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TSANZ: ORAL ABSTRACTS

RESPIRATORY NURSES SIG: ORAL SESSION

TO-001

ILLUMINATING THE PATHS: RESPIRATORY NURSE PRACTITIONERS

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An increasing number of respiratory nurses are overcoming the challenges of completing clinical and academic training and achieving Nurse Practitioner (NP) endorsement to establish novel roles to meet the needs of the populations they service. These roles are not completely new, however the detail on the path to a full scope of practice as an NP is largely hidden from current and prospective candidates.
Aim Our paper discusses the journey of two nurse practitioners from initial endorsement through the establishment of new roles and the evolution of their clinical practice from CNC to NP. The professional relationships with other clinicians and the interface with existing health roles and services are explored and the different opportunities and challenges between the acute care and community care settings are contrasted. The benefit that adding a Respiratory NP to the team can bring for patients in different care setting is described and the lessons shared.
Support Nil.
Nomination Best nursing oral.
Conflict of Interest No.

TO-002

LONG-TERM OUTCOMES OF A NURSE-LED COMMUNITY-BASED COPD EXACERBATION MANAGEMENT PROGRAMME

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Background Previous studies have established that self-management training and the use of COPD Action Plans focusing on early community-based management of COPD exacerbations (AECOPD) can improve hospital utilisation rates in the short term. In this study we assessed whether short-term benefits were sustained over a two to seven-year follow-up period.
Methods Patients were given self-management training and encouraged to contact the respiratory outreach nursing service at exacerbation onset. Community-management focused outreach nursing assessment and early use of broad-spectrum antibiotics and corticosteroids. Data were collected prospectively until patients died or were lost to follow-up. We assessed the impact of this service on hospital admission rates for management of COPD and the percentage of AECOPD events that could be managed in a community-setting.
Results One hundred fifty-two patients were followed for 2 to 7 years, mean follow-up time 3.3 years (range 1 to 7 years). The average annual admission rate in the 2 years prior to enrolment was 1.4 per year, and in the first 2 years post 1 per patient per year. Average annual bed-days in the year prior to enrolment was 8.5 days and < 6 bed-days per patient per year for the 5 years following enrolment. Twenty-three percent of patients died during the 7-year follow-up. Average annual bed-days increased significantly in the 12 months prior to death (average 12 months before death 13.8 bed-days per patient versus survivors 5 bed-days per annum, $P < 0.0001$).
Conclusion These results indicate that community-based exacerbation management programmes can decrease acute health care demand. Despite these measures acute health care utilization does however increase in the 12 months prior to death for most patients with COPD.
Conflict of Interest No.

TO-003

NURSING CARE PLAN FOR PATIENTS REQUIRING LONG TERM OXYGEN THERAPY

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In 2006 an alliance was formed by Registered Nurses from the Lower North Island of New Zealand who facilitate and manage home oxygen services. They met quarterly providing collegial support and peer review. They also developed a national oxygen database, an audit tool and standards of care specifically related to assessment, consultation and implementation of patients requiring home oxygen. The Respiratory Nursing Care Plan for Patients requiring Domiciliary Long Term Oxygen Therapy was developed to reflect a nursing model of care.
The care plan is a framework to guide the practice of interacting with complex patients prescribed long term oxygen therapy. Following requests for long term oxygen therapy, nurses undertake comprehensive consultation and assessment which includes negotiation with families/whanau and medical teams relating to the planned treatment and resource allocation. The care plan includes aspects of care across the care continuum from referral through to palliation. The care plan is aligned to the recently endorsed New Zealand Adult Respiratory Nursing National Knowledge & Skills Framework and is currently in the second phase of trial. The process of development and application of use will be discussed.
Conflict of Interest No.
Grant Support Nil.

