Review of the British Thoracic Society Winter Meeting 2016, 7–9 December, London, UK

Hannah V Woodcock,[1] Ricardo J José,[2] Gisli Jenkins,[3] on behalf of the BTS science and research committee

[1]Department of Respiratory Medicine, Whipps Cross Hospital, London, UK
[2]Centre for Inflammation and Tissue Repair, University College London, London, UK
[3]Centre for Respiratory Research, University of Nottingham, Nottingham, UK

Correspondence to
Professor Gisli Jenkins, Clinical Sciences Building, City Campus, Nottingham University Hospitals, Nottingham NG5 1PB, UK; Gisli.Jenkins@nottingham.ac.uk

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ABSTRACT

This article reviews the British Thoracic Society Winter Meeting 2016 and highlights the new developments in scientific and clinical research across the breadth of respiratory medicine.

INTRODUCTION

The British Thoracic Society (BTS) Winter Meeting 2016, not to be overshadowed by the Brexit discussions at the UK Supreme Court next-door, attracted more than 2200 delegates to London. At the BTS, world-renowned experts discussed the latest advances in respiratory science, and in clinical and translational research with a particular emphasis on how precision medicine is starting to transform the way respiratory diseases are treated. This article summarises a selection of key sessions.

BTS/British Lung Foundation/British Association of Lung Research early career investigators symposium

In one of the highlights of the winter BTS meeting, six budding academics presented outstanding research to a panel of judges, for a chance to win an early career investigator award. Dr Grogono (Cambridge) won the BTS Award for her work using whole genome sequencing and detailed epidemiology, to show that most *Mycobacterium abscessus* infections in patients with cystic fibrosis (CF) are acquired through patient-to-patient transmission and not from the environment, which challenges previously held beliefs.[1] The runner up was Dr Pengo (Padua, Italy), who carried out a randomised sham controlled trial to show that transcutaneous electrical stimulation of upper airway dilator muscles improves obstructive sleep apnoea (OSA).[2] Dr Nikolic (Cambridge) was awarded the British Association of Lung Research prize for showing that multipotent epithelial stem cells from human embryonic lung could engraft and repopulate a mouse lung following lung injury, suggesting that cell therapy could play a role in lung repair in the future.[3] Dr Adlakha (London) was highly commended for demonstrating that the dendritic cell response to *Aspergillus* is impaired by tacrolimus and is restored by interferon-gamma (IFN-γ).[4] This suggests the possibility that adjunctive immunotherapy with IFN-γ might be beneficial in lung transplant patients with invasive fungal disease. Dr James Allinson (London) won the British Lung Foundation (BLF) prize for his investigation of the relationship between early life respiratory tract infection and development of adult chronic mucus hypersecretion using data from the 1946 national birth cohort.[5] Finally, Dr Finney (London) received the highly commended BLF award for demonstrating that human rhinovirus directly impairs phagocytosis of bacteria by monocyte-derived macrophages isolated from patients with COPD, which may explain why viral infections cause secondary bacterial infection during COPD exacerbations.[6]

Best of *Thorax*

Four important manuscripts were showcased in the second year of the 'Best of Thorax' session. Professor Friedland's group (London) used positron emission tomography (PET) scans with the hypoxic-specific tracer (^{18}F-labelled fluoromisonidazole), to show for the first time that pulmonary TB lesions are severely hypoxic and that hypoxia upregulates the collagenase matrix metalloproteinase-1, an important contributor to the cavitation and lung destruction seen in this disease.[7] This was followed by Professor Lederer (New York, USA), who showed that higher levels of rheumatoid arthritis (RA) autoantibodies, even in the absence of clinically evident RA, are associated with subclinical interstitial lung disease (ILD) on CT imaging, particularly in smokers. This suggests that targeting autoimmunity in at-risk patients could be a novel strategy to prevent ILD.[8] Professor Foronjy (New York, USA) demonstrated that inhaled nicotine e-cigarette solution leads to airway inflammation and airspace enlargement in mice, suggesting that in addition to being the addictive component of cigarettes, nicotine also plays a key role in the initiation and progression of COPD.[9] Finally, Dr Melissa McDonnell (Newcastle) discussed different bronchiectasis severity measures in seven European cohorts, and showed that the Bronchiectasis Severity Index was superior at predicting clinically useful outcomes such as hospitalisation, exacerbations, lung function decline and quality of life.[10]

Plenary scientific symposium

This session gave a platform to four leading researchers to present their work. Professor Mark Lindsay (Bath) gave an excellent overview of the role of non-coding RNAs in respiratory disease.[11] He explained that microRNA expression is altered in a wide variety of respiratory conditions and can be manipulated for the treatment of lung disease. For example, oligonucleotide therapies are already in development for the treatment of respiratory syncytial virus, asthma and COPD. Professor Simon Johnson (Nottingham) described the complexity of matrix proteases in the lung. Dr Elizabeth Sapey (Birmingham) outlined how neutrophil function is impaired with ageing and how this can be

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modulated. For example, neutrophils from older patients migrate haphazardly up a chemotactic gradient, but phosphoinositide 3 kinase inhibition restores accurate migration associated with the 'younger' neutrophil phenotype, giving hope for all those aged neutrophils out there.[12] Finally, Professor Adrian Martineau (London) presented exciting data on the role of vitamin D in protecting against infections. He explained that daily or weekly vitamin D supplementation in profoundly deficient (25(OH) vitamin D <25 nmol/L) patients significantly reduces the risk of respiratory tract infection with a number needed to treat (NNT) of only four.[13]

The Snell memorial lecture

In the last ever Snell lecture, Professor Christopher Dye, the director of strategy at WHO, discussed what it would take to eliminate TB, the world's biggest infectious killer. The ambitious goals of the WHO's 'end TB' strategy include reducing TB cases by 90% and deaths by 95% between 2015 and 2035, and ensuring that no family is burdened with catastrophic expenses due to TB.[14] To reach these targets by 2035, he explained that significant investment into research for new point-of-care diagnostics, vaccines and simpler treatment regimens is urgently required.

