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Review of the British Thoracic Society Winter Meeting 2015, 2-4th December, London, UK

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Abstract

The British Thoracic Society Winter Meeting 2015 is reviewed in this article. Over 3 days in December this annual scientific meeting attracted over 2300 delegates and up-to-date respiratory research was presented by leading United Kingdom and international speakers. This article reviews a number of symposia and selected abstract presentations from the meeting.

Introduction

Looking out from the 6th floor of the QEII Conference Centre, the magnificent sight of The Shard, the London Eye and Big Ben all in one view reflected the equally outstanding meeting that we were about to experience over three days. This year the British Thoracic Society (BTS) Winter Meeting brought over 2300 delegates to London, and provided an exceptional forum for clinicians, scientists, allied health care professionals and students from the UK and abroad. A total of 146 speakers (27 from overseas) and chairs participated in delivering outstanding Symposia, which complemented presentations from the 460 accepted abstracts (131 in the spoken sessions, 291 posters, 32 moderated posters and 6 for the Early Career Investigator competition).

BTS/BLF/BALR early career investigators symposium

The BTS/BLF/BALR early career investigator symposium is an opportunity to see the future of UK respiratory medicine as 6 young academics present in front of a multidisciplinary judging panel for the opportunity to be named this year's Early Career Investigator winner.

Dr Rachel Dancer (Birmingham University) received the British Lung Foundation (BLF) award for demonstrating that Vitamin D supplementation reduces extravascular lung water, a surrogate marker of lung injury, after oesophagectomy in the brilliantly named VINDALOO trial [1] (confirming Birmingham as the home of UK Indian Cuisine after the equally delicious BALTI trial! [2]). Her group previously reported that vitamin D deficiency appears to contribute to the development of acute respiratory distress syndrome (ARDS)[3] and now demonstrate that vitamin D supplementation reduces peri-operative extravascular lung water but not oxygenation.[1] The immunomodulatory effects of vitamin-D (or the absence of them!) has been a recurring theme of our 3 years reporting from the BTS winter meeting and we look forward to large confirmatory studies.[4,5] Dr Richard Lee (King's Health Partners, London) was the runner-up in the BLF competition for his study evaluating MET targeted therapy in non-small cell lung cancer.[6]

Dr Aran Singanayagam (Imperial College London) was the recipient of the British Association for Lung Research (BALR) award for his study demonstrating that inhaled fluticasone caused an outgrowth of new bacteria within the mouse microbiome, particularly *Stenotrophomonas sp.* and was accompanied by impaired clearance of bacteria and viruses.[7] Given the clinical data linking fluticasone to an increased risk of pneumonia, this seems important and plausible.[8] We await confirmation in humans. The runner up was Dr Megan Jackson (Queen's University Belfast) who demonstrated that mesenchymal stem cells can enhance macrophage phagocytosis suggesting a potential therapeutic role in ARDS.[9]

Finally, the BTS award was won by Dr Alex Rothman (University of Sheffield). He described the role of MicroRNA-140-5p and SMURF1 in experimental and human pulmonary arterial hypertension (PAH).[10] Low levels of microRNA were associated with pulmonary hypertension in human and

animal PAH, while restoring this pathway preventing PAH development in rats. The runner-up for the BTS award was Dr Ahsan Akram (University of Edinburgh), who reported a novel in-vivo imaging method of detecting bacteria using fluorescent antimicrobial peptides.[11] The method has the potential to improve the diagnosis of conditions such as ventilator associated pneumonia where existing diagnostic methodologies are limited and treatment remains largely empirical.[12]

Plenary Scientific Symposium

Four of the UK's leading clinician scientists presented their cutting edge translational research during this Symposium.

