTER OF OUR DISCONTENT

Or at least of the usual influx of respiratory syncytial virus positive infants needing ventilation or worse into our pitifully inadequate numbers of paediatric intensive care beds. Understanding the pathophysiology of the disease is a high priority; efforts to find a vaccine have failed, pharmacotherapy is non-existent and prevention with Palivizumab is so expensive and inconvenient that it will never be offered to low-risk babies, who form the bulk of the numbers of patients. Two manuscripts in this issue of *Thorax* address novel mechanisms of disease. McNamara *et al* showed that BAFF (B cell activating factor of the tumour necrosis factor family) was increased in bronchoalveolar lavage in severe RSV disease, and was produced in vitro by epithelial cells via an interferon-β dependent pathway (***see page 76***). Appropriately enough for a winter disease, APRIL was nowhere to be found. In a second manuscript, Triantafilou *et al* demonstrated that the creation of viral ion channels through the SH RSV viroporin activates inflammasomes, which induces membrane permeability and activation of caspase 1 and the release of pro-inflammatory cytokines (***see page 66***). For the BAFFLed, turn first to *Basic Science for the Chest Physician* for a masterly exposition of the immune and inflammatory responses to respiratory viral infections, and then read the original articles (***see page 108***).

DON'T PLAY MISTY FOR ME

Drug safety is an important theme this month and next. Dong and colleagues (***see page 48; Hot Topic***) provide further evidence of a dose-related increase in cardiovascular mortality with Tiotropium Respimat. The likely mechanism—increased heart rate and potential for dysrhythmias – is discussed by Singh and colleagues (***see page 114***). Evidence is accumulating that this preparation of Tiotropium is associated with increased cardiac risk, possibly reflecting increased systemic bioavailability because of greater peripheral deposition of the drug. We have previously questioned whether mortality reduction should be the pre-eminent goal of pharmacotherapy for chronic disease in the elderly; living well might be a more important priority for some. However, Tiotropium given via the Respimat does not make patients more well than Tiotropium delivered via the Handihaler, and the Handihaler does seem to be safe, at least in a population with no overt cardiac or renal disease. We therefore agree with Jenkins and Beasley (***see page 6***) that it is hard to justify the continued use of the Respimat preparation, at least in the current doses. Can we not learn from the past? Berotec was given the death sentence by Helen Clark in New Zealand to the accompaniment of much squawking and protest largely because there were known safer alternatives. Time for the black cap here?

CONTROL YOURSELVES!

Volbeda and colleagues (***see page 19***) report that patients with asthma that is judged to be controlled have less eosinophilic airway inflammation than patients with uncontrolled disease. For us the striking finding of the study was the considerable overlap in measures of inflammation between clinical control categories. Longitudinal studies show even greater dissociation: neither Mepolizumab nor inflammation guided steroid treatment modify symptom control despite having a large beneficial effect on inflammation and the risk of attacks. Is it time that control of symptoms and inflammation were considered separate and independent goals of management? The continued belief that they are causally linked might be good enough for GINA and great for inhaled steroid sales, but it is it good medicine?

DIAL D FOR DILATATION (OF THE AIRWAY)

Vitamin D turns up, or rather fails to turn up in many diseases—now including non-cystic fibrosis bronchiectasis. Chalmers *et al* (***see page 39***) studied 402 patients with bronchiectasis and showed that normal Vitamin D status was as rare as an honest banker. Low levels were associated with worse spirometry, more evidence of inflammation in sputum and more infection with *Pseudomonas aeruginosa*. Good to see a big research study in this orphan group of patients. Challengingly, although they could not dissect out in a cross-sectional study whether Vitamin D deficiency was cause or consequence of more severe disease, they found elevated vitamin D binding protein (VDBP) in sputum correlating with higher levels of markers of neutrophilic inflammation. We know VDPB binds Vitamin D and has intrinsic immunomodulatory properties, and it may be the crucial missing link. However, bring on data not discussion! We must have a moratorium on cross-sectional studies and do the much more challenging longitudinal and intervention work.

THE DARK SIDE OF THE BRONCHUS

What the bronchoscopist saw is shown in the figure; what did it mean to this middle aged man in whom sarcoid had been diagnosed previously when non-caseating granulomas were found on transbronchial biopsies? Sort it out, then turn to ***page 117***.