Review of the British Thoracic Society Winter Meeting 2013, 4–6 December, London, UK

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Received 25 January 2014 Accepted 27 January 2014 This article reviews the British Thoracic Society Winter Meeting 2013, the annual scientific meeting attended by over 2000 delegates and representing the depth and breadth of UK respiratory medicine. This year's meeting from 4 to 6 December in London featured cutting-edge research alongside keynote symposia from international experts in respiratory science, epidemiology and clinical trials. This article reviews the key symposia and selected abstract sessions from the 2013 meeting.

INTRODUCTION

ABSTRACT

For many the draw of 3 days in London in December would be Oxford Street, leaving with still warm credit cards and multiple bags of Christmas presents. For 2133 delegates, however, the highlight was the British Thoracic Society Winter Meeting 2013, and they left with something far more rewarding and considerably cheaper! This article reviews the important new data presented at this year's meeting. As it is impossible to review 23 major symposia, 149 spoken abstracts and 287 presented posters, we present some of the authors' selected highlights from the British Thoracic Society (BTS) 2013.

Early career investigator symposium

A highlight of the BTS meeting each year is the early career investigator symposium, a showcase for the best basic, translational and clinical research submitted to the winter meeting. Six early career investigators gave presentations to a panel of judges from the BTS, British Lung Foundation (BLF) and British Association of Lung Research (BALR), hoping to win one of the prestigious awards.

The BTS prize was won by Dr Liam Hurst from Cambridge, who presented in vivo and in vitro evidence that tumour necrosis factor- α down-regulated expression of bone morphogenetic protein receptor II (BMPR-II) in vitro and increased expression of ADAM 10 and 17. These cleaved BMPR-II to further impair BMP signalling. BMPR-II mutations are present in a substantial proportion of patients with familial pulmonary arterial hypertension (PAH), and BMP signalling is thought to be very important in idiopathic PAH. This work demonstrates a link between inflammation and pulmonary artery smooth muscle proliferation, suggesting TNF- α inhibition as a therapeutic approach in PAH.

The BLF prize was awarded to Dr Belton from Imperial College London, who presented a fascinating mechanistic study into the role of hypoxia in regions of pulmonary tuberculosis infection. Using PET-CT with the hypoxia tracer 18F FMISO, severe hypoxia was demonstrated in pulmonary tuberculosis (TB) lesions. Hypoxia increased MMP-1 and MMP-9 in bronchial epithelial cells, an effect that was dependent on the hypoxia regulator hypoxia inducible factor (HIF) 1α .

The BALR prize was awarded to Dr Ourradi from Bristol, who investigated the role of vascular endothelial growth factor (VEGF) isoforms in human umbilical vein endothelial cells (HUVEC) and human lung microvascular endothelial cells treated with two different VEGF isoforms. The researchers demonstrated differential effects of the alternative spliced products on vascular permeability, suggesting an alternative pathway for therapeutic manipulation.⁴

Runners-up were Dr Kalirai from Birmingham, who described an epidemiological study evaluating the impact of COPD on employment and the factors associated with employment in working-age patients with COPD;5 Dr Paschalaki from Imperial College, who investigated senescence markers in blood outgrowth endothelial cells from patients with COPD and smokers;6 and Dr Ritchie from Glasgow, who demonstrated the complexity of in vivo pneumococcal pneumonia models by showing that interleukin-17 receptor A knockout mice were either significantly more susceptible to bacteraemia or protected from mortality, depending on the strain of Streptococcus pneumoniae used and the strain's relative resistance or susceptibility to neutrophil phagocytosis.7

Following the presentation of the awards, Professor Ann Millar began her term as president of the British Thoracic Society with a wide-ranging speech. Evoking Charles Dickens, Professor Millar's 'Christmas Carol' touched on the Societies' Christmas past, present and future, emphasising the importance of respiratory science and scientists to the Society and pointing out that while the Society membership has grown and broadened over the past decades, still only two members described themselves as non-clinical scientists last year.

Plenary scientific symposium

The scientific symposium is an opportunity each year to hear from four of the UK's leading clinician scientists presenting cutting-edge translational research. This year was a real showcase for the depth and breadth of UK respiratory research, opening with Dr Tom Wilkinson from Southampton presenting research into T cell responses to influenza infection. Dr Wilkinson and colleagues have used human challenge models of influenza infection to identify T cells responses associated with protected against influenza