Dr Nicholas Hart (London) started his presentation by highlighting the importance of mentorship, support and encouragement in research. His research showed how critically ill patients develop a rapid deterioration in muscle bulk, which is greater in multi-organ failure and he explored its underlying mechanisms.[13] Additionally, his patient focused research demonstrates that neural respiratory drive measured by parasternal electromyography (EMG) is feasible and can detect inpatient deterioration and predict early readmissions in those with COPD exacerbations.[14,15]

Professor Jacky Smith (Manchester) presented her research into the mechanisms and therapeutics for cough, a common respiratory symptom that is particularly troublesome in smokers.[16] Her work confirms that neuronal dysfunction is an important driver of cough and that specific neuro-phenotypes may exist.[17] Finally, her group has conducted a randomised control trial of the P2X3 receptor antagonist (AF-219) and demonstrated that this novel agent reduces cough frequency and is a promising anti-tussive for the future, once the taste disturbances are resolved.[18]

Dr James Chalmers (Dundee) presented his work into neutrophilic inflammation in bronchiectasis. His work shows that increased bacterial load in the airways is associated with increased airway and systemic inflammation, which is associated with exacerbation frequency.[19] Additionally, he highlighted novel findings that bronchiectasis sputum neutrophils produce extra-cellular traps, a mechanism for pathogen entrapment and killing, but have reduced phagocytic capacity. These are important findings for our understanding of neutrophil function in the airways where strategies are needed to achieve a fine balance between host defence and neutrophil-associated injury.[20] Furthermore, James chairs the pan-European network and registry in bronchiectasis (EMBARC) with the support of the European Respiratory Society (ERS), so if any BTS members would like to contribute, please visit <https://www.bronchiectasis.eu/register>.

Dr Pandurangan Vijayanand (Southampton and La Jolla, USA), presented work where his group identified new genes that contribute to asthma by using an unbiased approach. He highlighted genetic areas of the genome that are highly active in diseased cells, but inactive in healthy cells.[21]

BTS president's address/The Moran Campbell Lecture

A unique address from Professor Mike Morgan (Leicester) combined the Presidents address, as he took over from Professor Ann Millar as BTS president, and the Moran Campbell lecture, an invited lecture celebrating achievements in pulmonary physiology. The talk, "from pain to gain" emphasised the importance of exercise in lung health both in maintaining health and also in the assessment of pathology, while reflecting on the achievements and life of Moran Campbell himself.[22] He then

analogised that working with political organisations, commissioners and policy makers, in his role as President may also require a pain to gain approach.

BTS Lecture

This year's BTS lecture was a particular highlight within the programme and received great praise for the conference delegates. Professor Alvar Agusti (Barcelona), board of member for the GOLD group, provided insight into the complexity and direction of personalised treatment for Chronic Obstructive Pulmonary Disease (COPD). He described the multiple components that contribute to COPD and how COPD populations are heterogenous with different traits present in individuals.[23]. To address this complexity he proposed we think of a COPD "control panel" with the different aspects of the disease combining to make multiple different phenotypes.[24] We were also treated to the concept of "treatable traits" where by identifying characteristics that are amenable to specific interventions we may make a difference. Identifying these traits are important and there may be practical methods, such as using a individualised patient focussed problem-based approach.[25]

Rare (and not so rare) lung infections

Primary ciliary dyskinesia was well represented at the BTS winter meeting, both in the spoken sessions where several high quality abstracts were reported, and by the patient support group present throughout the conference. Dr Shah reported data from 151 adult PCD patients at a tertiary referral centre in London. Risk factors for lung function decline related to severity of disease on HRCT and ciliary ultrastructure but interestingly was not associated with *P. aeruginosa* colonisation.[26] *P. aeruginosa* was more common in patients diagnosed late, as was lower lung function, emphasising the importance of picking up the disease early.[27]

Fungal infections are an important cause of morbidity and mortality post-transplantation. Our inaugural award for coolest video of the BTS goes to the same Dr Shah who demonstrated lateral transfer of *Aspergillus fumigatus* from dying macrophages to new cells, a process hindered by calcineurin inhibitors, a standard treatment post-transplant.[28] These inhibitors were shown in a separate abstract to inhibit maturation of dendritic cells, further impairing host defence against *A. fumigatus* infection.[29]