TO-004

DEVELOPMENT AND AUDIENCE TESTING OF A COPD EDUCATION DVD

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Most educational resources for patients with COPD are in the form of written text. Few other media are available to support patient education. **Aim** To develop and audience test an interactive COPD DVD to support patient education.
Methods The DVD chapters were chosen based on the prevalence of the clinical problems identified in older people with COPD (1). A project team was convened involving leading content experts. Each expert developed and presented a chapter in the DVD, including: (i) An overview of COPD; (ii) Flare ups; (iii) Inhaled medications: (iv) Exercise and Pulmonary Rehabilitation; (v) Breathlessness (vi) Eating well; and (vii) Stopping Smoking. Following development and before the final cut the DVD was reviewed by 14 clinicians and 14 patients with COPD. Feedback was sought via a written evaluation tool purposefully developed for the project. The tool included a 7 point likert scale (1 = strongly disagree and 7 = strongly agree). The feedback of both groups was used to edit the final product.
Results A 50-min DVD that can be viewed in full or as individual chapters was produced. Clinicians and patients rated the quality of the DVD as a mean (SD) of 6.7 (0.4) and 6.5 (1), respectively. In terms of patient centredness, it was rated by clinicians and patients as 6.7 (0.4) and 6.2 (0.7). After watching the DVD, patients strongly agreed that they felt more able to manage their disease (6.3 (.06)), motivated to exercise (6.3 (0.6)) and more able to manage their breathlessness (6.6 (0.6)). All clinicians said they would recommend it to patients.
Conclusions The DVD can be a valuable addition to clinical practice and COPD patient education. As well, the DVD was very well accepted by both patients and clinicians.
Reference McDonald VM *et al.* Age and Ageing 2011; 40; 42–9.
Supported by The Department of Veterans' Affairs.
Conflict of Interest No.

ASTHMA & ALLERGY SIG AND CELL BIOLOGY & IMMUNOLOGY SIG: COMBINED ORAL SESSION

TO-005

β2-ADRENOCEPTOR (ADRβ2) HAPLOTYPE PAIRS AFFECT ADRβ2 FUNCTION AND RESPONSE TO FORMOTEROL IN SEVERE ASTHMATICS

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Background Effective treatment of asthma relies on efficient drug – receptor interaction. The functional & clinical relevance of ADRβ2 polymorphisms is controversial due, in part, to a lack of haplotypic analysis and differing cohorts. We compared surface ADRβ2 expression (*s*ADRβ2) and activation between severe asthmatics who had one of three common ADRβ2 haplotype pairs (HP) 22, 24 and 44, before and after formoterol (FOR). Secondary end points were FEV1 and acute bronchodilator response (BDR), tested before and after 4 weeks of FOR 12μg BD.
Methods *s*ADRβ2 (via FACS) and ADRβ2 activation (via cAMP ELISA) of lymphocytes were measured at time 0 (after 4 weeks of FOR), and repeated 12 h later, after a dose of FOR *in vitro*. *s*ADRβ2 was defined as fold change in mean fluorescence over negative controls. There were six severe asthmatics per HP group.
Results HP24 showed the highest *s*ADRβ2 at time 0 (24 vs 22 vs 44: 5.84, 4.3 and 2.7; $P = 0.03$) but marked FOR-induced downregulation. For HP22, *s*ADRβ2 was unchanged post FOR and had the highest cAMP at 12 hrs ($P < 0.001$) and the best improvement in FEV1 (80 mls, $P = 0.04$) and AM PEFR (18 L/min, $P = 0.02$) on FOR vs no LABA. While HP24 had a fall in FEV1 on FOR (100 mls, $P > 0.05$), it had the greatest BDR (190 mls, $P = 0.03$), with a significant correlation between ADRβ2 activation and higher *s*ADRβ2 ($r = 0.67$, $P < 0.001$). In stark contrast, HP44 showed low *s*ADRβ2 and cAMP, poor *s*ADRβ2-activation correlation ($r = –0.2$, $P = 0.08$), and a fall in baseline FEV1 (850 mls, $P = 0.09$) while on FOR without any BDR (–20 mls).
Conclusions ADRβ2 haplotype pairs determine ADRβ2 expression and activation and possibly clinical response in severe asthmatics. In particular, patients who are HP44 appear to show suboptimal response to LABA or SABA.
Nominations Ann Woolcock YIA, Janet Elder and TSANZ Travel Award.
Conflict of Interest Nil.

