

# Thorax: the Cappuccino years

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We are now about half way through our term of office (unless we are prematurely fired for terminal misbehaviour); here we review where we are, and where we are going, and have the first instalment of the showcase of some of our best articles from last year. We have maintained our second position with an improved impact factor (6.84) over 2011, we continue to attract very high quality manuscripts, and handling times have come down (all good news). We owe these achievements to our associate editors and editorial board, the reviewers, and especially those who have submitted such great manuscripts. An especially large bouquet to the editorial staff, in particular Renuka Patel for her work on Hot Topics and marketing, Bryony Skinner, who has stepped magnificently into the breach, Allison Lang and our unsung heroine Sarah Szatkowski, who keeps us sane when ScholarOne is driving us to Prozac or haloperidol or both. Don't leave us! We acknowledge we need to speed up further, and get the impact factor higher—both are a work in progress. However, average time from submission to first decision for all manuscripts is less than 30 days, and accepted manuscripts appear on-line in an average of 25 days. We have had our first randomised controlled trial protocol to review for consideration for fast-track publication when the study is completed—an offer which does *not* depend on the result being positive—investigators please note. *Hot off the Breath* continues to generate controversy—totally drug resistant tuberculosis (TB) and the roaring *PANTHER* being cases in point. We have had two themed issues (North American, to coincide with American Thoracic Society and cystic fibrosis (CF), to coincide with the US CF Foundation annual meeting). In 2013, we will have a Tuberculosis themed issue for World TB day (March 24th) and plan a Pneumonia themed issue for World

Pneumonia day (November 12th). We are continuing to use Podcasts and are keen to explore better use of electronic media—suggestions (and help for the terminally e-illiterate) are welcome. We would also welcome ideas for further themed issues.

We have been fortunate in publishing some great manuscripts in 2012. We have chosen four areas to highlight, and, in the Olympic Year, we have awarded gold, silver and bronze in each category. There is no overall winner; can you compare Michelangelo's David with Beethoven's ninth symphony? Apologies if your manuscript is missed or you think you should have won the prize; the rules were that the editors' own manuscripts were automatically disqualified, and the umpires' verdict is both final and arbitrary. Better luck next year, keep the great manuscripts coming. This month we showcase Paediatric and Adult Thoracic Medicine; next month, epidemiology and basic science.

## PAEDIATRIC LUNG DISEASE

The main themes have been asthma and CF, respectively the most common problem in childhood and the area where there is the most game-changing research going on. Asthma is much more than reaching for the prescription pad. We can and should do our best to improve the environment. Tobacco (again!) is the lead culprit, with paternal as well as maternal tobacco abuse being shown to be important by the ISAAC programme.<sup>1</sup> We need to look beyond the home; the COPSAC group reported the association between short-term exposure to air pollution and hospital admissions for asthma.<sup>2</sup> The strong relationship in infants is a puzzle, given one would expect them to be outside the home less than older children, but maybe this reflects the extreme vulnerability of the developing lung. School air quality was also highlighted as an area for improvement.<sup>3</sup> Allergens are another perennial theme, and a long-term prospective study from the Isle of Wight demonstrated that an intensive allergen avoidance programme starting from birth reduced the risk of asthma onset in genetically predisposed individuals<sup>4</sup>; this is the Bronze medal manuscript, a whisker behind the silver medal position, for a superb, long-haul effort. A randomised, double-blind, placebo controlled trial of allergen

