

Making Education Easy

September 6-10, 2014; Munich 2014

In this review:

- Sleeping on animal fur during 1st 3 months of life reduces later asthma risk
- Insulin use increases asthma risk in diabetics
- Stepwise ICS withdrawal and lung function in COPD treated with dual bronchodilation
- Cognitive impairment in acute COPD exacerbation
- Anti-inflammatory effects of targeted lung denervation in COPD
- Audit of CTPA requests at a UK hospital
- Diagnostic gain of mediastinoscopy following mediastinal staging by EBUS-TBNA
- Systematic vs. 'hit and run' endosonographic lung cancer staging
- Telemedicine-based CPAP follow-up in OSA
- A sleep position trainer for positional OSA

Abbreviations used in this review

COPD = chronic obstructive pulmonary diseaseCPAP = continuous positive airway pressureCT(PA) = computed tomography (of pulmonary
angiogram)EBUS = endobronchial ultrasoundESS = Epworth Sleepiness ScaleFEV1 = forced expiratory volume in 1 secICS = inhaled corticosteroidLABA = long-acting β-agonistLAMA = long-acting muscarinic antagonistOSA = obstructive sleep apnoeaPE = pulmonary embolismPET = positron emission tomographyTBNA = transbronchial needle aspiration

Welcome to this Conference Review highlighting ten abstracts from the largest respiratory conference in the world, the European Respiratory Society (ERS) International Congress 2014, held in Munich. This congress has morphed from humble beginnings to a truly global affair. While taking a refreshment, I found myself at a small table with an advanced trainee from Kazakhstan, glad to be able to learn for the benefit of his people, a physician from Lithuania, proud to contribute her part to the European congress by sharing a session, a Professor from Australia giving a key note lecture and Prof Spiro, the author of one of the key text books of respiratory medicine.

While cosmopolitan and truly democratic, the **ERS is setting standards**. The new GINA standards were presented by Helen Reddel from Australia (<u>www.ginaasthma.org</u>), the ERS/ATS guidelines for the management of severe asthma were detailed (<u>Eur Respir J 2014;43[2]:343–73</u>) and the new guidelines for the management of PE in co-operation with the European Cardiological Society were presented. These guidelines come with a user-friendly, free-to-download app (<u>www.escardio.org/guidelines</u>). The ERS is gaining momentum in creating tuberculosis guidelines, lung cancer guidelines and a worldwide registry of patients with idiopathic pulmonary fibrosis.

Idiopathic pulmonary fibrosis was also the 'buzz' topic at the meeting. 'Respiratory medicine will never be the same!' was Athol Wells' interpretation of the fact that with pirfenidone and nintedanib, we will soon have two agents available to treat this common and most aggressive interstitial lung disease (see <u>Respiratory Research Review issue 104</u>). This 'watershed' moment was celebrated with enough posters to fill this entire Conference Review, reporting factors predicting response, 7-year experience, possible combinations and a possible extension of the indication for pirfenidone. This is certainly an area to watch.

However, in this review I have tried to keep a **balanced view**, reporting two abstracts for each of the topics of asthma, COPD, PE, lung cancer and sleep-disordered breathing. I hope you enjoy the selection, and I am happy to receive comments, feedback and questions for more information.

Abstracts, slides and posters from the meeting can be found at <u>http://www.ers-education.org/events/</u> international-congress.aspx

Kind regards Dr Lutz Beckert lutzbeckert@researchreview.co.nz

Sleeping in animal fur in the first three months of life reduces the risk of asthma in later childhood

Authors: Tischer C et al.

Summary: This research investigated the effect of sleeping on an animal skin during the first 3 months of life on asthma and allergies out to age 10 years in 2441 children from the LISAplus birth cohort, 55% of who had slept on animal skins as described. Logistic regression analyses showed that sleeping on an animal skin was inversely associated with ever wheezing, physician-diagnosed asthma and physician-diagnosed hay fever out to age 10 years (respective adjusted odds ratios 0.75 [95% Cl 0.60–0.94], 0.62 [0.39–1.00] and 0.65 [0.46–0.92]), but not eczema or allergic sensitisation to aero-allergens; analyses using generalised estimating equations yielded similar results.

Comment: In the 1990s, it was trendy for German newborns to sleep on an animal fur, mainly sheepskins. These researchers reported on almost 2500 children from Munich and Leipzig who spent at least 3 months sleeping on an animal fur. The authors postulated that sleeping on an animal fur, a reservoir for microbiological compounds, may serve to provide similar protective mechanisms to growing up on a farm or rural environment. The authors reported a significant reduction in asthma and a trend towards less hay fever; the effect was stronger if the parents had allergic disease. Bottom line: sleeping on sheepskins in early life may protect from asthma in later life.

