TSANZ & ANZSRS 2019 Annual Scientific Meeting Conference Review™

Making Education Easy

Mar 29 to Apr 2, 2019; Gold Coast

In this review:

Abbreviations used in this review:

CF = cystic fibrosis; **COPD** = chronic obstructive pulmonary disease; **FOT** = forced oscillation technique; **IPF** = idiopathic pulmonary fibrosis; **QOL** = quality of life; **RCT** = randomised clinical trial.

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Welcome to this review of the 2019 Annual Scientific Meeting of the TSANZ (Thoracic Society of Australia and New Zealand) and ANZSRS (Australian and New Zealand Society of Respiratory Science),

the Annual Scientific Meeting for leaders in lung health and respiratory science, including numerous presentations from a range of international and local researchers. The meeting was during March 29 to April 2, 2019, at the Gold Coast Convention and Exhibition Centre. Among the many attendees who convened to hear the latest respiratory research was Conjoint Professor Peter Wark from Newcastle who has provided the commentary for this review. Abstracts for the meeting's oral presentations included in this review can be found here (Respirology 2019;24(S1).

We hope you enjoy this Conference Review. We value your comments and feedback.

Kind Regards,

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TSANZ Plenary: Emerging strategies for the management of bronchiectasis

Why doesn't treatment for CF bronchiectasis work for non-CF related bronchiectasis?

Presenter: Hoffman L, University of Washington, USA

Summary/comment: Luke Hoffman gave a comprehensive description of the differences and similarities between CF (cystic fibrosis) and bronchiectasis not associated with CF to try and determine why many trials for bronchiectasis have failed to produce positive findings. He highlighted the wide clinical disparities seen in those with bronchiectasis as a major reason why demonstrating effectiveness can be difficult. He also highlighted important differences in pathophysiology between CF and bronchiectasis, where in many cases this is now much better defined and homogenous in the case of CF. The importance of a high DNA content in sputum and the efficacy of inhaled dornase alfa was given as an example. The heightened local inflammatory response in the airways that precedes bacterial colonisation was also cited as a potentially modifiable factor in CF through early intervention with chest physiotherapy, early antibiotic treatment and now CFTR modulators. He did highlight the emergence of evidence though, especially the work. An important aspect though about this disparity may be the relatively poor organisation of services to address the needs of those with bronchiectasis as opposed to what has become a very well organised and multidisciplinary approach to CF, with a strong evidence base and momentum for both research and monitoring outcomes.

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Where are we at with the chronic management of bronchiectasis?

Presenter: Polverino E, Barcelona, Spain

Summary/comment: Eva Polverino presented on the EMBARC (European Multicentre Bronchiectasis Audit and Research Collaboration) registry, which is a prospective, pan-European observational study of patients with bronchiectasis. The inclusion criterion is a primary clinical diagnosis of bronchiectasis consisting of: i) a clinical history consistent with bronchiectasis; and ii) CT demonstrating bronchiectasis. She highlighted the lack of evidence around bronchiectasis, especially the epidemiology and natural history of the condition. In this aspect, the EMBARC aims to make a major contribution to understanding the natural history of the disease, as well as guiding evidence-based decision making and facilitating the development of large-scale RCTs. Details on EMBARC can be found at https://www.bronchiectasis.eu.

Eva Polverino highlighted the ERS guidelines for bronchiectasis statement (Eur Respir J 2017;50:1700629) and the approach whereby a multidisciplinary group representing respiratory medicine, microbiology, physiotherapy, thoracic surgery, primary care, methodologists and patients considered the most relevant clinical questions (related to management). They generated nine key clinical questions and a systematic review was conducted to identify published systematic reviews, RCTs and observational studies that answered these questions. They used the GRADE approach to define the quality of the evidence and the level of recommendations. The resulting guideline addresses the investigation of underlying causes of bronchiectasis, treatment of exacerbations, pathogen eradication, long-term antibiotic treatment, anti-inflammatories, mucoactive drugs, bronchodilators, surgical treatment and respiratory physiotherapy. While this is an important first step, she highlighted the lack of evidence that existed to inform in all of these areas.

The protracted bacterial bronchitis – bronchiectasis paradigm

Presenter: Chang A, Queensland

Summary/comment: Anne Chang gave a comprehensive overview of protracted bacterial bronchitis, comparing and contrasting it to bronchiectasis in childhood. She described how protracted bacterial bronchitis is the commonest cause of chronic wet cough in children attending Australian respiratory clinics. She also highlighted that it is a possible forerunner to other chronic suppurative lung diseases, such as bronchiectasis. Finally accurate identification is important, certainly in allowing treatment with relative short-course antibiotics that can be highly effective.