reduction using a commercially available device aiming to reduce allergen exposure to producing nocturnal, temperature controlled laminar airflow during sleep showed improved quality of life and reduced systemic inflammation, but unfortunately no effect on exacerbations.<sup>5</sup> Of course pharmacotherapy is important, and we debated the hot topic of whether continuous or intermittent inhaled corticosteroids were correct for children with mild asthma.<sup>6,7</sup> However, whatever the outcome of the debate in the rarefied atmosphere of the hospital clinic, it is likely in practice that families will do their own thing in real life! One issue is that you cannot treat that which is not perceived, and we also published a great manuscript showing that, in inner city asthmatic children, perception of asthma is poor but can be improved by appropriate feedback, at least in the short-term<sup>8</sup>; this is accompanied by improved adherence to therapy. This manuscript wins the Silver medal in recognition of the difficulty of doing research in such a challenging environment. Finally, for connoisseurs of public fist-fights, two papers about monitoring severe asthma<sup>9,10</sup> triggered Leicester-London internecine warfare in the editorial columns<sup>11,12</sup> and correspondence.<sup>13,14</sup> Judge between the editors: is induced sputum useful in childhood severe, therapy-resistant asthma, and if not, why not?

CF was the second major topic. Three manuscripts covered CF new-born screening (NBS) and outcomes.<sup>15-17</sup> Strategies of NBS were compared in a prospective study,<sup>15</sup> especially to inform countries where DNA screening may not be acceptable, and reassuringly, all strategies performed well. Australian-UK controversy is heating up nicely ahead of the Ashes series, in terms of outcomes; the Australian group reported deterioration in structural lung disease with worsening infection and inflammation in their NBS group<sup>16</sup>; the UK London collaboration resolved the controversy about whether CF NBS babies have impaired lung function shortly after diagnosis (they do),<sup>17</sup> but their follow-up data, so far only presented in abstract, may tell a different story. Don your helmet, watch this space and be ready for the sledging and short-pitched bowling! Space precludes reviewing a number of excellent CF randomised controlled trials, but we highlight two areas where what was thought to be simple has become complex. The first is diagnosis—as medical students we were taught that the sweat test was the be-all and end-all of diagnosis, but we are now

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finding that it may be normal in milder or single-organ atypical cases; however, *pace* Oscar Wilde, in this case the UK and North America have the same language in common, and largely agree on diagnostic criteria.<sup>18 19</sup> Second, we were taught that CF was a polymicrobial disease; now molecular techniques have taught us that the CF airway is teeming with multiple organisms, and the community stays largely stable in a given individual, despite antibiotic therapy.<sup>20</sup> In an accompanying editorial, LiPuma charts a path for the confused, as well as re-assuringly demonstrating to the intellectually challenged that even the serious scientists are struggling with the implications of these novel data.<sup>21</sup>

Finally, *Thorax* was not a two horse show in 2012. Important manuscripts included guidelines on the management of neuromuscular disease in children,<sup>22 23</sup> which gives a comprehensive overview of how to look after a group of conditions which are becoming of increasing importance in adult practice; a randomised controlled trial of oral antibiotics in chronic wet cough<sup>24</sup> (showing our forebears were not as stupid as we thought! Keep doing the same thing long enough and you will be back in fashion); and a further testing of the special relationship in a USA-UK debate about what makes a diagnosis of primary ciliary dyskinesia<sup>25–28</sup>—genes versus not the environment but function—decide for yourself. The gold medal winner is in this category; we all know (or should know) that survivors of very preterm birth and intensive neonatal interventions have long term respiratory morbidity and premature airflow obstruction. This manuscript, based on the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort showed that late pre-term (33–34 weeks gestation) infants have just as severe lung function decrements as 25 week gestation babies,<sup>29</sup> and there are a whole lot more pretermers. For sure there was some improvement by the late teenage years in the late pre-term group, but this has considerable importance for adult practice; do not be complacent just because the baby was ‘a bit early’!