The BTS lecture

Epithelial alarmins are three innate cytokines, interleukin (IL)-25, IL-33 and thymic stromal lymphopoietin (TSLP) released by the airway epithelium in response to noxious environmental stimuli, including respiratory viruses. Professor Paul O'Byrne (McMaster, Canada) discussed the evidence that inhaled allergens also stimulate the production of these cytokines leading to airway eosinophilia and airway hyperresponsiveness in asthmatic airways.[15] This involves activation of the innate and adaptive immune response with increased production and stimulation of myeloid dendritic cells, type 2 innate lymphoid cells and type 2 helper cells. All of the epithelial-derived alarmins have been implicated in the inhaled allergen-induced airway response in asthma, but the best evidence exists for TSLP. A monoclonal antibody directed against TSLP can normalise baseline biomarkers of airway inflammation (blood and sputum eosinophilia and FeNO) and attenuate allergen-induced bronchoconstriction in allergic asthmatic subjects.[16] O'Byrne suggested that IL-33 and TSLP in particular are excellent targets for new therapies for severe eosinophilic asthma.

Sarcoidosis

It was standing room only at the sarcoidosis session, reflecting the interest from the respiratory community in this heterogeneous multisystem disease. Professor Moller (Baltimore, USA) described how granulomas form as a result of major histocompatibility complex class II antigen presentation leading to an exaggerated type 1 helper cell response, characterised by increased tumour necrosis factor-α, IFN-γ and IL-6 levels.[17] Numerous studies have suggested microbial-derived antigens play a causative role but despite evidence of previous mycobacterial infection in >50% of patients with sarcoidosis, there is no convincing evidence of active infection. Professor Moller hypothesised that sarcoidosis is actually a protein aggregation disease characterised by deposition of serum amyloid A in response to mycobacterial infection, which then perpetuates the T-cell response leading to persistent granulomatous inflammation.[18] He described immune modulation strategies, including enhancing regulatory T-cell function, targeting IFN-γ secreting T helper 17 cells and IL-6 receptor antibodies, as potential future therapies.[19 20]

Dr Cleaver (Cleveland, USA) discussed the challenges of diagnosing cardiac sarcoidosis (CS). While a positive endomyocardial biopsy establishes the diagnosis of CS, the sensitivity of biopsy is low due to the patchy involvement of disease. The World Association for Sarcoidosis and Other Granulomatous Disorders (WASOG) guidelines suggest that patients with suspected CS should undergo cardiac MRI and/or PET imaging.[21] MRI and PET have similar diagnostic accuracy (80%–90% sensitivity and specificity). MRI is excellent for detecting myocardial fibrosis (late gadolinium enhancement (LGE)), whereas ^{18}F-fluorodeoxyglucose (FDG)-PET is more sensitive for detecting and monitoring of active inflammation. Furthermore, combining ^{18}F-FDG-PET with rubidium-82 perfusion scanning allows detection of both inflammation and scar tissue. He explained that LGE or increased ^{18}F-FDG uptake are associated with increased risk of ventricular arrhythmias and mortality and are superior to other functional parameters such as left ventricular ejection fraction (LVEF) for stratifying high-risk patients.[22 23] Steroids are used to treat CS, without any support from randomised controlled trial (RCT) data. Early immunosuppression improved LVEF and reduced ventricular arrhythmias in a retrospective study.[24]

Professor Ling-Pei Ho (Oxford) gave a practical talk on the management of sarcoidosis. There have only been five RCTs in sarcoidosis, so there is little evidence to guide treatment. Patients with 'simple' sarcoidosis, defined by nodularity on high resolution computed tomography (HRCT) scan, often regress and may not require treatment. Perihilar disease, conglomeration or consolidation on CT imaging are signs that the patient will develop fibrosis and these patients should be treated even in the absence of organ dysfunction. A CT activity score for sarcoidosis is able to predict forced vital capacity (FVC) response to treatment.[25] She shared her own treatment strategy with prednisolone as first-line therapy, and azathioprine or methotrexate as second-line therapy. If >10 mg/day prednisolone is required despite second-line therapy, mycophenolate, leflunomide or infliximab should be considered as third-line therapy.

Interstitial lung disease

Idiopathic pulmonary fibrosis (IPF) remained a hot topic at this year's meeting. Professor Garcia (Texas, USA) gave an excellent overview of the genetics of sporadic and familial pulmonary fibrosis (PF).[26] Genome-wide association studies have identified common variants (>5% minor allele frequency) associated with pulmonary fibrosis, which probably account for a third of the risk of developing IPF. The most widely replicated is the *MUC5B* promoter polymorphism. In addition, genetic sequencing has identified rare variants in multiple genes involved in telomere maintenance in familial PF,[27] with telomerase reverse transcriptase (*TERT*) the most commonly mutated gene.[28] The UK 100 000 genomes project will hopefully shed more light on the contributions of common and rare genetic variants to the development of fibrosis. Regarding the treatment of IPF, Professor Noble (Los Angeles, USA) presented pooled data from phase III studies showing that pirfenidone significantly reduces FVC decline in all patients, regardless of baseline demographics or lung function,[29] similar to nintedanib.[30] These data suggest that patients with IPF with preserved lung function should also be offered treatment, in contrast to current National Institute for Health and Care Excellence (NICE) recommendations. The ILD team from Oxford found that in patients with intolerable side effects or disease progression on pirfenidone, switching to nintedanib was well tolerated.[31] IPF guidelines currently advocate the use of proton pump inhibitors in patients with IPF,

without any prospective RCT data. However, Professor Kreuter (Heidelberg, Germany) presented results from a retrospective study to show anti-acid treatment alone or in combination with pirfenidone had no beneficial effect in patients with IPF, and on the contrary was associated with increased pulmonary infections.[32]