Breathing dysfunction and complex breathlessness in asthma

Presenters: Fowler S, Depiazzi J & Clifton-Smith T

Summary/comment: This symposium highlighted an important but challenging area of management for clinicians. Stephen Fowler gave an excellent overview on assessment and diagnosis of complex dyspnoea in adults and adolescents. He highlighted the path to diagnosis in intermittent laryngeal obstruction and breathing pattern disorder, and the importance of identifying and managing comorbidities such as asthma, rhinosinusitis, gastro-oesophageal reflux disease, obesity and tracheomalacia. He also gave an overview of the role of speech therapy and physiotherapy in management. His talk was based on his excellent recent review in Eur Respir J from 2016 (Eur Respir J 2016;25:287–94). He was supported by Julie Depiazzi who outlined nonpharmacological treatments of dyspnoea and Phil Bardin who went over assessment and treatment of paradoxical vocal fold movement, while Tania Clifton-Smith spoke about dyspnoea, dysfunctional breathing and anxiety.

TSANZ Symposium

Independent commentary by Conjoint Professor Peter Wark

Prof Peter Wark is a senior staff specialist in Respiratory and Sleep Medicine at John Hunter Hospital, Newcastle, Australia and a conjoint Professor with the University of Newcastle. In addition, he is a senior investigator with the Priority Research Centre for Healthy Lungs and the Vaccines Immunology Viruses and Asthma research group at the Hunter Medical Research Institute. He is also a chief investigator in the National Health and Medical Research Council Centre of Excellence in Severe Asthma. His research interests are in the area of infection and the impact this has on inflammatory airways disease, with a particular interest in viral respiratory infections and acute exacerbations of chronic airways disease.

RESEARCH REVIEW — The Australian Perspective Since 2007

Bugs behaving badly

Presenters: Grimwood K, Hoffman L & Rodgers G

Summary/comment: This session combined views from clinical medicine and microbiology with the emerging science of the microbiome. Keith Grimwood spoke on the microbiome dynamics in paediatric lung disease. He highlighted the work that he has been involved in demonstrating the role of the microbiome. He highlighted how the nasopharyngeal microbiome in CF differed by 2 months. He highlighted though the difficulties faced applying microbiome studies in subjects with CF. Challenges around contamination and the presence of low-level pathogens were also highlighted. A consistent finding though appears to be the lower biodiversity seen as people with CF age and their lung disease progresses. He raised an important point in microbiome studies as to what matters – is it the overall abundance of bacteria or the biodiversity that better reflects a disease state?

Luke Hoffman followed with an excellent talk on the same area, somewhat philosophically asking the question as to what constitutes a pathogen and how this could be considered in the context of working with the microbiome as opposed to traditional microbiological definitions of infection. He pointed out that Koch's postulates were really designed to look at infection within a sterile place, such as the blood. Realisation that the airways are not sterile has changed this concept considerably. He highlighted there was a poor relationship between the abundance of organisms present and clinical outcomes in the setting of CF studies. He also highlighted that in the case report of the lungs from an individual who was transplanted, the organisms present varied in different parts of the airways. There was also the issue raised that antibiotic use probably was driving selection of micro-organisms in the setting of chronic disease, such as CF.

Geraint Rodgers from South Australia then concluded discussing the importance of the microbiome on a much larger scale, and the important role played by the gut microbiome in overall health. He outlined the role played in oligosaccharides in breast milk establishing a healthy enteric microbiome and how this is protective against enteric infection. He briefly outlined the importance of the gut microbiome in regulating immune function and referred the audience to an important recent review of this topic (Budden KF *et al.* Nat Rev Microbiol 2017;15:55–63). In concluding with the role of the gut microbiome in respiratory disease, he also spoke about how short-chain fatty acids have been shown in asthma to influence microbial metabolites and are therefore protective (Thorburn A *et al.* Eur Respir J 2013;42:P3140).

ANZSRS/TSANZ Joint Plenary

Efficacy of oral antibiotics for non-severe exacerbations of bronchiectasis in children

Authors: Goyal V et al.

Summary: This RCT reported that both amoxicillin-clavulanate and azithromycin were better than placebo for treating children with nonsevere bronchiectasis exacerbations in the absence of *Pseudomonas aeruginosa* infection.

