

**Review of the British Thoracic Society Winter Meeting 2014, 3-5 December,
London, UK**

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of the BTS Science and Research Committee

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Abstract

The British Thoracic Society Winter Meeting 2014 is reviewed in this article. The annual scientific meeting had its largest number of delegates ever and over three days in December presented some of the world's most up to date Respiratory research, as well as delivering reviews of current thinking in Respiratory Science and Clinical Academia. This article reviews a number of symposia and selected abstract presentations from the meeting.

Introduction

"When shall we three meet again? In thunder, lightning, or in rain?" And so plans to attend the British Thoracic Society Winter Meeting 2014 were made. A record number of delegates attended this year's meeting with 24 major symposia (including 18 international speakers), 3 Guest Lectures, 26 Spoken Sessions, with a total of 144 spoken and 304 poster abstracts. Here, a selection of the authors' highlights are presented.

Plenary Scientific Symposium

This year we heard from four of the UK's leading clinical academics that showcased their foremost research in respiratory medicine. Professor Stephen Gordon (Liverpool) spoke about his research into mucosal defence against *S. pneumoniae*, the most common cause of community-acquired pneumonia. Mucosal immunity is an important host derived mechanism for the naturally acquired protective immunity against lung infection with this pathogen(1). Additionally, he discussed the experimental human pneumococcal carriage

model used by his group to investigate clearance of *S. pneumoniae* and protection against infection(2).

Dr Alison Condliffe (Cambridge) described her research that led to discovery of a novel genetic mutation in which there is glutamic acid to lysine substitution at residue 1021 (E1021K), causing a primary immunodeficiency known as activated PI3K-δ syndrome(3). This specific immunodeficiency has been reported in a number of families and causes recurrent respiratory infections.

Professor Luca Richeldi (Southampton) discussed his research trying to identify patients with interstitial lung disease earlier with the aim of in the future improving patient outcomes by commencing anti-fibrotic treatment before patients have had decline in lung function(4). His research has identified good agreement between electronic interpretation of acoustic patterns of fibrotic lung sounds and the assessment by expert physicians. Furthermore, he is investigating the correlation of these sounds obtained from recordings with electronic stethoscopes to HRCT images.

Guest Lectures

The guest lectures were a particular highlight this year, encompassing multiple aspects of Respiratory Medicine.

Professor Sally Wenzel delivered the BTS Lecture from the Asthma Institute, University of Pittsburgh, on asthma phenotypes and the evolution from clinical to molecular approaches(5). She reviewed the clinical and physiological features that historically been used to type asthma and then introduced more objective ways of phenotyping patients using cluster analysis(6, 7). These methods demonstrate how the different pathobiology and biomarkers can relate to the

clinical characteristics and establish separate sub-groups of asthmatics. Importantly, treatments that target specific pathways are now available for particular phenotypes. Finally, Professor Wenzel described the less-well understood non-T_H2 asthma, in particular neutrophilic asthma, which is less responsive to corticosteroids.

The Morriston Davies Lecture was given by Professor Sir David Spiegelhalter (Cambridge) on communicating risk and uncertainty to the public and policy makers. This highly entertaining lecture was directly relevant to all those involved in talking to patients, as managing uncertainty is one of the most difficult skills. Using real life examples- such as the nationally reported risks of eating a rasher of bacon a day- he presented different ways of communicating risk and it is likely that expected frequencies and tree diagrams will become part of standard reporting of trials, rather than absolute or relative risk. Indeed they are already appearing on patient information leaflets around disease screening.

This year's Snell memorial lecture was given by Professor Douglas Young (London), taking us back in time through phylogenetic trees to determine the origins of *Mycobacterium tuberculosis*. Although it is advocated that human tuberculosis was distributed throughout the world following the dispersal of humans from Africa, it is now suggested that sea mammals played a key role in transmitting the disease across oceans and to the different continents(8).

The president's address was given by the current American Thoracic Society (ATS) president, Professor Thomas Ferkol (Washington, USA), who detailed his journey as a clinical academic leading discovery science in cystic fibrosis, as well as highlighting recent emerging therapies that will change the outlook for these patients. Professor Ann Millar will continue as BTS president for another term

as the elected president for this year, Professor Wisia Wedzicha (London) has taken up the role as the first non-American and first female editor-in-chief of the American Journal of Respiratory and Critical Care Medicine. During this session we were informed that the BTS members will be able to attend the ATS 2015 meeting at ATS member rates.