Professor Fischer (Colorado, USA) advised the consideration of underlying connective tissue disease (CTD) in younger, female patients with ILD, especially if they have a non-specific interstitial pneumonia (NSIP) or organising pneumonia (OP) pattern on HRCT and a positive antinuclear antibody (ANA) or other autoantibody. He explained many patients with ILD have some subtle features of CTD, but do not meet the diagnostic criteria for a specific CTD, and are now classified as having interstitial pneumonia with autoimmune features (IPAF).[33] Patients with IPAF have similar outcomes to patients with IPF, but worse than those with CTD-ILD.[34] Immunosuppressive therapy is first-line therapy in all patients with clinically significant or progressive CTD-ILD, independent of radiological or histological features, although the only data are extrapolated from studies in patients with systemic sclerosis ILD. Dr Maher (London) described an ongoing trial comparing rituximab and cyclophosphamide in progressive CTD-ILD (the RECITAL study, NCT01862926) and emphasised that further studies are needed to guide the roles of immunosuppression and antifibrotic therapy in usual interstitial pneumonia (UIP) patterns of CTD-ILD.

Lung cancer

A new symposium focused on the overlap between COPD and ILD with lung cancer. Professor Hubbard (Nottingham) explained the epidemiological links between these diseases, with the risk of lung cancer doubled in patients with COPD and 5–10 times higher in IPF. He explored whether this could all be explained by smoking but showed that although smoking partly confounds the COPD link, it does not affect the risk of cancer in patients with IPF. On the basis of these data, he suggested that IPF and COPD diagnoses should be included in risk stratification for lung cancer screening. Dr Spira (Boston) explained that the presence of emphysema in patients with COPD is particularly associated with a high risk of developing cancer and discussed mechanistic links between COPD and cancer. He shared exciting data regarding a gene-expression classifier that can distinguish smokers with lung cancer from smokers without lung cancer in cytologically normal bronchial epithelial cells collected at bronchoscopy, even in patients with distant nodules or malignancy.[35] Dr Jo Porter (London) explored the parallels between IPF and lung cancer, and outlined active signalling pathways, transcriptomic and epigenetic signatures identified in IPF that overlap with cancer. This has led to the successful repurposing of the oncology drug nintedanib for patients with IPF and may lead to further shared therapies.[36]

In the thoracic surgery session, the video-assisted thoracoscopic surgery (VATS) versus open lobectomy debate continued with VATS winning with better short-term outcomes, including reduced postoperative pulmonary complications (PPC) and shorter length of stay.[37] The importance of preoperative smoking cessation was emphasised, as smoking significantly increases the risk of PPC following VATS lobectomy.[38] Data from Manchester showed that the adequacy of intraoperative lymph node sampling has dramatically improved over 5 years, but that further improvement is needed to meet current International Association for the Study of Lung Cancer (IASLC) guidelines.[39] Dr Kennedy (Leeds) described real-world data showing higher recurrence rates in patients with stage 1 cancer treated radically with stereotactic ablative radiotherapy (SABR) compared with lobectomy and spoke about weighing up the risks of SABR recurrence and surgical mortality when considering patients for radical intent therapies.[40]

Pleural disease

The pleural symposium presented RCT data to guide management of malignant pleural effusion (MPE). Professor Maskell (Bristol) spoke about the difficulties in trial design in this group of patients with a poor prognosis and advised that the prognostic LENT score (calculated on the basis of pleural fluid lactate dehydrogenase, performance status, serum neutrophil-to-lymphocyte ratio and tumour type) should be taken into account when making management decisions in MPE.[41] Professor Rahman (Oxford) explained that the first Therapeutic Interventions in Malignant Effusion (TIME) trial challenged accepted wisdom by suggesting a 24 Fr drain is superior to a 12 Fr drain for talc pleurodesis, and that non-steroidal anti-inflammatory drugs do not alter pleurodesis success.[42] He suggested that it is reasonable to offer either chest drain/talc pleurodesis or indwelling pleural catheter (IPC) as first-line therapy in MPE, as both interventions improve breathlessness and quality of life scores.[43] Furthermore, outpatient autopleurodesis is possible with IPC and is achieved more quickly with daily compared with alternate day drainage.[44] The ongoing IPC PLUS trial is examining the efficacy of talc pleurodesis via IPC and results are expected in summer 2017. Professor Maskell spoke about the high run-in failure in this study, mostly caused by high rates of trapped lung, which is difficult to know how to avoid or how to manage. The use of preprocedural thoracic ultrasound to identify trapped lung was discussed in the poster session.[45] The results of the MESOtrap trial, comparing VATS pleural decortication to IPC in mesothelioma, should help to guide management of these patients in the future.