To cite: Chalmers JD, Greening NJ, José RJ, *et al. Thorax* 2014;**69**:378–382. infection, opening a potential new avenue for vaccine development.⁸ This was followed by Professor Martin Tobin from Leicester, whose group is studying genetic determinants of lung function and lung disease in the UK Biobank, a resource consisting of detailed medical information and DNA from half a million people in the UK.9 The potential of these kinds of huge bioresources when combined with cutting-edge genetic techniques is clear and may finally start to resolve the complex relationships between individual variation, smoking, lung function and respiratory health. This was followed by Dr Sarah Walmsley from Sheffield, who presented her work on the effects of hypoxia on neutrophil function. Hypoxia prolongs neutrophil lifespan, delaying apoptosis and thereby potentially preventing the effective resolution of inflammation. 10 Dr Walmsley's group described multiple effects of hypoxia on neutrophil function, including describing a novel hypoxia-regulated neutrophil survival factor, Prolyl hydroxylase 3 (PHD3), effects of hypoxia preventing bacterial killing of Staphylococcus aureus and describing the role of HIF 2a in regulating neutrophil survival. 10-12 Unlike HIF1α, which has multiple effects on neutrophil function, HIF2α knockouts had reduced neutrophil survival and less inflammation in lung models but without defects in respiratory burst, chemotaxis or phagocytosis, thereby suggesting a therapeutic target for neutrophil-driven diseases like COPD or bronchiectasis where resolution of inflammation is desirable without increasing susceptibility to bacterial infection.12

The symposium was closed by Professor Gavin Perkins, who described the trials and tribulations of important multicentre trials in critical care. Initial randomised controlled trials had demonstrated potential efficacy of intravenous salbutamol in patients with acute lung injury, with a trial published in 2006 showing a reduction in extravascular lung water and other benefits. This was followed up by the multicentre BALTI-2 trial, randomising 162 patients to salbutamol and 164 patients to placebo. The trial was stopped early due to safety with an increase in 28-day mortality reported in the salbutamol arm and a general poor tolerance of the therapy. There followed an interesting discussion on the challenges of modern clinical trial design, from choosing endpoints in early-phase studies to the difficulties of translating benefits seen in experimental models into patient benefit in late-phase clinical trials.

This was a record-breaking year for abstracts at the BTS with 436 presented over the 3 days of the conference. Here we review a mix of the symposia highlights and selected abstracts across the major disease areas.

TUBERCULOSIS AND RESPIRATORY INFECTIONS

TB remains a global health problem, and it featured prominently at this year's conference. The 'New frontiers in tuberculosis' symposium was well attended by delegates and started with Professor Aljit Lalvani (London) highlighting the increasing incidence of TB in London despite it being a decade since the health protection agency declared war against TB. He focused on the need for a coordinated national screening programme, and that this should probably be taken up by GP services and be more targeted to improve efficiency. 15 This was followed by Professor Kheertan Dheda (Cape Town) sharing his experience of multidrug resistance (MDR) and extensively drug-resistant (XDR) TB in South Africa, where more than 80% of patients diagnosed with XDR-TB were resistant to 10 or more drugs, leaving clinicians with no effective antimicrobial drugs. Importantly, despite this only representing 0.2% of cases in the country, it consumed over half of the budget. Fortunately, some new drugs are emerging in the pipeline, including inhaled TB

therapy, but the cost and access to these drugs by countries such as South Africa will be a limitation to their use. He also discussed the importance of new diagnostic tests and showed that Xpert MTB/RIF, a fully automated diagnostic test, can be performed by nurses in community clinics and that increases same day diagnosis of TB and detection of drug resistance. This symposium then came to a close with Dr Philip Monk (Leicester) talking about the 100 000 genome project in England, which will include the sequencing of pathogens including *Mycobacterium tuberculosis* with the aim of early identification of the pathogens, predicting antibiotic susceptibility and epidemiological typing that will improve current contact-tracing strategies. Many lessons will be learnt from analysing these data, but ultimately this will be a move towards personalised medicine for TB patients.

Professor Lalita Ramakrishnan (Seattle) delivered the 2013 Snell Memorial lecture on the 'Immunological and therapeutic insights into human TB from the zebra fish', a model that does not have lungs but has enabled detailed investigation of the TB granuloma that resembles human TB. ¹⁷ Additionally, she demonstrated how the findings made in the zebra fish have been translated to humans and are leading to new therapeutic intervention strategies. Ultimately, this was an enthusiastic and entertaining lecture that was much enjoyed by the delegates.

Highlights of the non-TB pulmonary infections included an expert symposium describing the epidemiology, immunology and management of pulmonary fungal infections and the description of the first clinical prediction tool for patients with non-CF bronchiectasis. 18 It was noticeable that multiple abstracts in fields as ranging from idiopathic pulmonary fibrosis (IPF)¹⁹ to bronchiectasis and cystic fibrosis^{20 21} reported data on the airway microbiome using modern sequencing techniques based on the bacterial 16s ribosomal RNA gene. This technique, which has comprehensively disproven the old textbook teaching that the healthy airways are sterile, is changing our view of infectious lung disease and also appears to have relevance to inflammatory lung diseases like IPF. Much has been written regarding the possible damaging effects of vitamin D deficiency in pulmonary infections (see more below!), but a randomised controlled trial by Martineau and colleagues sounds a note of caution. They performed a double-blind cluster-randomised placebo controlled trial of high-dose versus low-dose vitamin D supplementation to residents and staff of sheltered housing schemes aiming to reduce the incidence of respiratory tract infections. After enrolling 240 participants, high-dose vitamin D replacement was associated with a significant increase in LRTIs. It appears you really can have too much of a good thing and illustrates another example that translating observational studies into clinical trial benefit is not always straightforward.²²