BTS/BALR

The BTS and BALR have had a long tradition of setting up joint sessions and this year we heard talks from exceptional speakers in two sessions on the topic of “Modelling respiratory disease: current concepts for drug discovery”. Professor Clive Page (London) described the usefulness of *in vivo* models to identify new drugs for respiratory disease, whilst Dr Chris Scotton (Exeter) spoke about novel ways to use *in vivo* imaging in murine models of lung disease(9), and Professor Stephen Renshaw (Sheffield) described how the zebrafish, which does not have lungs, is a useful model to study pulmonary inflammation(10). In the second session, Professor Eric White (Michigan, USA) discussed novel 3D cell culture models to study fibrotic lung disease, Professor Donna Davies (Southampton) described how novel tissue engineered constructs with microfluidics platforms to deliver inflammatory cells will be used to develop novel therapeutic for asthma, and Dr Carmel Nanthakumar (London) discussed how novel *in vitro* platforms are being used in industry to develop new anti-fibrotic drugs.

BTS/BPRS

This year’s BTS/BPRS symposium covered the emerging body of evidence on the role of the microbiome in respiratory disease. Professor Hans Bisgaard

(Copenhagen) gave a very impressive talk on the role of the microbiome in viral induced wheeze in children and interestingly found that most cases were actually associated with bacteria and not viruses(11), suggesting that childhood wheeze should be treated with antibiotics. A probable link was also demonstrated between births from normal vaginal delivery and caesarian-section, whereby infants born following caesarian-section may have a less variable microbiome, which may affect health in later life(12). Professor William Cookson (London) discussed the microbiome in asthma and COPD and showed that those with severe disease are associated with higher frequencies of Streptococcal species in the lung microbiome. Professor Stuart Elborn (Belfast) talked about the complex microbiome in cystic fibrosis patients where the distinction between what is a pathogen and commensal organisms is difficult to ascertain; These also seems to be a correlation between low species richness (i.e. number of different bacterial species) and poor outcome in this group of patients.

Chronic Obstructive Pulmonary Disease (COPD)

Improving the outcome from exacerbations of COPD was the first symposium of the BTS. Dr Jennifer Quint (London) reviewed the risk from exacerbations and described how the complexity and multifactorial nature of these events made prediction of outcome difficult. This was followed by three interventions that have been of increasing interest and proposed to improve outcome. Dr Neil Greening (Leicester), presented around peri-exacerbation pulmonary rehabilitation, demonstrating good evidence for post exacerbation rehabilitation but poor uptake(13), and new evidence from an impressively large randomised

controlled trial of early rehabilitation starting at time of hospitalisation that had a negative primary outcome with no change in hospitalisation frequency or differences in physical performance, though large natural recovery was seen(14). Tele-health was presented next with Dr Hiliary Pinnock (Edinburgh), showing that the evidence is not as robust as Government announcements would suggest(15). Finally there were more positive outcomes presented by Dr James Calvert (Bristol), on findings from the BTS COPD admission bundle. Correct oxygen prescription and rapid treatment were associated with improved mortality, two of the five elements of the care bundle. Correct oxygen management and acidosis management elements of the care bundle were also associated with a lower length of hospital stay. Further abstracts on exacerbations of COPD were presented later in the BTS with Dr Kon (London) demonstrating that a measure of frailty, the 4 metre gait speed, which can be performed near the bed side, predicts mortality following hospitalisation(16). The extra pulmonary effects were also demonstrated with premature cardiovascular ageing in COPD using aortic pulse wave velocity(17).

Away from specific diseases and covering the symptoms of breathlessness Professor Miriam Johnson (Hull), covered the management of refractory breathlessness. All clinicians who manage patients with advanced disease with recognise the difficulties with this. Treatments included facial airflow, low dose opiates and oxygen therapy with a systematic review and meta-analysis for the last published the same day in Thorax demonstrated a benefit of oxygen on breathlessness symptoms, but with a limited evidence based(18). Dr Kyle Pattison (Oxford) proved the importance of the brain and neural mechanisms for breathlessness using fMRI(19).