Professor Gary Lee (Perth, Australia) considered a different approach to management of MPE and explored why pleural cancers produce large quantities of pleural fluid and how we can 'turn off the tap'. He explained the chemokine MCP-1 is a key driver of exudative pleural fluid formation and may be a useful target for the treatment of MPE.[46] He also showed mesothelioma pleural fluid is not an innocent bystander, but is a rich source of growth factors that actively drive tumour growth. Targeting fibroblast growth factor (FGF)-9, which is highly expressed in pleural fluid, showed encouraging results in experimental models and this has paved the way for a phase II trial of an FGF-9 inhibitor in patients with mesothelioma, who have progressed on first-line or second-line chemotherapy.[47]

Pulmonary hypertension

Professor Morrell (Cambridge) gave a fascinating talk about the genetic mutations and molecular mechanisms underlying familial pulmonary arterial hypertension (PAH). Over 75% familial cases (and >20% sporadic cases) are associated with a mutation in *BMPR2* gene, which encodes the bone morphogenetic protein (BMP) type II receptor (BMPR-II), a receptor member of the transforming growth factor-β superfamily.[48] It is the most common cause of PAH and patients with *BMPR2* mutations present at a younger age with more severe disease.[49] Restoration of BMPR-II signalling with delivery of BMPR-II ligands has been shown to reverse PAH in experimental models and is a promising therapeutic strategy in PAH.[50]

Dr Wort (London) explained that most pulmonary hypertension (PH) is not due to PAH and gave a comprehensive overview of PH due to left heart disease, lung disease and chronic thromboembolic pulmonary hypertension (CTEPH). Unlike other forms of PH, CTEPH is potentially curable by pulmonary endarterectomy so all patients with PH should be screened for CTEPH even in the absence of acute PE.[51] For selected non-operable patients with CTEPH, management options include balloon pulmonary angioplasty or riociguat, which has recently been shown to improve exercise and functional capacity for up to 1 year.[52]

Professor David Kiely (Sheffield) described the CT characteristics of PH and explained that centrilobular ground glass opacification in patients with unexplained breathlessness should alert us to the possibility of PAH.[53] CT is also useful for prognostication in PAH, with pleural effusions, septal lines and inferior vena cava dilatation predicting increased mortality. There is growing interest in using cardiac MRI to diagnose PH and a recent study showed MRI measurements of pulmonary artery haemodynamics and right ventricular function can diagnose PH with high accuracy, potentially reducing the need for invasive right heart catheterisation.[54]

Cystic fibrosis

Until recently, management of CF was based on supportive treatments to mitigate the consequences of defective cystic fibrosis transmembrane conductance regulator (CFTR) function. The CF symposium focused on the rapid evolution of precision medicine in CF brought about by the development of genotype-specific small molecules that modulate the CFTR defect.[55] There are two main strategies to modulate CFTR function that have been approved. CFTR potentiators recover the chloride transport function of CFTR disrupted in class III mutations and CFTR correctors improve intracellular folding and trafficking of CFTR with class II mutations. Ivacaftor (CFTR potentiator) is approved for patients aged 2 years plus with at least one G551D allele in the USA, Europe and Canada.[56 57] However, >90% of patients with CF do not have this mutation and will not benefit from ivacaftor monotherapy. Professor Elborn explained that targeting the most common mutation, F508del, has proved more challenging because this mutation is associated with class II and class III functional defects. This may explain the failure of lumacaftor (CFTR corrector) monotherapy to have a clinical benefit in F508del homozygous patients.[58] However, a dual approach using a combination of CFTR correctors and potentiators has proven to be more promising in improving CFTR function in these patients. Lumacaftor-ivacaftor (Orkambi) treatment in F508del homozygous patients led to a significant, but modest (~3%), improvement in FEV_1 compared with the placebo arm in phase III trials.[59] As a result, the Food and Drug Administration approved this drug combination for patients with CF with this homozygous mutation in 2015. In contrast, NICE did not approve Orkambi, primarily due to its substantial cost and modest effects on lung function. There are ongoing trials investigating other CFTR correctors (eg, VX-661) with ivacaftor in patients with homozygous and heterozygous mutations. Professor Amaral (Lisbon, Portugal) discussed her work using *ex vivo* experimental models and high-throughput screening technologies to identify further novel CTFR corrector small molecules for clinical use. The emergence of novel targeted therapies in CF is exciting, but the long-term benefits of CFTR modulators are not known and affordability remains a huge issue.

Asthma

Professor Liam Heaney (Belfast) emphasised the difference between 'difficult' and 'severe' asthma. Around 13% of patients have a difficult clinical problem, but attention to inhaler technique, adherence and exogenous factors reduces the numbers with truly severe asthma to 3.5%. He placed new emphasis on smart inhaler technology and FeNO monitoring to understand adherence in patients with poorly controlled asthma. This underpins the Refractory Asthma Stratification Programme (RASP) study, which identifies suitable patients for novel biological treatments only when they are adherent to optimised inhaled corticosteroid (ICS) therapy.[60] Joseph Arron (Genentech) described using biomarkers from large observational studies to guide study design for new biological therapies in asthma. Phase III studies of lebrikizumab (anti-IL-13 monoclonal antibody) were stratified by serum periostin, and although studies failed to show a consistent reduction in exacerbations in the periostin-high group,[61] he hypothesised this could be due to a large placebo response, or the occurrence of non-eosinophilic exacerbations unresponsive to lebrikizumab.