TO-006

ROSIGLITAZONE OVERCOMES RESISTANCE TO BOTH SHORT-ACTING AND LONG-ACTING β_2-ADRENOCEPTOR AGONISTS IN SMALL AIRWAYS IN MOUSE LUNG SLICES

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Background and Aim Chronic use of β_2-adrenoceptor agonists induces receptor downregulation and desensitization, potentially limiting their capacity to oppose airways hyperresponsiveness in asthma. The aim of this study was to characterize *in vitro* responses to the novel bronchodilator rosiglitazone (RGZ) under conditions where small airways are resistant to the effects of β-adrenoceptor agonists.
Methods Lung slices (150 μm) were prepared from male Balb/C mice. Using phase-contrast image analysis, changes in small airway lumen diameter in response to RGZ, salbutamol, isoprenaline or formoterol were assessed following precontraction with methacholine (MCh). Dilator responses were also compared after overnight incubation with salbutamol (SABA, 100 μM) or formoterol (LABA, 100 nM). A potential mechanism underlying differences in reactivity was explored using Ca^{2+}-permeabilized slices pharmacologically clamped at constant $(Ca^{2+})_i$, with subsequent airway size changes due to regulation of Ca^{2+}-sensitivity alone.
Results RGZ, but not β-adrenoceptor agonists, maintained dilator potency and efficacy (maximum relaxation 91 ± 3%, $n = 4$) in maximally contracted airways. Relaxation to RGZ was maintained in the presence of SABA- or LABA-induced desensitization (RGZ EC_{50}: 10 ± 1 μM, in vehicle- and formoterol-treated slices, $n = 4$). Relaxation in Ca^{2+}-permeabilized slices was markedly delayed for all β-adrenoceptor agonists, with the degree of relaxation significantly impaired for formoterol only. In contrast, slower relaxation to RGZ was only slightly delayed.
Conclusions Small airway relaxation to RGZ occurs via a different mechanism to β-adrenoceptor agonists. Since RGZ is resistant to the functional antagonism that limits airway relaxation in response to β-adrenoceptor agonists, and works under conditions of homologous β_2-adrenoceptor desensitisation, further exploration of its potential as a novel bronchodilator for the treatment of asthma is warranted.
Supported by NHMRC.
Conflict of Interest No.

TO-007

THE ACTIVATION OF THE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (RAGE) CONTRIBUTES TO THE INDUCTION OF HDM-SPECIFIC T_H2 RESPONSES

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The receptor for advanced glycation end products (RAGE) is a pattern-recognition receptor (PRR) which interacts with a diverse repertoire of endogenous ligands involved in the host immune response to injury, infection and chronic inflammation. RAGE can function as a molecular platform for the recognition of various ligand complexes via its collaboration with other PRRs including TLR4. Since TLR4 has been shown to be crucially involved in the airway response to inhaled allergens, we investigated whether RAGE contributes to the development of allergic airway inflammation in an animal model of asthma. Intranasal sensitization and challenge with house dust mite (HDM) resulted in the translocation of the RAGE ligand HMGB1 from the nucleus to the cytoplasm in both wild-type (WT) and RAGE-deficient ($RAGE^{-/-}$) mice. In the absence of RAGE, gene expression of T_H2 and T_H17 cytokines in the lung was attenuated. In addition, draining lymph node cells cultured from $RAGE^{-/-}$ mice produced significantly less HDM-specific IL-5 and IL-17A. $RAGE^{-/-}$ mice were protected against eosinophilic inflammation, but had a more pronounced neutrophilic response, despite reduced expression of pro-neutrophilic cytokines and chemokines (IL-17A, CXCL1, CXCL2, CCL3). These findings provide the first evidence that RAGE contributes to the development of T_H2- and T_H17-associated allergic airway inflammation. Further studies interrogating the mechanisms by which RAGE mediates the allergic inflammatory response; particularly as to whether this involves direct recognition/interaction with allergenic proteins, and/or occurs secondary to the release of endogenous RAGE ligands, and the co-requirement for TLR4 signalling, may expose new pathogenic processes that promote the onset of asthma.
Conflict of Interest No.