The National Secondary Care COPD audit was collected earlier in 2014 and its results were presented by Dr Robert Stone (Taunton). The largest ever COPD patient dataset was collected and showed improvements in palliative care, non-invasive ventilation and early discharge services, but a number of issues were identified including access to spirometry, smoking cessation and pulmonary rehabilitation.

Respiratory infections

Bronchiectasis was prominent at this year's winter meeting. The reason for this was perhaps best demonstrated by Navaratnam et al, who used hospital episode statistics to demonstrate a near doubling in the number of hospital admissions for bronchiectasis in England from 2004 to 2011(20). Bronchiectasis is becoming more common and more costly (figure 1).

This was the setting for the symposium "new developments in bronchiectasis" on Friday morning. The session began with Dr Tony De Soyza (Newcastle) discussing important new developments in bronchiectasis research. The award of a large MRC grant to establish a UK bronchiectasis network and biobank was celebrated as the first step towards facilitating a better understanding of this disease. Alongside International initiatives including the European Respiratory Society sponsored European Bronchiectasis Registry (EMBARC) these networks should facilitate better clinical trials and Dr De Soyza emphasised that the UK is already a leading destination for commercial and academic clinical studies in bronchiectasis. Emerging antibiotic and anti-inflammatory therapies for bronchiectasis were discussed, reflecting on the fact that this once neglected disease now has an impression pipeline of potential new therapies.

Dr Charles Haworth (Cambridge) outlined the challenges of treating chronic *P. aeruginosa* infection. This pathogen is associated with higher mortality, faster lung function decline and worse quality of life but there remains no consensus on how best to deal with it(21). Dr Haworth presented an international randomised controlled trial of inhaled colistin which he led, which narrowly failed to meet its primary end-point of improved time to first exacerbation, but which had a highly significant effect on this end-point and on quality of life in patients that had adhered to therapy(22). A timely reminder that patients have to take their treatment in order to derive benefit. Dr Michael Loebinger (London) gave an excellent talk on the growing worldwide problem of non-tuberculous mycobacterial infection. Although the incidence is increasing at rate of 2.9-8.2% per year, it is also frequently underdiagnosed and underestimated(23). Data point to a unique immunological phenotype and even morphotype and Dr Loebinger presented data again linking NTM infection with defects interferon gamma.

The final presentation on the role of macrolides provided an excellent platform for discussion. Several trials now support the use of macrolides in bronchiectasis but there is no agreement on the best choice of drug, duration or dose. Dr Hill (Edinburgh) provided the evidence to date(24).

Statins were once promoted as a panacea to treat a range of inflammatory airways diseases. Animal and experimental models of asthma, COPD and infections show remarkable anti-inflammatory effects, but clinical trials have been very disappointing, most recently an RCT of 885 COPD patients randomized to simvastatin or placebo found no impact on exacerbations(25). Statins made a minor comeback at the winter meeting with a report by Mandal et al that

atorvastatin significantly improved cough in a randomized controlled trial (30 patients atorvastatin vs 30 patients receiving placebo), possibly by promoting neutrophil apoptosis(26).

Saleh et al used a recently described severity assessment tool for bronchiectasis to study the extent of bronchiectasis in patients with primary immunodeficiency(27, 28). They found that, consistent with other reports, patients managed in specialist immunodeficiency services have a good prognosis with preserved lung function and a low frequency of colonisation with *P. aeruginosa*.

The winter meeting coincided with the publication of the NICE guidelines for pneumonia and so this was always bound to be a hot topic at the meeting(29). One of the major findings of that guideline was an almost complete lack of UK data on the management of hospital acquired pneumonia (HAP) and so it was refreshing to see a study by Burton et al describing the incidence and risk factors for HAP in a large cohort (1302 patients). Perhaps not surprisingly, aspiration was a major risk factor and mortality was high(30). HAP is a key area of unmet need in respiratory medicine.

Hospitalisations for pneumonia are increasing, a message reinforced by Millett and colleagues who could find no clear explanation for the rise and suggested the possibility that changes in the health service may be driving an increased tendency to refer patients to hospital(31). The likelihood of hospitalisation for pneumonia increased by almost 30% over 10 years, suggesting a major shift in practice that could have important implications for healthcare costs.