Dr Dominick Shaw (Nottingham) emphasised that non-eosinophilic asthma is much more difficult to treat and is often associated with a rapid decline in lung function. Small molecules targeting neutrophilic inflammation, such as a CXCR2 antagonist, reduce sputum neutrophils but have no significant impact on exacerbations.[62] He cautioned against the use of azithromycin, which failed to significantly reduce exacerbations in asthma, but suggested an empirical trial of a mucolytic agent may be helpful in these patients.[63]

Dr Hannah Durrington (Manchester) described the many circadian clock functions that are relevant to asthma, with peak expiratory flow rate (PEFR), methacholine challenge, sputum eosinophil counts and symptoms all worse overnight.[64] Drug treatments should be timed to account for this. She showed that it is best to give ICS at 15:00, and suggested that targeting new once-daily treatments to the correct time would improve efficacy.

The importance of the 'middle airway' in asthma was emphasised by Dr James Hull (London). About one-third of patients with severe asthma have abnormal laryngeal movement on CT, but it is unclear if this is a cause or consequence of asthma. He described the four-question Vocal Cord Dysfunction (VCD) Index, which is useful for discriminating VCD from asthma, and proposed that vocal cord assessment will soon become routine with the use of portable devices and involvement of multidisciplinary teams.[65] New techniques for the treatment of VCD, such as laser supraglottoplasty and unilateral botox injection, need RCT assessment.

Chronic obstructive pulmonary disease

The value of home non-invasive ventilation (HMV), in comparison with home oxygen therapy (HOT), after admission with life-threatening ventilatory failure due to severe COPD is a particularly challenging topic. In a randomised study likely to change clinical practice, Murphy *et al*[66] found that patients with persistent hypercapnia ($PaCO_2$ >7 kPa) following discharge treated with combined HMV/HOT had fewer 28-day re-admissions and a significant reduction in 12-month exacerbation rate compared with HOT alone. Dr Morris (Manchester) reviewed end-of-life planning in relation to community oxygen prescribing, and found that although median survival was low at around 6 months, only 33% had discussed a DNACPR ('Do not attempt cardiopulmonary Resuscitation') decision prior to death.[67] This suggests that the General Medical Council

recommendations on future care for those at risk of respiratory arrest are not being followed and should be considered when prescribing home oxygen.

'Real-world' data were a feature of several poster presentations in COPD. Dr John Hurst (London) examined the factors associated with step-up from long-acting muscarinic antagonist (LAMA) to triple therapy and showed that exacerbations and COPD severity significantly influenced a step-up in treatment. Women and patients with diabetes were significantly less likely to be stepped-up.[68] According to guidelines, patients were overtreated, with 39% of patients on triple therapy in Global Initiative for Chronic Obstructive Lung Disease (GOLD) A and B categories. On the same theme, Dr Vince Mak (London) showed that 40% of patients with COPD are being overtreated with high-dose inhaled corticosteroid/long-acting beta agonist (ICS/LABA) combination treatments and expressed concern about potential harm and waste associated with high-cost ICS combinations. Over the last 18 months with the introduction of lower cost generic ICS combination therapies, the monthly cost of prescriptions has reduced by 14.5% (to £18 million/month!), but the number of inappropriate prescriptions for high-dose combinations is only down 8.4%. Dr Mak concluded 'doing the wrong thing cheaper does not make it right'. However, both speakers accepted that guidelines derived from registration studies might not be applicable to the general population. For example, Dr Kostikas (Novartis) presented pooled 'Ignite' RCT data on the effect of indacaterol/glycopyrronium on exacerbation rates,[69] in which the trial population contrasted with real-world RCT data from the Salford Lung Study (SLS; fluticasone furoate/vilanterol) with an annual exacerbation rate half that of SLS.[70]

Smoking cessation

The emergence and widespread use of e-cigarettes has led to much debate on their use in smoking cessation. Professor Peter Hajek (London) discussed the Public Health England report[71] that advocates the use of e-cigarettes in smoking cessation because they are less harmful than cigarettes.[72] In contrast, Dr Charlotta Pisinger (Copenhagen, Denmark) presented her data from a large systematic review of health effects of e-cigarettes,[73] which questioned the safety of e-cigarettes on the basis that carcinogens and volatile organic compounds are found in exhaled breath of e-cigarette smokers.[74] She noted that approximately 75% of e-cigarettes contain diacetyl, a chemical approved for food use but associated with respiratory disease (popcorn worker's lung) if inhaled.[75] Subsequently, in the spoken session, e-cigarette vapour condensate was shown to be toxic to alveolar macrophages in vitro, especially in the presence of nicotine[76] and the flavouring in e-cigarette vapour extracts was shown to alter macrophage function.[77] Dr Onno Van Schayk (Maastricht, The Netherlands) discussed the development of nicotine vaccines for the treatment of tobacco addiction. Four conjugated nicotine vaccines have been tested in humans and although they lead to the development of antibodies, there is no impact on smoking abstinence, which suggests we do not fully understand the complexities of addiction.[78] Finally, we heard from health psychologist Professor Susan Michie (London) who discussed the design, delivery and impact of behaviour change interventions in relation to smoking cessation. She reminded all of us of our important role in offering opportunistic smoking cessation advice.

CONCLUSION

Once again, the BTS Winter Meeting 2016 #BTSwinter2016 brought together scientists, clinicians, nurses and therapists from the UK and wider afield, with the aim of improving respiratory healthcare. The latest scientific research was showcased, useful clinical experiences were shared and new collaborations established. We are already looking forward to the 2017 meeting #BTSwinter2017. In the meantime, log on to twitter and review the details of #BTSwinter2016, follow @thoraxbmj for the latest *Thorax* publications and #resped for up-to-date respiratory news and education.