TO-008

SERUM AMYLOID A (SAA) INDUCES IL-17A DEPENDENT NEUTROPHILIC INFLAMMATION IN THE LUNG

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Introduction The pro-inflammatory cytokine IL-17A has been implicated in lung diseases where neutrophilic inflammation is prominent including severe asthma, cystic fibrosis and COPD. Although IL-17A promotes the recruitment and activation of airway neutrophils, the endogenous mediators that regulate its production in COPD are unclear. We have recently identified SAA as a candidate pathogenic mediator in COPD, where BAL levels of SAA positively correlated with neutrophilic recruitment. Furthermore, exogenous delivery of SAA into murine airways promoted an acute neutrophilic response.
Aim To determine the role of IL-17A in SAA-induced airway neutrophilia.
Methods Male BALB/C mice (6–8 weeks of age) were treated intranasally with recombinant SAA (2 μg per mouse) or saline (control) for 6–72 h. BAL and lungs were then harvested for characterization of immune cells (B, T, NKT, DC, macrophage and neutrophils) (Flow Cytometry) and QPCR used to determine expression of IL-17A in sorted cell populations. Data was expressed as mean ± SEM and significance determined using a *t*-test.
Results Significantly greater numbers of neutrophils were observed in the BAL of SAA-treated mice compared to saline-treated mice at 6, 24 and 48 h. Furthermore, anti-IL-17A significantly reduced the number of lung (0.27 ± 0.04 vs $2.95 \pm 1.20 \times 10^4$, $P = 0.043$) and BAL (0.81 ± 0.42 vs $5.93 \pm 2.23 \times 10,^5$ $P = 0.006$) neutrophils compared to isotype-treated mice 24 h post SAA. IL-17A expression was detected only in $CD4^+$T cells but not in other cell types in the lung.
Conclusion SAA-induced recruitment of airway neutrophils is dependent on IL-17A from CD4 T-helper cells (T_H17 cells).
Supported NHMRC Australia.
Conflict of Interest No.

TO-009

SILENCING OF MDA5 AND TLR3 DOES NOT REDUCE INNATE IMMUNE RESPONSES TO RHINOVIRUS IN DEFECTIVE ASTHMATIC BRONCHIAL EPITHELIAL CELLS

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Background Rhinoviruses (RV) are the most frequently isolated virus associated with acute exacerbations of asthma and Chronic Obstructive Pulmonary Disease (COPD). Bronchial Epithelial Cells (BECs) detect the presence of RV infection through innate immune sensors; MDA5 and TLR3. These are thought to initiate the interferon (IFN) response, but these pathways have not been well characterized in primary BECs (pBECs) from different disease groups.
Methods We investigated the expression patterns and roles of TLR3 and MDA5 using siRNA knockdown transfection for TLR3 and MDA5. Following knockdown, healthy and asthmatic pBECs were infected with RV-1B. A specific inhibitor of TBK1 and IKKϵ, BX795, was used to further elucidate innate signalling pathways. mRNA for TLR3 and MDA5 were measured by qPCR. IL-6, CXCL-8 and CXCL-10 were measured using cytometric bead array. Supernatants and whole cell lysates were collected for IFN-β, pSTAT-1 and PKR. IFN-λ was measured using ELISA. RV replication was measured by cell titration assay and $TCID_{50}$ calculated.
Results Asthmatic pBECs had significantly reduced release of IL-6, CXCL-8 and IFN-λ in response to RV-1B infection compared to healthy pBECs. Knockdown of > 80% was achieved with siRNA for MDA5 and TLR3. In healthy pBECs, siMDA5, siTLR3 and BX795 all reduced release of IL-6, CXCL-10 and IFN-λ to infection. In contrast, in asthmatic pBECs where responses were already reduced, there was no further reduction in IL-6 and IFN-λ, though there was in CXCL-10.
Conclusion Defective innate asthmatic pBEC immune responses to RV infection are not further impaired by preventing signalling via MDA5 and TLR3, as they are in healthy pBECs.
Nomination Cell Biology/Immunology
Conflict of Interest None.