Tuberculosis

TB remains a major challenge, but our own problems pale into insignificance compared to those in Eastern Europe, which now has an unwanted status as a world leader in multidrug resistant TB (MDR). For example, a recent study from Belarus showed that 35% of new TB diagnoses and $\frac{3}{4}$ of new TB cases in those having previously treated for TB were MDR or XDR-TB cases(32). Professor Christoph Lange (Borstel, Germany) outlined this growing problem, emphasising the need for solutions at a European and global level.

Professor Stephen Gillespie (St Andrews) next presented a ground breaking clinical trial- the ReMOX TB trial. This was an extraordinary international effort, randomising 1931 patients in South Africa, India, Tanzania, Kenya, Thailand, Malaysia, Zambia, China and Mexico(33). The study aimed to reduce the duration of antibiotic therapy for TB from 6 months to 4 months using a moxifloxacin based regime. Despite moxifloxacin resulting in a more rapid bacterial killing, the shorter regimes containing moxifloxacin showed a higher relapse rate than the standard 6 month regime, which will consequently remain the standard of care internationally. Finally Professor Beate Kampmann (London) reviewed the specific clinical challenges of treating TB in children, including latent TB infection in children. London sees a high burden of UK TB cases. Ferenando et al presented an abstract describing a very high frequency of latent TB infection in hard to reach groups (homeless people, substance misusers and prisoners) in London along with high rates of blood borne virus co-infection(34). A higher than expected prevalence of blood borne viruses in TB cases was confirmed in a separate abstract by Potter et al, who advocated changing national guidelines to recommend routine screening for hepatitis B and

C in patients with active tuberculosis(35). Vitamin D deficiency was an important discussion topic in the 2013 winter meeting review, but in a study by Sloan et al was found not to have any effective on treatment response during TB infection in adults in Malawi(36).

Interstitial Lung Disease

Idiopathic pulmonary fibrosis has recently gained much interest from the respiratory community as two important clinical trials have been published that demonstrate a positive effect on clinical outcomes by two drugs, Pirfenidone(37) and Nintedanib(38). At this year's BTS Winter meeting the IPF sessions were very well attended with full auditoriums. Dr Martin Kolb (Ontario, Canada) kicked off with an interesting lecture that not only reminded us that IPF has worse outcomes than most cancers but that their pathobiology have many similarities, and that in the future this disease may need to be targeted in the same way that oncologists have managed cancer. Dr Gisli Jenkins (Nottingham) discussed the role of imaging in the diagnosis of IPF and using features of the disease on computed tomography chest scans to assist with outcome prediction, whilst biomarkers such as MMP3 and CXCL13(39) may in the future allow for stratification of IPF patients and targeted therapies, moving into an era of personalised medicine. Dr Andrew Wilson (Norwich) discussed the pulmonary microbiome in IPF and suggested that antibiotics may have a role in improving patient outcomes(40). Dr Nik Hirani (Edinburgh) ended the session by demonstrating how patient's treated in his local practice would not fulfil criteria to enrol in recently conducted IPF clinical drug trials making it hard to generalise results of these trials to the majority of IPF patients seen in clinical practice. The

basic mechanisms in IPF session highlighted novel basic science research in this field, including identification of the kinase selectivity profiles of compounds trialled for the treatment of IPF(41). In this session Miss Al-Juffali (London), winner of the BTS medical student prize, presented her elegant research on the use of nanodiamonds to deliver VEGF to promote fetal lung development in a rat model of congenital diaphragmatic hernia(42).

Acute Lung Injury

Acute lung injury (ALI) is a major cause of morbidity and mortality and this year the BTS heard from experts in this field that a working on understanding the mechanisms of acute lung injury for drug development. Professor Rachel Chambers (London) gave an insightful overview of the known pathomechanisms leading to the development of ALI in particular focusing on novel work from her group on the interplay between coagulation and inflammation(43), in particular the role of neutrophilic inflammation(44). Professor Danny McAuley (Belfast) discussed his experience of investigator led studies for the translation of findings from experimental models to human clinical trials in the development of new therapeutics for patients with acute lung injury, which is a difficult task that is made even harder by the heterogeneity associated with the disease(45). Due to the paucity of effective therapeutics for the treatment of ALI, Dr Daniel Talmor's (Boston, USA) talk focused on identifying patients at risk and focusing therapeutic strategies at preventing the development of the acute respiratory distress syndrome in this group of patients. Finally, Dr Andrew Bayliffe (London) discussed the important contribution of the pharmaceutical industry