#### ADULT LUNG DISEASE

There have been strong contributions in lung cancer, idiopathic pulmonary fibrosis (IPF) and obstructive lung disease. Screening for lung cancer was very much the topic of the year. We are more sceptical of the benefits of this approach than many and are keen that we do not commit ourselves to an expensive

screening protocol without being absolutely sure that it is efficacious, feasible and acceptable to participants. Saghir *et al*<sup>30</sup> raised some concerns about efficacy in a preliminary report from the Danish Lung Cancer Screening Trial, suggesting that the main impact of screening was bringing forward early disease rather than a reduction in mortality. The concept that some cancers may be innocent bystanders rather than active players in the development of morbidity and death is important, and when Thoracic Surgeons start talking about it,<sup>31 32</sup> we should take note. Attitudes to participation in lung cancer screening clearly depend on the likely benefits but understanding other factors is important in a population who might be nihilistic about health promotion initiatives. Patel *et al*<sup>33</sup> found that the screening tests were acceptable to most but that the factors contributing to the decision to participate were complex and probably difficult to modify. Might it be better to focus more on increasing public awareness of symptoms and promoting earlier diagnosis? Some progress is being made as resection rates are increasing in the UK<sup>34</sup> but there is still along way to go. Simon *et al*<sup>35</sup> assessed public awareness of symptoms using a new assessment tool and found that it was low, particularly in the most high risk groups. Athey *et al*<sup>36</sup> recognised that increasing awareness of lung cancer might be a way of tackling the high lung cancer mortality in Doncaster and developed a multi-faceted intervention to improve public awareness of symptoms. The initiative was informed by local qualitative research and was highly imaginative, including coughing phone boxes, billboards and illustrated beer mats. It appeared to be effective, increasing chest X-ray referrals and lung cancer diagnoses. This is an excellent example of identifying and responding to local health concerns in an innovative and effective way; it is a richly deserved winner of the Silver medal in the adult category.

The IPF field was rocked by the findings of the PANTHER trial, highlighted first in a Hot off the Breath article in *Thorax*.<sup>37</sup> How could our treatment approach have been so spectacularly wrong for so long? We must ensure that this never happens again. To paraphrase St Paul, if I speak with the words of the wise, but have not solid evidence, I am a noisy gong or a clanging cymbal. However, the study does provide us with an opportunity to begin exploring other, potentially more fruitful treatment strategies. Proteasomal inhibition with Bortezomib<sup>38</sup> and promotion of

the effects of the death receptor ligand tumour necrosis factor-related apoptosis-inducing ligand<sup>39</sup> both look like promising approaches. Before embarking on clinical trials in IPF we need to be sure we use the most appropriate outcome measures. We agree with Athol Wells and colleagues<sup>40</sup> that mortality should not be the be all and end all of these trials and that other patient centred and physiological endpoints still have a role. The King’s brief interstitial lung disease health status questionnaire<sup>41</sup> and sarcoidosis questionnaire<sup>42</sup> look potentially useful and the good old forced vital capacity holds up well as a marker of disease progression, whether expressed as a relative or absolute percentage change.<sup>43</sup>

New and existing measures of obstructive lung disease have been discussed in a number of papers. The use of the acute bronchodilator response has had a serious mauling in two studies evaluating this measure cross-sectionally and longitudinally in big populations.<sup>44 45</sup> When something can neither be measured repeatedly nor shown to relate to any important patient event, it’s time to abandon it. There remains controversy about the best criteria for diagnosing chronic obstructive pulmonary disease (COPD),<sup>46–48</sup> a debate that we suspect will never be resolved to everyone’s satisfaction. Potentially new CT based measures<sup>49</sup> might provide a fresh and important perspective as might novel blood and urine biomarkers.<sup>50 51</sup> Previously promising markers of disease have had a bad year: Rinaldi *et al*<sup>52</sup> failed to confirm a previous finding of anti-elastin antibodies in COPD although blood and urine desmosine, an elastin degradation product, has emerged as a promising biomarker.<sup>51</sup> We suspect that the future is to view these measures as risk factors rather than arbitrary defining characteristics, as has been cogently pointed out by Guy Marks in a ‘must read’ opinion article.<sup>48</sup> COPD lung attacks have been the focus of a number of excellent papers in 2012. Aaron *et al*<sup>53</sup> suggested that attacks could be classified by their temporal pattern. Could these patterns be associated with different causes and treatment responses? Better risk stratification of patients presenting with an attack is an important priority, particularly if the current trend for devolving management to less specialised settings continues. We liked the Dyspnoea, Eosinopenia, Consolidation, Acidaemia and atrial Fibrillation score,<sup>54</sup> developed after a realisation that existing scoring systems were inadequate,<sup>55</sup> as it looks feasible, has good performance characteristics and benefits