TO-010

EXPRESSION AND ROLE OF CATHEPSINS IN ASTHMATIC AIRWAYS

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Rationale Tumstatin is an anti-angiogenic collagen IV α3 fragment, absent from the airways of asthmatics. Its absence may be due to the degradation by extracellular matrix (ECM) proteases. Cathepsins play a role in ECM remodelling, with cathepsin D, H and K (CTSD, CTSH and CTSK) being associated with lung diseases. CTSD modulates the NC1 domains of collagen molecules including tumstatin, while CTSH and CTSK are involved in ECM degradation. The role of these cathepsins in the regulation of tumstatin in the lung has not previously been examined.
Methods Gene expression of asthmatic and non-asthmatic airway smooth muscle cells (ASMCs) was compared using microarrays and verified by real-time PCR (RT-PCR). Antibodies specific for CTSD, CTSH and CTSK were used in immunohistochemistry (IHC) on formalin fixed human airway sections and staining was quantified by image analysis. CTSD and CTSH activity were analysed in human bronchoalveolar lavage fluid (BALF) samples. Recombinant tumstatin was exposed to commercial CTSD, CTSH and CTSK *in vitro*. Digestion patterns were examined over a time course (15 min–8 h) by SDS-PAGE and densitometry.
Results ASMCs from asthmatic individuals had decreased expression of CTSH and CTSK mRNA. There was no difference in the expression of CTSD, CTSH and CTSK between asthmatic and non-asthmatic airway tissue sections. CTSD and CTSH activity in BALF showed no difference between asthmatics and non-asthmatics; however, the activity of CTSH in asthmatics was increased post 6 weeks corticosteroid treatment ($n = 8$, $P < 0.0001$). CTSD, CTSH and CTSK all significantly degraded recombinant tumstatin within 15 min.
Conclusion Our results showed the presence of CTSH in the asthmatic airways and its activity is increased in asthmatics after corticosteroid treatment. How this contributes to the absence of tumstatin from asthmatic airways remains to be investigated.
Support NHMRC and Asthma Foundation NSW.
Conflicts of Interest No.

COPD SIG: ORAL SESSION 1

TO-011

FOREHEAD SENSORS ARE MORE ACCURATE THAN FINGER SENSORS WHEN MEASURING ARTERIAL OXYGEN SATURATION VIA OXIMTERY

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Introduction In people with COPD, arterial oxyhaemoglobin saturation is commonly measured by finger sensor pulse oximetry (SpO_2). As finger sensors may produce erroneous measures, we sought to determine whether a forehead sensor yielded more accurate measures of SpO_2 in people with COPD.
Methods During a standard aerobic exercise task, SpO_2 was measured continuously by two Masimo pulse oximeters (radical 7); one attached to a finger sensor and one attached to a forehead sensor. Before and after the task, arterialized capillary samples were collected as a minimally invasive gold standard measure of oxyhaemoglobin saturation.
Results Thirteen participants completed the study (FEV_1 = 36 [16]% predicted; 6 males). Compared with measures obtained in capillary blood, on average, the finger sensor under-read SpO_2 by 2% (limit of agreement [LOA] 3%) and the forehead sensor over-read SpO_2 by 2% (LOA 4%). The mean change in oxyhaemoglobin saturation during the task was similar between the finger, forehead and capillary samples being –7%, –7%, –7%, respectively (P = 0.44).
Conclusion Arterialized capillary samples comprise a mixture of arterial and venous blood and therefore the oxyhaemoglobin saturation in these samples is slightly less than that of arterial blood. As oxyhaemoglobin saturation measured using the forehead sensor was higher than that measured in the capillary sample, it is likely that this sensor produced measures that were more concordant with oxyhaemoglobin saturation in arterial blood. Both sensors were accurate in detecting the magnitude of exercise-induced desaturation.
Support SCGH Research Advisory Committee and Curtin University.
Conflict of Interest No.
Nomination Physiotherapy Prize.