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REFERENCES

1 Grogono D, Bryant J, Rodriguez-Rincon D, *et al*. T4 global spread of mycobacterium abscessus clones amongst cystic fibrosis patient. *Thorax* 2016;71(Suppl 3):A2.
2 Pengo MF, Xiao S, Ratneswaran C, *et al*. Randomised sham-controlled trial of transcutaneous electrical stimulation in obstructive sleep apnoea. *Thorax* 2016;71:923–31.
3 Nikolic M, Johnson J, Sun D, *et al*. T5 towards human lung regeneration in end-stage respiratory failure: genetically-modifiable 3d organoid culture of human embryonic lung stem cells enables for the first time the study of human lung development in vitro. *Thorax* 2016;71(Suppl 3):A3.
4 Adlakha A, Armstrong-James D, Lenhard B. T1 calcineurin inhibition impairs the dendritic cell transcriptional response to aspergillus fumigatus infection in lung transplant recipients. *Thorax* 2016;71(Suppl 3):A1.
5 Allinson J, Hardy R, Donaldson G, *et al*. T2 early-life respiratory tract infection and adult susceptibility to chronic mucus hypersecretion—a prospective 64 year national birth cohort study. *Thorax* 2016;71(Suppl 3):A1–2.
6 Finney L, Belchamber K, Mallia P, *et al*. T3 human rhinovirus impairs the innate immune response to bacteria in monocyte derived macrophages from patients with chronic obstructive pulmonary disease. *Thorax* 2016;71(Suppl 3):A2.
7 Belton M, Brilha S, Manavaki R, *et al*. Hypoxia and tissue destruction in pulmonary TB. *Thorax* 2016;71:1145–53.
8 Bernstein EJ, Barr RG, Austin JHM, *et al*. Rheumatoid arthritis-associated autoantibodies and subclinical interstitial lung disease: the Multi-Ethnic Study of Atherosclerosis. *Thorax* 2016;71:1082–90.
9 Garcia-Arcos I, Geraghty P, Baumlin N, *et al*. Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner. *Thorax* 2016;71:1119–29.
10 McDonnell MJ, Aliberti S, Goeminne PC, *et al*. Multidimensional severity assessment in bronchiectasis: an analysis of seven European cohorts. *Thorax* 2016;72:1110–8.
11 Booton R, Lindsay MA. Emerging role of microRNAs and long noncoding RNAs in respiratory disease. *Chest* 2014;146:193–204.
12 Sapey E, Greenwood H, Walton G, *et al*. Phosphoinositide 3-kinase inhibition restores neutrophil accuracy in the elderly: toward targeted treatments for immunosenescence. *Blood* 2014;123:239–48.
13 Martineau A, Jolliffe D, Hooper R, *et al*. S102 vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of individual participant data. *Thorax* 2016;71(Suppl 3):A60–1.
14 Uplekar M, Weil D, Lonnroth K, *et al*. WHO's new end TB strategy. *Lancet* 2015;385:1799–801.
15 Mitchell PD, O'Byrne PM. Epithelial derived cytokines in asthma. *Chest*. Published Online First: 3 Nov 2016. doi:10.1016/j.chest.2016.10.042.
16 Gauvreau GM, O'Byrne PM, Boulet LP, *et al*. Effects of an anti-TSLP antibody on allergen-induced asthmatic responses. *N Engl J Med* 2014;370:2102–10.
17 Chen ES, Moller DR. Etiologies of sarcoidosis. *Clin Rev Allergy Immunol* 2015;49:6–18.
18 Chen ES, Song Z, Willett MH, *et al*. Serum amyloid a regulates granulomatous inflammation in sarcoidosis through Toll-like receptor-2. *Am J Respir Crit Care Med* 2010;181:360–73.
19 Prasse A, Zissel G, Lützen N, *et al*. Inhaled vasoactive intestinal peptide exerts immunoregulatory effects in sarcoidosis. *Am J Respir Crit Care Med* 2010;182:540–8.
20 Facco M, Cabrelle A, Teramo A, *et al*. Sarcoidosis is a Th1/Th17 multisystem disorder. *Thorax* 2011;66:144–50.
21 Judson MA, Costabel U, Drent M, *et al*. The WASOG sarcoidosis organ assessment instrument: an update of a previous clinical tool. *Sarcoidosis Vasc Diffuse Lung Dis* 2014;31:19–27.
22 Blankstein R, Osborne M, Naya M, *et al*. Cardiac positron emission tomography enhances prognostic assessments of patients with suspected cardiac sarcoidosis. *J Am Coll Cardiol* 2014;63:329–36.
23 Coleman GC, Shaw PW, Balfour PC Jr, *et al*. Prognostic value of myocardial scarring on CMR in patients with cardiac sarcoidosis: a systematic review and meta-analysis. *JACC Cardiovasc Imaging* 2017;10:411–20.