Session 234; Abstract 1944

Insulin use increases risk of asthma but metformin use reduces the risk among patients with diabetes in a Taiwanese population cohort

Authors: Chen CZ et al.

Summary: These researchers used Taiwanese insurance claims data to prospectively compare the incidence of asthma between 19,428 case patients with diabetes and 38,856 matched controls. They also conducted a nested case-control study of 3596 patients from the NHI database to explore the relationship between antidiabetes agents and asthma risk. Patients with diabetes had a significantly higher incidence of asthma than those without diabetes (adjusted hazard ratio 1.33 [95% Cl 1.26, 1.41]). Furthermore, the risk of asthma was significantly increased in patients with diabetes treated with insulin (odds ratio 1.16 [95% Cl 1.02, 1.31]), but not any oral antidiabetes agent.

Comment: These Taiwanese authors presented data exploring whether insulin treatment may facilitate the onset of asthma. From the Taiwanese population registry, they identified about 20,000 case patients with diabetes who developed asthma over a 10-year follow-up period; they matched these to a nonasthmatic diabetic population controlled for age, gender and body mass index. Diabetes seemed to increase the risk of developing asthma 1.3-fold. The control cohort had the same body mass index, so the main difference was the use of asthma medications. Bottom line: treatment with insulin increases the risk of asthma 2.2-fold, and treatment with metformin may reduce the risk of developing asthma by 25%.

Poster 2989

The impact of stepwise withdrawal of inhaled corticosteroids on lung function in COPD patients receiving dual bronchodilation

Authors: Watz H et al.

Summary: WISDOM trial participants with GOLD 3–4 COPD and a history of exacerbation treated with LAMA plus LABA therapy (n=2485) received tiotropium 18µg once daily, salmeterol 50µg twice daily and fluticasone 500µg twice daily for a 6-week run-in period and were then randomised 1:1 to continue this regimen or withdrawal ICS treatment in a stepwise manner (dose reduction every 6 weeks) over a 12-week period. Compared with continued treatment, participants in the ICS withdrawal group had a 38mL greater adjusted mean decrease in baseline trough FEV₁ at week 18 (p<0.0001), and similar results were seen at week 52.

Comment: This study was one of the hot topics, presented by the institution where I spent my sabbatical period. The authors explored the benefit of background ICSs in COPD patients receiving LABA plus LAMA therapy. They recruited 2500 COPD patients receiving ICSs, LABAs and LAMAs, and in a stepwise manner withdrew ICSs in half of the participants. FEV₁ remained stable until the patients were taking ICS 100µg twice daily; thereafter the FEV₁ dropped by 43mL in the ICS withdrawal group. Their primary outcome is the **bottom line: the withdrawal of ICS in patients with severe, stable COPD did not cause increased exacerbations.**

Session 260; Abstract 2423

RESPIRATRY RESEARCH REVIEW IS BROUGHT TO YOU BY RESEARCH REVIEW

We offer over 50 different Reviews in various clinical areas. Subscription costs nothing – go to **www.researchreview.co.nz**





Cognitive impairment in patients hospitalized with acute COPD exacerbations

Authors: López-Torres I et al.

Summary: These researchers measured cognitive impairment using the MOCA (Montreal Cognitive Assessment) tool in 200 patients hospitalised with an acute COPD exacerbation. The total MOCA score was low, which translates to high cognitive impairment, with particularly low scores in the abstraction and memory subscales.

Comment: This is a fascinating observational study from Spain. The researchers recruited 200 patients admitted with an acute exacerbation of COPD and asked them to perform a standardised 8-item minimental test, the MOCA. This cognitive assessment showed an impressively poor performance, particularly in aspects of abstraction and memory subscales. If validated, this may mean that the time of admission is not a good time to make major decisions; data on performance are still being collected. **Bottom line: patients with an acute exacerbation of COPD scored 17/30 in the MOCA cognitive test.**

Session 366; Abstract 3551

ABOUT RESEARCH REVIEW

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas. Research Review publications are intended for New Zealand medical professionals.

ABOUT CONFERENCE REVIEWS

Conference Reviews are prepared with independent commentary from relevant specialists. To become a reviewer or to commission a conference review contact admin@researchreview.co.nz

SUBSCRIBE AT NO COST TO ANY RESEARCH REVIEW

Respirator

NZ health professionals can subscribe to or download previous editions of Research Review publications at www.researchreview.co.nz

Respirat

NZMA

12

Anti-inflammatory effects of targeted lung denervation in patients with COPD

Authors: Kistemaker L et al.