Comment: A major feature of the conference this year was infection. Goyal *et al.* presented an important RCT that looked at the efficacy of oral antibiotics in children with nonsevere exacerbations of bronchiectasis. One-hundred-and-ninety-seven children were randomised to receive amoxicillin-clavulanate 22.5 mg/kg twice daily (n=63), azithromycin 5 mg/kg/day (n=67) or placebo (n=67) for 14 days. Resolution of the exacerbation (defined as return to baseline) by 14 days was the primary outcome. They excluded children colonised with *P. aeruginosa*. Exacerbations had resolved by day 14 in 41, 41 and 29 children from the amoxicillin-clavulanate, azithromycin and placebo groups, respectively. Compared with placebo, the relative risks of resolution by day 14 were 1.50 (95% CI 1.08–2.09) and 1.41 (1.01–1.97) with number-needed-to-treat for benefit values of 5 (95% CI 3–21) and 6 (3–97) in the respective amoxicillin-clavulanate and azithromycin groups. Compared with the placebo group, the median exacerbation duration was significantly shorter in the amoxicillin-clavulanate group (7 vs. 10-days [p=0.018]), but not in the azithromycin group (8 vs. 10 days [p=0.242]). No significant differences were seen for time to the next exacerbation. The trial demonstrated that both antibiotic-containing regimens were superior to placebo, with amoxicillin-clavulanate showing some benefits over azithromycin. It provides important evidence that targeted antibiotic use in this at-risk population is beneficial, at least in the short term. It also further adds to what is unfortunately a very sparse field in the area of management for bronchiectasis.

TSANZ Oral Presentation TO-003

Temporal variability of forced oscillation mechanics from home telemonitoring is related to symptoms and quality of life and changes before acute exacerbations in COPD

Authors: Zimmermann S et al.

Summary: This research found that variability in FOT (forced oscillation technique) measures obtained by home telemonitoring reflects COPD symptoms and QOL, and may be useful for the early detection of acute COPD exacerbations.

Comment: While telemonitoring for COPD has not always been a success, it remains promising. This study was interesting as it combined telemonitoring with a novel measure of lung function, the FOT, to determine and respond to exacerbations. The investigators enrolled 16 COPD participants (aged 69 ±9 years, with percent predicted FEV_1 of 40.7 ±14.0). They measured FOT as well as change in symptoms as measured by the CAT (COPD assessment test) and SGRQ (St Georges Respiratory Questionnaire). Of all the FOT parameters, variability of inspiratory X was related to CAT and SGQR score (respective fixed-effect estimate coefficients, 1.56 [95% CI 0.63–2.50; p=0.001] and 4.64 [0.17–9.11; p=0.04]); these relationships were consistent over 7-, 10- and 14-day windows. Variability of inspiratory X and mean CAT score over 7 days both changed significantly 1 day prior to acute COPD exacerbation (respective p values 0.03 and 0.009). In this small sample size, changes in FOT appeared to reflect the change seen in symptoms, suggesting that as a technique it may be more responsive to changes in acute physiology in these patients.

TSANZ Oral Presentation TO-006

The cystic fibrosis gut microbiome: a major reservoir of transmissible antibiotic resistance

Authors: Taylor S et al.

Summary: These researchers comprehensively defined the intestinal resistome for a cohort of adults with CF. They found that the gut microbiome in CF is a major reservoir of transmissible resistance against clinically important antibiotics in the management of respiratory infections, and that the efficacy of antipseudomonal treatment might be reduced by gut-derived tobramycin resistance.

Comment: Resistance to antibiotics is a major problem globally as well as in important rare diseases such as CF. Despite this, transmission of antibiotic resistance genes is poorly understood. Investigators from South Australia assessed the gastrointestinal resistome for a cohort of adult CF patients. They used shotgun metagenomic sequencing on faecal samples from 19 CF patients and 16 healthy adults. There was a significant difference in the faecal resistome between the patients with CF and the healthy adults (Pseudo-F = 4.675 [p=0.0004]). Resistance genes that are transmissible between species were significantly higher in the patients with CF than the healthy controls (p=0.0027). Notably, patients with CF had significantly greater carriage of plasmid-mediated aminoglycoside-modifying genes (p<0.0001), which is consistent with widespread use of drugs like tobramycin. Tobramycin-resistant *Klebsiella pneumoniae* and *Escherichia coli* isolated from CF faecal samples harboured the transmissible tobramycin-resistant genes aac(6')-Ib' and aac(6')-Ib7, which were also present in tobramycin-resistant *P. aeruginosa* in the same patients, meaning that the gastrointestinal microbiome is likely to be an important source of microbial resistance gene transmission.