The growing national interest in bronchiectasis was reflected by increased abstract numbers. Koustas *et al* identified no correlation between IL-8, IL-17 and the recently described severity tool, the Bronchiectasis Severity Index, finding no clinical value of these biomarkers.[30,31] *P. aeruginosa* had a dedicated session at this years BTS reflecting its importance in driving disease progression in CF and bronchiectasis.[32] Interesting data were presented on phage therapy for CF, [33] the absence of good evidence of cross infection in a UK centre in Exeter,[34] and evidence from an observational study from Belfast to suggest that the addition of an inhaled antibiotic enhances eradication.[35]

Streptococcus pneumoniae remains an important pathogen in community-acquired pneumonia.[36] Pneumolysin is a major virulence factor and work presented at the BTS suggests that this pore-forming toxin dampens early inflammation allowing growth of the bacteria by evasion of the immune system.[37] Furthermore, challenging humans with *S. pneumoniae* is a useful experimental model to investigate responses to colonisation and unlike in children where colonisation events appear to be symptomatic (although confounding factors may exist) it has now been reported that in adults colonisation events are asymptomatic.[38]

Antibiotic resistance

Combatting antibiotic resistance is a national priority and this was reflected in a high profile symposium. Opened by an introduction from Chairs Professor McShane (Oxford) and Dr Forthergill (Liverpool), the symposium heard the latest public health England and British Society of Antimicrobial chemotherapy (BSAC) data from David Livermore (Norwich) – *S. pneumoniae* remains the dominant pathogen in pneumonia, even in patients with frequent healthcare contacts and resistance remains low.[39] There are additional causes for optimism, for example in the decline in MRSA as a proportion of *S. aureus* cases in the UK, but an increasing global threat from carbapenemase resistant Gram-negatives and other multidrug resistant organisms.[40]

Professor Stuart Elborn (Belfast) reviewed the potential role of microbial diagnostics, from PCR to sequencing based “microbiome” characterisation and how this could be used to both rationalise antibiotic use and to identify resistance.[41,42] He also demonstrated experiments suggesting that interactions between different species within the microbiome could dramatically change antibiotic susceptibility. He suggested that traditional methods of defining resistant (R) and sensitive (S) from in-vitro growth may not always predict in-vivo effectiveness of antibiotics.

Finally, Professor Grant Waterer (Perth, Australia) gave a global view on antibiotic resistance, describing important differences in care that contribute to differences in antibiotic resistance rates internationally. He finished optimistically, suggesting that we remain far from the antibiotic apocalypse, but also challenged the audience to consider that tackling antibiotic resistance would need to include targeting antibiotic prescribing in children. Additionally, that we need to discuss the ethics of end of life care, as increasing numbers of patients worldwide acquire multidrug resistant pathogens in intensive care units and long term ventilation facilities near the end of life.

COPD

The two major COPD symposia were popular as ever with overflowing rooms. The COPDMAP is a large consortium of MRC and industry partners, supporting close collaboration between some of the top centres in the UK investigating COPD phenotypes, biomarkers and mechanisms which may lead to new therapeutic targets. Much of the work presented here was novel and had not previously been shown, providing attendees with the latest in understanding. Professor Donnelly (London) provided evidence that increasing bacterial load is associated with increased airway inflammation, which is in part due to defects in macrophage phagocytosis and efferocytosis. Despite the importance of these sentinel resident phagocytes the role of alveolar macrophage independent clearance mechanisms during lung infection are often overlooked.[43] Professor Adcock (London) spoke around the physiological roles of mitochondria, showing multiple roles, beyond the traditional model that it's only role is for ATP production. He talked about mitochondrial dysfunction, which affects inflammation and proliferation. In the final talk, Professor Polkey (London) took a different steer, looking at one of the systemic effects of COPD in skeletal muscle dysfunction. Here distinct muscle-specific phenotypes have been described, as well as interventions to understand mitochondrial targets. Finally he described the programme of activity to inform regulatory bodies around using exercise tests as a recognised outcome in COPD.