Summary: The effect of targeted lung denervation on inflammation was explored in seven patients with moderate-to-severe COPD: LAMA therapy was withheld for 7 days prior to the procedure. Analyses of bronchial wash fluid samples obtained on day 0 (before the procedure) and again on day 30 showed that five participants experienced a decrease in their percentage of neutrophils during this time, four had reductions in CXCL8 levels and six had reductions in CCL4 (MIP-1b) levels. Bronchial brush samples taken at the same timepoints showed that six participants had a decrease in CXCL8 gene expression, five had decreased IL-6 expression, six had decreased TGF-b gene expression and five had decreased MUC5AC gene expression.

Comment: Conferences are always places to showcase technological advances - the ERS is no exception. One of these innovations is a fascinating proof-of-concept study presenting a cooled catheter that allows for localised denervation of the bronchus to reduce the vagal, cholinergic effect on the airway. Although the study included only seven patients, it showed a significant reduction in inflammatory markers. I guess while the gastroenterologists went from selective vagal separation to protonpump inhibitors, we respiratory physicians may move from LAMAs to targeted denervation. Bottom line: targeted lung denervation may produce an anticholinergic and antiinflammatory effect on the lung.

Session 365; Abstract 3333

Privacy Policy: Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Research Review publications are intended for New Zealand health professionals.

Audit of computed tomography pulmonary angiogram (CTPA) requesting at Hammersmith Hospital

Authors: Purcell M & Ellis H

Summary: Using retrospective data, these authors sought to determine the proportion of 76 CTPAs performed during June to August in 2013 that used Well's scores or D-dimer measurements in accordance with the UK NICE guidelines. Eight CTPAs resulted in a diagnosis of PE, three had a Well's score calculated and D-dimer level measurements were obtained for 49. There were a range of other respiratory pathologies identified, including consolidation and malignancy. A re-audit of 2014 data showed that more Well's scores were being calculated, but there was no increase in PE diagnoses.

Comment: This abstract is included to provide a degree of reassurance to all of us who struggle with excessive CTPA requests and the associated radiological burden. This study caused a sense of déjà vu, as the findings are very similar to results published by my colleagues and myself in NZ. The author presented an audit and re-audit after an educational intervention about CTPA scans performed at Hammersmith Hospital. Despite the intervention, only 14.5% had the Wells score and 57% a D-dimer performed. Bottom line: electronic ordering may provide an opportunity to improve CTPA ordering – the new PE app (www.escardio.org/guidelines) may also help.

Session 255; Abstract 2330

No additional diagnostic gain of mediastinoscopy following systematically and thoroughly performed mediastinal staging by EBUS-TBNA

Authors: Kempa A et al.

Summary: These authors reviewed clinical data to assess the diagnostic value of a systematic biopsy, obtained using rigid bronchoscopy under general anaesthesia, of the mediastinal lymph node zones for patients with either a central lesion or suspected hilar or mediastinal involvement on imaging. EBUS-TBNA was performed in 192 patients during the study period, followed by radical surgery and systematic lymphadenectomy. An average of 2.89 lymph node zones were biopsied in each patient. Systematic lymph node sampling was undertaken in 57% of patients (including at least lymph node zones 4L, 4R and 7), while 33 of the patients had an N2-situation on EBUS-TBNA, which was confirmed by systematic lymphadenectomy. One patient had a false-positive EBUS finding, and two had a false-negative finding at lymph node zone 5/6L. The respective sensitivity, specificity and negative predictive values for mediastinal involvement were 93.93%, 99.81% and 99.6%. Mediastinoscopy was performed in 13 patients with PET and CT findings suggestive of mediastinal involvement and negative EBUS-TBNA. All these patients had confirmed preoperative N-staging, although two had an N2 stage on systematic lymphadenectomy.

Comment: In this German study, the authors reviewed their data on 192 patients who underwent EBUS-TBNA and then went on to have radical surgery and systematic lymphadenectomy. According to current guidelines the authors performed mediastinoscopy in 13 patients in whom CT-PET scans were suggestive of mediastinal involvement but EBUS-TBNA was negative. Although they had one false-positive N2 node and two false-negative N2 nodes, EBUS-TBNA had a sensitivity of 94%, specificity of 99.8% and a negative predictive value of 99.6%. Bottom line: if EBUS-TBNA is performed systematically, a mediastinoscopy does not add additional information.

Session 388; Abstract 3563

Independent commentary by Associate Professor Lutz Beckert.