TSANZ Oral Presentation TO-016

Prognosis of adults with idiopathic pulmonary fibrosis without effective therapies

Authors: Khor Y et al.

Summary: This was a systematic review and meta-analysis of data from 154 cohort studies and 16 RCTs reporting survival rates for patients with IPF (idiopathic pulmonary fibrosis) without effective therapies. The respective 1-year and 5-year survival rates for such patients were found to be 86% and 42%. The authors concluded that despite the significant heterogeneity in study design and population, these findings can inform treatment discussions for patients with IPF and be used in comparisons in future studies with new therapies.

Comment: Outcomes for patients with IPF are a source of considerable concern, especially while the treatments currently available have a lot of side effects. This was a large and wide scoping review that aimed to evaluate the survival of patients with IPF without effective therapies. They systematically reviewed 154 cohort studies and 16 RCTs published between 1972 and 2018 across the globe. They were hampered by changes in the diagnostic criteria that occurred in that time, and this is likely to account for some of the study heterogeneity. They found that the survival rates for patients with IPF without effective therapies were 86% at 1 year and 42% at 5 years. This work is helpful in understanding the expected mortality effect this disorder has and will be useful for clinicians weighing up treatment decisions.

TSANZ Oral Presentation TO-021

Patients' perceptions of opioids postprescription for breathlessness in advanced COPD

Authors: Moran T et al.

Summary: Cross-sectional, qualitative, in-depth interviews were undertaken to explore perceptions regarding the use of opioids for managing severe chronic breathlessness in ten outpatients with advanced COPD. The results identified a number of barriers to opioid therapy acceptance for refractory breathlessness, even in patients with current or prior opioid prescriptions. The authors concluded that services focussing on building strong relationships, continuity and co-ordinated care using a multi-professional patient-centred approach are important for enabling safe and effective opioid prescribing.

Comment: Intractable breathlessness is common in patients with severe COPD. Opioids are often prescribed but there is a reluctance for patients to use them and this may limit their effectiveness. These investigators explored perceptions regarding opioids for the management of severe chronic breathlessness, with cross-sectional, qualitative, in-depth interviews analysed using both a descriptive and exploratory thematic analysis framework. Participants described barriers related to their initial fear of opioid use, concerns regarding side effects, difficulties accessing the medications, social stigma and generalised aversive tendencies, although fatalistic perspectives and addiction risk were not reported as barriers. Key facilitators included better QOL after starting opioids, a strong trusting relationship with the health professional who recommended opioids and having realistic expectations in terms of symptom improvement. These results are important to better understand what barriers may exist in the prescription of opioids and their acceptance by patients. The importance of introducing this in the context of a strong therapeutic relationship is clearly important.

TSANZ Oral Presentation TO-033

Clinical response to mepolizumab in patients with severe eosinophilic asthma

Authors: Harvey E et al.

Summary: Patient characteristics and response to mepolizumab for the treatment of severe eosinophilic asthma were described for 212 patients entered in the Australian Mepolizumab Registry (a multicentre postmarketing surveillance registry), who had been prescribed mepolizumab prior to PBS subsidisation. It was found that the patients in this registry with severe eosinophilic asthma had a very significant and long-standing disease burden, but that their disease burden was significantly reduced with the use of mepolizumab. However, despite the recorded improvements, the condition remained uncontrolled for most of the patients.

Comment: Prescription of monoclonal antibodies has made a large impact on severe asthma care, with trials promising a substantial benefit. The Australian Mepolizumab Registry is looking at how effective they have been to asthma care in Australia. Between January 2017 and June 2018, 212 registered patients commenced mepolizumab. Among the patients commenced, 48% were taking maintenance oral corticosteroids. During the 12 months prior, they had required a median of three oral corticosteroid courses and 28% had been hospitalised for exacerbations. After 3–5 months of treatment, there were significant improvements in asthma symptom control, QOL and lung function. At 6–8 months after commencement, 106 of 120 assessable patients were classified as responders, 14 had discontinued mepolizumab due to adverse drug reactions (n=3), failed asthma control (ACQ) response (n=7) and other reasons (n=4), and 92 were awaiting assessment. However, 53% of the patients had an ACQ5 score of ≥1.5 at this timepoint. The Australian population was older than that seen in the trials, had a very high burden of illness and despite treatment with mepolizumab, still had a high asthma symptom burden. In the rush to introduce monoclonal therapies, we should not forget the complexity of disease in our patients. More work needs to be done to see what further improvements could be applied to care in these individuals.

TSANZ Oral Presentation TO-040

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