24 Padala SK, Peaslee S, Sidhu MS, *et al*. Impact of early initiation of corticosteroid therapy on cardiac function and rhythm in patients with cardiac sarcoidosis. *Int J Cardiol* 2017;227:565–70.
25 Benamore R, Kendrick YR, Repapi E, *et al*. CTAS: a CT score to quantify disease activity in pulmonary sarcoidosis. *Thorax* 2016;71:1161–3.
26 Mathai SK, Newton CA, Schwartz DA, *et al*. Pulmonary fibrosis in the era of stratified medicine. *Thorax* 2016;71:1154–60.
27 Stuart BD, Choi J, Zaidi S, *et al*. Exome sequencing links mutations in PARN and RTEL1 with familial pulmonary fibrosis and telomere shortening. *Nat Genet* 2015;47:512–17.
28 Diaz de Leon A, Cronkhite JT, Katzenstein AL, *et al*. Telomere lengths, pulmonary fibrosis and telomerase (TERT) mutations. *PLoS ONE* 2010;5:e10680.
29 Noble P, Albera C, Chou W, *et al*. S97 annual rate of FVC decline in various patient sub-groups with idiopathic pulmonary fibrosis treated with pirfenidone: pooled analysis from 3 pivotal studies. *Thorax* 2016;71(Suppl 3):A57.
30 Costabel U, Inoue Y, Richeldi L, *et al*. Efficacy of nintedanib in idiopathic pulmonary fibrosis across prespecified subgroups in INPULSIS. *Am J Respir Crit Care Med* 2016;193:178–85.
31 Rathnapala A, Fries A, Ruggiero C, *et al*. S101 single centre experience of switching patients with idiopathic pulmonary fibrosis from pirfenidone to nintedanib. *Thorax* 2016;71(Suppl 3):A60.
32 Kreuter M, Spagnolo P, Wuyts W, *et al*. S98 antacid therapy and disease progression in patients with idiopathic pulmonary fibrosis (IPF) under pirfenidone treatment. *Thorax* 2016;71(Suppl 3):A58.
33 Fischer A, Antoniou KM, Brown KK, *et al*. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J* 2015;46:976–87.
34 Oldham JM, Adegunsoye A, Valenzi E, *et al*. Characterisation of patients with interstitial pneumonia with autoimmune features. *Eur Respir J* 2016;47:1767–75.
35 Silvestri GA, Vachani A, Whitney D, *et al*. A bronchial genomic classifier for the diagnostic evaluation of lung cancer. *N Engl J Med* 2015;373:243–51.
36 Mercer PF, Woodcock HV, Eley JD, *et al*. Exploration of a potent PI3 kinase/mTOR inhibitor as a novel anti-fibrotic agent in IPF. *Thorax* 2016;71:701–11.
37 Agostini P, Lugg S, Adams K, *et al*. S63 postoperative pulmonary complications and physiotherapy requirements after open thoracotomy versus vats lobectomy: a propensity score-matched analysis. *Thorax* 2016;71(Suppl 3):A38.
38 Agostini P, Lugg S, Adams K, *et al*. S61 risk factors and short-term outcomes of developing postoperative pulmonary complications after vats lobectomy. *Thorax* 2016;71(Suppl 3):A36–7.
39 Edwards T, Balata H, Tennyson C, *et al*. S62 adequacy of intra-operative lymph node sampling during surgical resection of NSCLC: influencing factors and its relationship to survival. *Thorax* 2016;71(Suppl 3):A37.
40 Kennedy M, Lummis K, Spencer K, *et al*. S64 Rates and sites of recurrence following radical treatment of stage I lung cancer. *Thorax* 2016;71(Suppl 3):A38–9.
41 Clive AO, Kahan BC, Hooper CE, *et al*. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. *Thorax* 2014;69:1098–104.
42 Rahman NM, Pepperell J, Rehal S, *et al*. Effect of opioids vs NSAIDs and larger vs smaller chest tube size on pain control and pleurodesis efficacy among patients with malignant pleural effusion: the TIME1 randomized clinical trial. *JAMA* 2015;314:2641–53.
43 Davies HE, Mishra EK, Kahan BC, *et al*. Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. *JAMA* 2012;307:2383–9.
44 Wahidi MM, Reddy C, Yarmus L, *et al*. Randomized trial of pleural fluid drainage frequency in patients with malignant pleural effusions. The ASAP trial. *Am J Respir Crit Care Med* 2017;195:1050–7.
45 Corcoran J, Talwar A, Hallifax R, *et al*. P2 incorporation of an in-depth thoracic ultrasound assessment into routine pre-procedural evaluation of patients with pleural effusions. *Thorax* 2016;71(Suppl 3):A83–4.
46 Stathopoulos GT, Psallidas I, Moustaki A, *et al*. A central role for tumor-derived monocyte chemoattractant protein-1 in malignant pleural effusion. *J Natl Cancer Inst* 2008;100:1464–76.
47 Cheah HM, Lansley SM, Varano Della Vergiliana JF, *et al*. Malignant pleural fluid from mesothelioma has potent biological activities. *Respirology* 2017;22:192–9.
48 International PPHC, Lane KB, Machado RD, *et al*. Heterozygous germline mutations in BMPR2, encoding a TGF-beta receptor, cause familial primary pulmonary hypertension. *Nat Genet* 2000;26:81–4.
49 Evans JD, Girerd B, Montani D, *et al*. BMPR2 mutations and survival in pulmonary arterial hypertension: an individual participant data meta-analysis. *Lancet Respir Med* 2016;4:129–37.
50 Long L, Ormiston ML, Yang X, *et al*. Selective enhancement of endothelial BMPR-II with BMP9 reverses pulmonary arterial hypertension. *Nat Med* 2015;21:777–85.
51 Pepke-Zaba J, Delcroix M, Lang I, *et al*. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. *Circulation* 2011;124:1973–81.