Associate Professor Lutz Beckert is the Head of Department of Medicine of the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board with particular clinical interests in Interstitial Lung Disease, Pulmonary Artery Hypertension, Respiratory Physiology and Venous Thrombembolic Disease.



FOR FULL BIO CLICK HERE

Systematic vs. 'hit and run' endosonographic staging of lung cancer

Authors: Crombag L et al.

Summary: The SCORE study enrolled 80 patients with suspected non-small-cell lung cancer and an indication for mediastinal nodal staging to undergo systematic EBUS followed by systematic 'EUS-B' (EBUS scope in oesophagus); nodal targets were defined based on CT-PET reports prior to endoscopy. Both target nodes and sonographically suspected and/or nodes with a short axis >8mm were sampled, and surgery with nodal dissection was the reference standard. NSCLC was the final diagnosis in 68 participants, SCLC in six, benign in four and other in two. Mediastinal nodal metastases were identified in 33 participants (41%). Systematic nodal staging added value compared with the targeted approach in seven participants (one N1, five N2 and one N3 disease). Six participants had false-negative findings.

Comment: Current guidelines suggest staging of mediastinal lymph nodes based on imaging. These Dutch authors explored whether the enlarged lymph nodes should be targeted or whether all lymph node stations should be sampled systematically. They presented a series of 80 case patients who had a full systematic EBUS and EUS-B for lung cancer staging. They analysed the data as if only the target lesion was sampled, and found that the systematic evaluation found additional nodal spread in seven patients (9%). **Bottom line: systematic staging of all nodal regions improves the yield compared with a targeted approach.**

Session 388; Abstract 3564

Telemedicine-based strategy for sleep apnoea management

Authors: Isetta V et al.

Summary: Patients with recently diagnosed OSA were randomised to receive CPAP follow-up either face-to-face or via an internet-based platform with 'visits' done via videoconference; 72/140 enrolled participants completed the trial. Compared with baseline, ESS scores had decreased significantly at 6 months in both the face-to-face group (10.7 vs. 5.4 [p<0.001]) and the internet-based group (10.7 vs. 6.7 [p<0.001]). In addition, most participants in the respective face-to-face and internet-based groups reported absence of either mask leaks (70.2% and 57.1% [p=0.327]) and nasal congestion (80.0% and 79.4% [p=1]).

Comment: A group of Spanish authors presented a randomised controlled trial of about 150 patients who had an indication for CPAP therapy with a baseline apnoea-hypopnoea index of about 50. All patients had an initial visit for CPAP titration and initial training. Thereafter they were randomised to receive face-to-face follow-up or teleconference follow-up at 1 and 3 months. At the end of the study, both groups had done equally well with regards to CPAP compliance, side effects of therapy and treatment effects on daytime sleepiness and quality of life. Bottom line: in this study, telemedicine-based CPAP follow-up was as effective as standard face-to-face follow-up.

Session 238; Abstract 2020

Subscribe at no cost to any Research Review

NZ health professionals can subscribe to or download previous editions of Research Review publications at **WWW.RESEARCHREVIEW.CO.NZ**

Long-term evaluation of positional therapy with the sleep position trainer (SPT) in the treatment of positional OSA (POSA)

Authors: Van Maanen JP & De Vries N

Summary: Adults with mild-to-moderate positional OSA (evaluable n=106) slept with a 'sleep position trainer', which vibrates when it detects the wearer lying in a supine position, strapped to their chests in this 6-month prospective observational study; use of the device could be discontinued early if it was not well tolerated. The compliance rate (device use for \geq 4 hours per night) was 64.4%. At 6 months, the median ESS score had decreased from 11 to 7, the FOSQ (Functional Outcomes of Sleep Questionnaire) score had increased from 91 to 103 and the PSQI (Pittsburgh Sleep Quality Index) score had decreased from 7 to 6. The device was associated with a rapid, persistent reduction in the median percentage of sleep time spent in supine position.

Comment: In earlier publications, these authors had shown that their sleep position trainer could treat mild-to-moderate positional OSA. The sleep position trainer is a small device that gently vibrates if the patient lies supine. Here the authors presented data on 145 patients with positional OSA treated for 6 months. The device was well tolerated, led to an almost complete reduction of supine sleeping over 2 weeks and a reduction of the participants' median ESS score from 11 to 7. **Bottom line: the sleep position trainer is effective and well tolerated over a long time, and improves quality of life.**

Session 238; Abstract 2015



This publication has been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and has been approved for CME for the General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes. Please <u>click here</u> to download your CPD MOPS Learning Reflection Form.



This publication has been created with funding from Rex Medical Limited. The content and opinions expressed in this publication do not necessarily reflect the views of Rex unless so specified.