The mechanistic insights into acute lung injury session had young investigators demonstrating their research in this field. The session included a description of a novel human model to study alveolar injury and repair, using precision cut lung slices(46), investigations highlighting important roles for TNFR1 in neutrophil-endothelial interactions(47) and proteinase-activated receptor-1 signalling in pneumococcal pneumonia-induced lung injury(48), as well as the role of lipoxin A4 in improving efferocytosis in ARDS(49).

Pleural disease

The symposium on pleural disease on the opening day of the BTS winter meeting was very well attended with emerging enthusiasm in pleural disease amongst our colleagues. This session included three entertaining and humorous pro-con debates on the use of the BTS guidelines for the management of primary spontaneous pneumothorax by Dr John Harvey (Bristol) and Dr Andrew MacDuff (Wolverhampton). We were reminded that even though there isn't a body cavity that can't be reached with a needle, we should always treat the patient and not the air on the chest radiograph. Dr Mark Slade (Cambridge) and Dr Mohammed Munavvar (Preston) debated the use of indwelling pleural catheters in the management of malignant pleural effusions; these catheters may change our management of these pleural effusions, facilitating outpatient care and improving integrated care.

#BTSSwinter

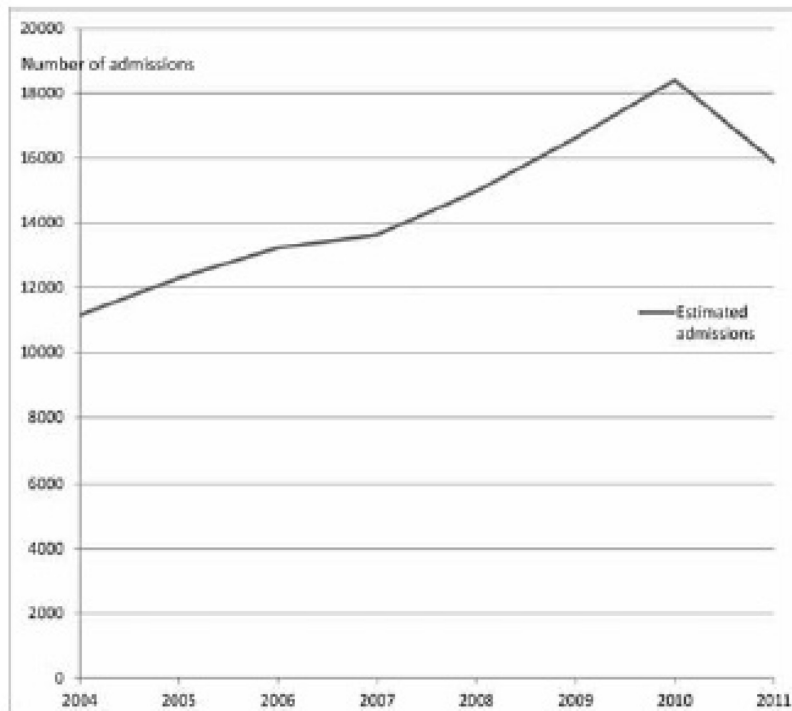
2014 saw further increased presence of the BTS Winter Meeting on social media. A total of 3,110 tweets from 431 participants saw discussions reaching beyond

the walls of conference centre, and debate by delegates within sessions. Figure 2 shows the most used words in tweets for the meeting, an insight to the particular areas of debate and interest.

Conclusions

The 2014 Winter BTS meeting provided delegates with both fantastic reviews of cutting edge Respiratory Science and Research and presentations of original data. For those busy digesting all this information and preparing for the obligatory New Year resolutions of more exercise and better diet the final abstract in this review is reserved for Curtis et al, who presented an interventional cross-over study of supplemental beetroot juice with cycle ergometry, showing a significant reduction in oxygen consumption and diastolic blood pressure in patients with COPD(50).

Figure 1: Increasing rates of hospitalisation for bronchiectasis.



Abstract P81 Figure 1 Hospital admissions from bronchiectasis in England from 2004–2011

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