from a very catchy title (although to be critical, the editors at least maintain that coffee without caffeine is like a honey-moon without sex). The use of beta-blockers by patients with COPD was surprisingly shown to be associated with a trend to a better outcome in patients presenting with an attack<sup>56</sup> supporting the truth universally acknowledged (pace Jane Austen) that interventions that reduce heart rate improve life expectancy (and vice-versa; more on this in 2013).

Otherwise it has been a quiet year for new treatments for obstructive lung disease with only small advances in prospect.<sup>57–58</sup> A notable exception is the use of polymer sealant for lung volume reduction as, unlike endobronchial valves, efficacy appears to be independent of fissure integrity.<sup>59</sup> Fissure integrity can be assessed directly by hyperpolarised gas MRI<sup>60</sup> so potentially patients best suited for these different techniques can be identified. Our highlight, and the overwhelming winner of the gold medal in the adult category (and this award is not driven by pity at the disappointing medal haul of the Canadian Olympic team), is the paper by Suissa and colleagues<sup>61</sup> on the natural history of severe COPD lung attacks and mortality in a large community population. This team strike us as being the best sort of epidemiologists. They are not content with identifying marginal ORs of nebulous risk factors in poorly defined populations in studies with a high potential for confounding and, we suspect, have no desire to see their work featured in the Daily Mail. They ask important and highly clinically relevant question and provide answers that change the way we think about disease. Figure 3 of their paper should be seen and digested by all clinicians and health economists interested in chronic lung disease.

There have been a number of notable contributions in the sleep field. Whether obstructive sleep apnoea (OSA) is an independent risk factor for cardiovascular disease, insulin resistance and obesity have been hot questions for some time. In 2012 we learnt that, compared with controls, patients with OSA find it harder to lose weight and had a less complete metabolic response to a healthy eating and living initiative.<sup>62</sup> OSA was associated with increased levels of several coagulation factors,<sup>63</sup> and an increased incidence of 'wake-up stroke'<sup>64</sup> (a condition whose existence was news to us). On the other hand, two blinded appropriately controlled studies showed no evidence that treatment of OSA with continuous positive airway pressure (CPAP) improved markers of vascular risk.<sup>65–66</sup> We liked particularly

the Multicentre Obstructive Sleep Apnoea Interventional Cardiovascular Trial (MOSAIC) study<sup>65</sup> and commend the study team for a sustained and impressive contribution to research in this area, which includes pioneering the use of sham CPAP treatment. They are our unanimous choice for the bronze medal. CPAP remains an effective treatment for sleepiness in OSA and other sleep related breathing disorders<sup>67</sup> even if some of the effects can be explained by an expectation of benefit.<sup>68</sup>

We have quoted Hilaire Belloc before: 'Oh! Let no-one ever, ever doubt, What nobody is sure about' and 2012 has been a good year for doing just that. In our 2014 editorial address to the society, we will have a prize for the authors who have successfully toppled the most entrenched dogma, and also a WS Gilbert prize: 'On fire that glows With heat Intense I turn the hoe Of common sense And out it goes At small expense'. Finally, we will have a prize for the most ridiculous acronym smuggled into a serious article, following on from 'REPRINTED' and 'SCRAPPED'.<sup>69</sup>

**Competing interests** None.

**Provenance and peer review** Not commissioned; internally peer reviewed.

**To cite** Bush A, Pavord ID. *Thorax* 2013, **68**, 1–4.

Accepted 5 November 2012

*Thorax* 2013;**68**:1–4.

doi:10.1136/thoraxjnl-2012-202970

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