Highlights from this issue

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Cystic fibrosis (CF): the new TB?

Not because it is anything other than a very minor player in the men of death compared with that great global scourge, TB, but because CF is following TB into the epicentre of evidence based medicine. This CF themed issue of *Thorax*, coinciding with the US Cystic Fibrosis Foundation annual meeting, celebrates the achievements of the CF community in general, and the Foundation in particular, in driving through a series of focussed randomised controlled trials taking medications forward from the 'wouldn't it be good if' stage to FDA licensing. These are summarised in the review by Rowe *et al* ***(see page 882)*** and visually on the front cover of the journal. The review summarises the few failures as well as the many triumphs, and highlights lessons learned by the Foundation. We include a further trial, comparing two different, relatively short course (28 days) *Pseudomonas aeruginosa* eradication regimes which showed equivalence of inhaled colistin and tobramycin when combined with oral ciprofloxacin ***(see page 853)***. CF is a beacon for other diseases, and an inspiration for other patient groups as to what can be achieved. These trials worthy successors to the MRC trials on TB treatment from way back when.

Wrong from the start

Not another medical *cri du coeur* about health service reform, but CF lung disease in babies diagnosed by newborn screening (NBS). There is conflicting evidence about whether NBS CF babies have normal or abnormal lung function very early on, and then subsequently deteriorate. The issue of lung function early on is definitively nailed by Hoo *et al* ***(see page 874)*** in this issue of the journal. They showed that, compared with contemporaneous controls, more than a third of NBS CF infants age 3 months had abnormal lung function, namely airway obstruction using the raised volume squeeze technique, hyperinflation, or distal gas mixing (lung clearance index). What is not clear is whether these changes are due to early postnatal infection and inflammation, or, as the CF pig studies might suggest (*Am J Respir Crit Care Med* 2010;**182:**1251–61), a structural, antenatally-mediated effect of CFTR dysfunction. Either way, these data challenge the CF community to address the issues of early NBS CF lung disease, and find biomarkers for intervention trials in very young infants, as highlighted in the accompanying editorial by Cunningham ***(see page 849)***. What you can't see will undoubtedly come back to bite you.

Two's company, three's a crowd, and hundreds are baffling!

Life used to be so simple—the normal lower airway is sterile, and CF is paucimicrobial. It is now clear from sophisticated molecular microbiology that the normal lower airway is teeming with microorganisms, that this flora is an essential part of modulating immune maturation, and that the more diverse the species, the better for the child. Stressmann *et al* report on the longitudinal bacterial flora in CF ***(see page 867)***, and showed that airway flora were diverse and tended to be stable over the yearlong study period; interestingly, individuals with very different clinical courses seemed to have the same microbiological profiles (so what *is* driving their clinical course?); that antibiotics transiently perturbed the community, but for whatever reasons, the previous community usually soon reformed; and that lots of different organisms were a good thing. In his editorial ***(see page 851)***, LiPuma discusses the need to move from single organism thinking to the concept of a 'pathogenic unit', and, reassuringly for those of us who are struggling with the new microbiology, frankly sets out the large areas of ignorance we all share. Rightly he cautions against therapeutic nihilism or paralysis in the face of ignorance; current antibiotic strategies, albeit shooting in the dark, have been associated with marked improvements in prognosis. However, these new data will likely provoke a radical re-think, and the need for new intervention trials, as we (hopefully!) increasingly understand how favourably to modulate the microbiological soups that are bubbling away in every human airway.

'Why, sometimes I've believed as many as six impossible things before breakfast'

The White Queen could accomplish this feat with practice, and to our politicians six is mere child's play, but in our case-based discussion doing a mere two impossible (or at least mutually contradictory) things was quite a challenge. So what does the CT show, why is the management problematic, and what's it got to do with CF? Turn to page 932 to find out.