The other COPD symposium ran along a theme similar to Prof Agusti's BTS Lecture and focused on “beyond FEV₁” in COPD. The first three speakers each covered a different aspect of COPD, each

requiring differing assessment and treatment. Dr Kon (Harefield), spoke around functional measures of COPD, such as exercise capacity[44] and walking speed.[45] This is often overlooked as a measure, yet exertional dyspnoea is the symptom that is the hallmark of COPD. Dr Franssen (Maastricht, Netherlands) presented the importance of co-morbidities, in particular cardiovascular risk and lung cancer risk. Whilst the importance of co-morbidities has been long recognised, he also showed that groups of co-morbidities often co-exist with each other.[46] This is important as screening for all potential co-morbidities in every patient is time-consuming and expensive, so being able to identify groups allows targeted screening. Dr Bafadhel (Oxford) talked on targeting exacerbations. The different factors triggering an exacerbation have become more apparent over the last few years,[47] and we are now approaching a time when we give targeted treatment for specific factors, such as steroids only for eosinophilic exacerbations.[48,49]

Away from the major symposia, original research was presented in a number of spoken and poster sessions. Data from a large primary care cohort was used to identify patients at risk of hospital admission or death with COPD[50] which may help find the patients that need additional care. Cardiovascular risk in COPD was also a common theme in several sessions[51–53] including looking at arterial stiffness.[54,55] One pragmatic study, comparing venous and arterial blood gas analysis, and now *in press* in *Thorax*, could potentially change our management in COPD exacerbations and improve patient experience.[56]

Lung cancer

After years in the doldrums, lung cancer is now one of the most exciting areas in pulmonary medicine. Presentations from this years BTS/BTOG Symposium demonstrated revolutionary treatments for lung cancer are emerging, lung cancer will be identified at earlier stages by screening and that we are moving towards seeing personalised medicine in practice.

Of great interest was the presentation of an eminent oncologist, Professor Camidge (Denver, USA), who described lung cancer as an immunogenic tumour[57] and the emerging role of PD1 axis inhibitors. Nivolumab has demonstrated superior overall survival compared to docetaxel as a second line therapy for both squamous and non-squamous advanced non-small cell lung cancer,[58,59] and pembrolizumab has shown impressive response rates and progression free survival when the tumours express high levels of PDL1.[60] Dr Popat (London) then described the national Strat-Med 2 programme and the linked Matrix trial. In this national programme, over twenty mutations will be targeted with novel therapies. Certainly, targeted therapy will continue to change the way we treat lung cancer.[61]

Pulmonary embolism

The pulmonary embolism (PE) symposium was well attended and provided delegates with evidence based guidelines from the 2014 European Society of Cardiology on the diagnosis and management of new PE[62] presented by Dr Robin Condliffe (Sheffield). He highlighted the complexity of the algorithms and the use of pulmonary embolism severity index (PESI) to stratify patients. Although systemic thrombolysis is indicated in patients with high-risk PE and haemodynamic compromise other features suggesting that thrombolysis should be considered include the concurrent detection of deep vein thrombosis and a high blood lactate level.[63]

Dr Pepke-Zaba (Cambridge) gave an interesting talk on the pathobiology of chronic thromboembolic pulmonary hypertension (CTEPH) where she highlighted the contribution of inflammation and deficiency in angiogenesis to the pathogenesis of CTEPH and the use of pulmonary arterial hypertension-targeted therapies.[64]