52 Simonneau G, D'Armini AM, Ghofrani HA, *et al*. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension: a long-term extension study (CHEST-2). *Eur Respir J* 2015;45:1293–302.
53 Rajaram S, Swift AJ, Condliffe R, *et al*. CT features of pulmonary arterial hypertension and its major subtypes: a systematic CT evaluation of 292 patients from the ASPIRE Registry. *Thorax* 2015;70:382–7.
54 Lungu A, Swift AJ, Capener D, *et al*. Diagnosis of pulmonary hypertension from magnetic resonance imaging-based computational models and decision tree analysis. *Pulm Circ* 2016;6:181–90.
55 De Boeck K, Amaral MD. Progress in therapies for cystic fibrosis. *Lancet Respir Med* 2016;4:662–74.
56 Davies JC, Wainwright CE, Canny GJ, *et al*. Efficacy and safety of ivacaftor in patients aged 6 to 11 years with cystic fibrosis with a G551D mutation. *Am J Respir Crit Care Med* 2013;187:1219–25.
57 Ramsey BW, Davies J, McElvaney NG, *et al*. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Engl J Med* 2011;365:1663–72.
58 Clancy JP, Rowe SM, Accurso FJ, *et al*. Results of a phase IIa study of VX-809, an investigational CFTR corrector compound, in subjects with cystic fibrosis homozygous for the F508del-CFTR mutation. *Thorax* 2012;67:12–18.
59 Wainwright CE, Elborn JS, Ramsey BW, *et al*. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. *N Engl J Med* 2015;373:220–31.
60 Heaney LG, Djukanovic R, Woodcock A, *et al*. Research in progress: Medical Research Council United Kingdom Refractory Asthma Stratification Programme (RASP-UK). *Thorax* 2016;71:187–9.
61 Hanania NA, Korenblat P, Chapman KR, *et al*. Efficacy and safety of lebrikizumab in patients with uncontrolled asthma (LAVOLTA I and LAVOLTA II): replicate, phase 3, randomised, double-blind, placebo-controlled trials. *Lancet Respir Med* 2016;4:781–96.
62 Nair P, Gaga M, Zervas E, *et al*. Safety and efficacy of a CXCR2 antagonist in patients with severe asthma and sputum neutrophils: a randomized, placebo-controlled clinical trial. *Clin Exp Allergy* 2012;42:1097–103.
63 Brusselle GG, Vanderstichele C, Jordens P, *et al*. Azithromycin for prevention of exacerbations in severe asthma (AZISAST): a multicentre randomised double-blind placebo-controlled trial. *Thorax* 2013;68:322–9.
64 Durrington HJ, Farrow SN, Loudon AS, *et al*. The circadian clock and asthma. *Thorax* 2014;69:90–2.
65 Traister RS, Fajt ML, Landsittel D, *et al*. A novel scoring system to distinguish vocal cord dysfunction from asthma. *J Allergy Clin Immunol Pract* 2014;2:65–9.
66 Murphy P, Arbane G, Bourke S, *et al*. S115Hot-HMV UK trial secondary outcome analysis: early readmission is reduced by the addition of home mechanical ventilation to home oxygen therapy in COPD patients with chronic respiratory failure following a life-threatening exacerbation. *Thorax* 2016;71(Suppl 3):A68–9.
67 Morris C, Parry S, Holmes P, *et al*. P61 community oxygen prescriptions and DNACPR discussions in Stockport; an opportunity to improve end of life care planning? *Thorax* 2016;71(Suppl 3):A117–8.
68 Hurst J, Dilleen M, Morris K, *et al*. P59 factors influencing step-up to LAMA+LABA/ICS in COPD patients initially on LAMA monotherapy: a thin database study. *Thorax* 2016;71(Suppl 3):A116.
69 Kostikas K, Tsiligianni I, Fucile S, *et al*. P60 Effect of indacaterol/glycopyrronium (IND/GLY) on patient-reported outcomes in men and women with COPD: a pooled analysis from the ignite programme. *Thorax* 2016;71(Suppl 3):A116–17.
70 Vestbo J, Leather D, Diar Bakerly N, *et al*. Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice. *N Engl J Med* 2016;375:1253–60.
71 McNeill A, Brose LS, Calder R, *et al*. E-cigarettes: an evidence update. A report commissioned by Public Health England. (PHE publications gateway number: 2015260) London: Public Health England, 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457102/Ecigarettes_an_evidence_update_A_report_commissioned_by_Public_Health_England_FINAL.pdf
72 Hartmann-Boyce J, McRobbie H, Bullen C, *et al*. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2016;9:CD010216.
73 Pisinger C, Døssing M. A systematic review of health effects of electronic cigarettes. *Prev Med* 2014;69:248–60.
74 Marco E, Grimalt JO. A rapid method for the chromatographic analysis of volatile organic compounds in exhaled breath of tobacco cigarette and electronic cigarette smokers. *J Chromatogr A* 2015;1410:51–9.
75 Farsalinos KE, Kistler KA, Gillman G, *et al*. Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. *Nicotine Tob Res* 2015;17:168–74.
76 Scott A, Lugg S, D'Souza V, *et al*. S122 effects of vaped e-cigarette liquid condensate upon human alveolar macrophage function. to vape or not to vape that is the question? *Thorax* 2016;71(Suppl 3):A72.
77 Dacie R, Belchamber K, Donnelly L. S123 The effects of electronic cigarette flavourings on macrophage cytokine release and phagocytosis. *Thorax* 2016;71 (Suppl 3):A72–A3.
78 Hartmann-Boyce J, Cahill K, Hatsukami D, *et al*. Nicotine vaccines for smoking cessation. *Cochrane Database Syst Rev* 2012(8):CD007072.