CRITICAL CARE

The critical care sessions focused on issues of the postcritical care patient with the symposium topics covering the brain, nerves, muscles and rehabilitation. Professor Tarek Sharshar (Garches) highlighted the importance of recognising brain dysfunction in critically ill patients and made the recommendation for daily neurological examination of the acute and critically ill patient. Next, Professor Mark Rich (Ohio) reminded us all of the long-forgotten neurophysiology of the action potential, detailing his hypothesis on how sodium channel dysfunction during critical illness may be responsible for the weakness seen in these patients and that this may be a protective mechanism of the body during critical illness. ²³ Dr Nick Hart (London) demonstrated in this symposium and in the 'late breaking news'

session that critically ill patients have a reduction in the rectus femoris muscle cross-sectional area, which is greater in those experiencing multiorgan failure and is associated with depressed levels of protein synthesis as seen in fasted healthy controls. We were also reminded that immobility is associated with the loss of 2% muscle mass per day—a good reason to remain active. This work recently published in *JAMA* is one of the best reflections of a year of great British translational medicine. ²⁴

In the 'mechanisms of lung injury' spoken session, several studies were presented, demonstrating the high-quality basic science and translational research that is being conducted in this area in the UK. Research from Professor McAuley's group (Belfast) investigated the use of a novel inhaled domain antibody to TNFR1 in a human model of lung injury induced by inhaled lipopolysaccharide (LPS)²⁵ and the role of targeting Siglec-E receptors on activated macrophages with polymeric nanoconstruct surface-functionalised with sialic acid targeting moieties.²⁶ Additionally, work from Dr Thickett's group (Birmingham) showed that vitamin D deficiency increases the bacterial load in the bronchoalveolar lavage fluid and blood of mice following caecal-ligation and puncture²⁷ and that neutrophils in the elderly have normal phagocytic ability but their migratory ability is impaired.²⁸ The migratory accuracy could be restored with simvastatin, but unfortunately this modulatory effect was not seen in neutrophils from septic patients. Finally, Miss Zambianchi (London) demonstrated that silver nanoparticles used in many consumer goods to treat pulmonary infections are potentially toxic to the lung by inducing oxidative stress, DNA damage and increasing inflammation particularly in the presence of viral infection.²⁹

LUNG CANCER

This year's poster sessions highlighted the increasing interest in the investigation and management of incidental pulmonary nodules³⁰ –³³ and the use of PET-CT for the detection of nodal disease³⁴ and non-nodal extra-thoracic metastases.³⁵ In the 'mechanisms in carcinogenesis' spoken session, work from Professor Janes' group (London) offered some hope for identifying novel treatments for lung cancer³⁶ and pleural mesothelioma,³⁷ as well as the identification of novel targets.³⁸ In the 'late breaking news session', we heard the results of Lung-BOOST trial and the MesoVATS trial from Dr Navani (London) and Dr Rintoul (Cambridge), respectively. Current routine investigations have low sensitivity for nodal staging in non-small cell lung cancer. Endobronchial ultrasound (EBUS) has been shown to have a high negative predictive value and resulted in fewer investigations for patients. Additionally, the use of EBUS in the diagnostic pathway resulted in improved survival possibly by shifting the staging at the time of diagnosis. Historically, mesothelioma has been treated with talc pleurodesis and the MesoVATs trial compared this to video-assisted thoracoscopic surgery (VATS) pleurodesis. The latter intervention significantly improved control of recurrent accumulation of pleural fluid in the first 6 months after the procedure and improved quality of life for 12 months; however, there was no significant difference in survival.

COPD

The first major symposium of the Winter BTS covered the options for severe COPD. Mr David Waller (Leicester) looked at lung volume reduction surgery (LVRS) 10 years after the publication of the NETT trial.³⁹ He demonstrated an individualised risk score for patients, and there was healthy debate on imaging techniques to aid patient selection. This was followed by a talk

by Dr Nick Hopkinson (London), who gave a comprehensive overview of bronchoscopic LVRS where evidence appears to lag behind current physician appetite.