The session ended with an enthusiastic debate between Mr David Jenkins (Cambridge) and Dr Irene Lang (Vienna, Austria). Mr Jenkins provided compelling evidence for pulmonary endarterectomy as the treatment of choice in CTEPH, however expert opinion is required to determine operability and surgery should only be done in an experienced centre where the mortality is <5% [65]. This treatment is associated with improvement in symptoms and better prognosis. Despite hypothermic circulatory arrest, cognitive function does not decline post-surgery.[66] On the other hand, balloon angioplasty is a novel interventional option that may be beneficial in a well-selected group of patients with CTEPH who are not surgical candidates.[67]

Best of Thorax

Four presentations showcasing the best of this year's publications in *Thorax* were given in the "best of *Thorax*" symposium. This new session, which will become an annual event presented three diverse subjects in the one session, including mechanisms of idiopathic pulmonary fibrosis (IPF), treatment of multi drug resistant TB (MDR-TB) in Ethiopia, and COPD exacerbations.

Professor Natarajan (Chicago, USA) presented novel mechanistic findings for IPF. Sphingosine-1-phosphate lyase (S1PL) is a bioactive lipid that is key in regulating a number of signaling pathways.[68] In this study in both humans and mouse models, it was found to be elevated and correlated with disease severity and survival.[69] This mechanism may lead to new therapeutic targets.

The global importance of MDR-TB was highlighted and with less than 20% of patients with MDR-TB assessing treatment in 2012.[70] Professor Goldfeld (Boston, USA) presented the instigation, expansion and results of a standardised second line drug regime programme in Ethiopia. In approximately five years 1044 patients were treated with a 78.6% treatment success.[71] This represents a huge impact on this important problem in a setting with severe resource constraints and diverse geography.

The final two talks were focussed on COPD exacerbations. The impact of hospitalisation for an exacerbation of COPD has been well recognised and interventions to reduce readmissions have had mixed results.[72,73] It is clear that hospitalisation and its impact is a result of the interaction of the underlying condition and the severity of the acute event.[74] Identifying the response and recovery (both short and long-term) have always been based around clinical judgement. Dr Suh (Dartford) and Dr Kon (Harefield) presented two simple measures that may aid that clinical decision-making. Dr Suh presented measures of neural respiratory drive (NRD) to measure load on the respiratory system. Using this non-invasive measure he was able to demonstrate recovery, which was superior to other standard measures to predicting patients unlikely to be readmitted.[15] Dr Kon presented that long term outcome was predicted using a simple walking test on discharge, the four meter gait speed, which takes five minutes to perform.[75] This global measure of frailty shows the effects of COPD on the whole system. These two measures, and others recently described,[76] show that identification of individuals' at risk of hospital readmission or death following hospitalisation may be a realistic prospect, allowing for targeted intervention.

#BTSWinter2015

The new *Thorax* editors December editorial, highlighted the importance of social media in disseminating information [77]. From 1 December 2015 to 6 December 2015, 2771 tweets were sent with the *Twitter hashtag* #BTSWinter2015 by 543 participants at an average of 18 tweets per hour, resulting in 8761002 impressions, demonstrating the impact of this medium to share conference highlights with those in all continents that couldn't make it to this great scientific meeting. Beyond the conference following @thoraxbmj will continue to keep everyone updated with the latest publications from the journal and #respmed will be a way to connect on *Twitter* with respiratory knowledge and education.

Respiratory research for the 21st century

Finally Dr Kim Prisk from the North American Space Agency laboratory (San Diego, USA) presented the symposium talk "occupational disease in the 21st century: space as the final frontier". His work focuses on understanding the effects of zero gravity on lung function and pulmonary aerosol transport in preparation for the day that may arrive when humans spend more time on the lunar surface. In his entertaining presentation he not only showed some great pictures from outer space but transmitted to the audience the importance of passion and ambition in conducting research. On this note, we look forward to seeing all the stellar research performed by BTS members and colleagues at the BTS winter meeting of 2016.

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