The systemic consequences of COPD were the subject of the second COPD symposium, which is increasingly recognised as both important in the natural history of the disease but also an area with large potential for therapeutic development. Dr Charlotte Bolton (Nottingham) started by reviewing the cardiovascular consequences of COPD, which are closely linked and the cause of more deaths than a respiratory aetiology. Professor Michael Steiner (Leicester) followed with an overview of one of the most important systemic sequelae, namely, skeletal muscle dysfunction. He demonstrated both the functional and mechanistic changes longitudinally associated with resistance training and nutrition from an impressive intervention study. 40 Professor Michael Polkey (London) then highlighted specific phenotypes that may be identified within COPD and how this could lead to stratifying the right treatment for the right patient. The global successes of consortia working in COPD were reviewed by Dr Ruth Tal-singer (GSK) and how this was changing future research in COPD.41

Away from the symposia the number of abstracts presenting high-quality randomised controlled trials was striking. An investigation of the anti-inflammatory effects of statin therapy in COPD, while negative, provided novel thinking into treatments of the disease. For severe hospitalised exacerbations, the different response of eosinophilic and non-eosinophilic phenotypes further suggested that exacerbations may be a target for stratified treatment (and reducing harm of unnecessary drug prescription). In all yearly pilot work using laser capture micro-dissection to study gene expression in individual muscle fibres provided clues to novel mechanistic work that is likely to be presented at future meetings.

ASTHMA

Risk was the theme of Friday's asthma symposia. Dr Mark Levy discussed the lead up to the UK National Registry of Asthma Deaths (NRAD), with results planned for publication in April 2014. The lack of change in success since the 1970s when risk factors were first demonstrated was striking. 45

In order to act upon this, a risk assessment tool would be needed, and Dr John Blakey (Liverpool) gave a comprehensive overview on how this may be developed and what needed to be measured, demonstrating its many complexities and requirements if it was to work well for both the patient in clinic and whole populations.

Professor Ian Pavord (Oxford) followed with biomarkers that may help reduce the risk of 'lung attacks', which reduce lung function as much as smoking 20 cigarettes a day for a year. He demonstrated how stratified biomarker-led treatment improved outcome and how sputum eosinophils, blood eosinophils, periostin and FeNO are all bedside tools ready for this era. 46

Finally, Dr Samantha Walker, from AsthmaUK, presented novels ways to get patients involved, improved education and understanding and increase adherence, ranging from cutting-edge social media to dress up dragons. This is of vital importance as having news targeted biological agents will only work if the patient takes them (and correctly).

INTERSTITIAL LUNG DISEASE

The journal club for the Panther-IPF study was overflowing, demonstrating the interest and importance of IPF and the effect of this study on everyday practice. Professor Athol Wells (London) presented the context, study and aftermath of this

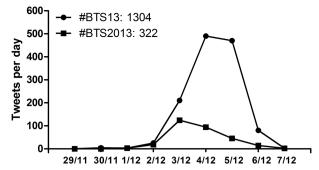


Figure 1 Tracking #BTS13 and #BTS2013 tweets from 29 November to 7 December 2013.

study, which found an increase in respiratory infections and mortality in IPF patients treated with N-acetylcysteine, corticosteroids and azathioprine ('triple therapy') compared with placebo.⁴⁷

He speculated on potential reasons for the harmful effects of treatment such as high-dose steroids in the first 16 weeks. ⁴⁷ Again, the theme of stratified medicine and the question around subpopulations that may do well were approached.

New therapies was the theme of the IPF symposium. Dr Gisli Jenkins (Nottingham) demonstrated the potential targets being identified in the laboratory, particularly through the TGF-β pathway and avβ6.⁴⁸ Next Dr Toby Maher (London) gave a preview of the Prospective Observation of Fibrosis in the Lung Clinical Endpoints study, due for publication soon.⁴⁹ This study will hopefully improve disease understanding, stratification and identify potential targets.⁴⁹ Professor Luca Richeldi then reviewed the measuring of endpoints in pulmonary fibrosis trials. This was particularly important with the publications of several large trials in the last couple of years and debate around acceptable outcome measures.⁵⁰

#BTS13

A final word to the virtual world of respiratory medicine. Delegates could not have helped but notice the large screen in the lobby of the Queen Elizabeth II conference centre displaying a live twitter feed as delegates discussed and reported the latest findings in 140 characters or less. As figure 1 shows, the combination of #BTS13 and #BTS2013 produced a total of 1600 tweets during the conference. A sign of the future as delegates share the latest research and clinical practice ideas with colleagues both within and outside the conference.

CONCLUSION

On reflection of the 2013 BTS in the Westminster arms, we considered Professors Millar's "Christmas future" for the BTS. We reflected that with an independence referendum in 2014 this may be last 'British' Thoracic Society for our Scottish members (or perhaps not). The British Thoracic Society's annual research meeting continues to highlight the very best of international respiratory research. 2014 is a world cup year, and it is pleasing to note that even if we cannot produce world beaters in Brazil, next December will at least see us continue to produce world leading science and research in respiratory medicine.

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