TO-012

FEASIBILITY OF HOME MONITORING IN COPD WITH FORCED OSCILLATION TECHNIQUE (FOT)

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Introduction Reactance measured by FOT (Xrs) has a potential role in COPD home monitoring because it is easy to administer, is highly repeatable in the laboratory setting and is sensitive to recovery from exacerbations. We previously found the day-to-day variability of Xrs, expressed as Sw (the within subject standard deviation), was 0.62 $cmH_2O/L/s$ in COPD. The variability of unsupervized, self-adminstered Xrs measurements is unknown. Our aim was to determine the feasibility of unsupervized Xrs measurements, and its variability in stable COPD subjects.
Methods Ten COPD subjects were trained at home, to use FOT. Xrs was measured under supervision on the training day. Subjects collected FOT measurements twice daily for 10 consecutive days. Medications were not withheld prior to testing. FOT data were transmitted to the lab via GSM.
Results Subjects had mean (SD) – age 68 years (8), smoking history 38.4 pack years (8.7), post-BD (post-bronchodilator) FEV1 42.4% predicted (12.0), FEV1/FVC ratio 0.45 (0.10), resistance (Rrs) 121.7 (26.1)% predicted, Xrs 746.8 (330.3)% predicted. The mean of the supervized measurements of Xrs from the training day (–4.07 (2.2) $cmH_2O/L/s$) was similar to the unsupervized (–4.29 (2.30) $cmH_2O/L/s$, $P = 0.52$). Compliance was high with 199 measurements transmitted out of the possible 200. The Sw of Xrs was 1.0 $cmH_2O/L/s$.
Conclusion In 10 moderate-severe COPD subjects, unsupervized home Xrs measurement is feasible with a high degree of adherence. Between session variability was similar to that of supervized recording. These results support the conduct of larger, long-term studies of FOT monitoring in COPD.
Support Asthma CRC, Australian Lung Foundation COPD Fellowship.
Nomination TSANZ Travel Grant, Janet Elder International Travel Award.
Conflict of Interest No.

TO-013

VAPOR TRIAL: 12 MONTHS EFFICACY AND SAFETY FOLLOWING ENDOSCOPIC THERMAL VAPOR ABLATION (INTERVAPOR™) FOR HETEROGENEOUS EMPHYSEMA

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Introduction We have previously described 6-month results following treatment with endoscopic thermal vapour ablation (InterVapor™) to achieve lung volume reduction by inducing inflammation and contraction fibrosis.
Aim To report observations from the 12-month assessment.
Methods: Multicenter, international, single-aim trial of InterVapor (unilateral upper lobe treatment) in patients with upper lobe predominant emphysema. Primary efficacy endpoints: FEV_1 or St George Respiratory Questionnaire (SGRQ) clinically meaningful improvement at 12 months. Secondary efficacy variables: lung volumes, mMRC dyspnea and 6MWD. **Results** Forty-four patients, 50% male received InterVapor (24 RUL, 20 LUL) of mean age 63 years, FEV_1 0.86 L (31% predicted), SGRQ 59 units and 6MWD 300 m. Mean FEV_1 improvement at 1 year 10% ($P = 0.005$), FEV_1 ≥12% in 46% patients, SGRQ – 11.0 units ($P < 0.001$), HRCT lobar volume change of –751.8 ml ($P < 0.001$), RV –302.8 ml ($P = 0.025$), mMRC score –0.83 ($P < 0.001$) and 6MWD +18.5 m ($P = 0.095$) compared with baseline. 78% patients achieved either FEV_1 ≥12% or SGRQ ≥–4 units. Thrirty-nine serious adverse events were reported in 23 patients over 12 months, with 25 events being respiratory in nature.
Conclusion Unilateral lobar InterVapor treatment of heterogeneous emphysema improves lung function and health outcomes at 12 months.
Conflict of Interest Nil.

TO-014

WHERE ARE THEY NOW? FOUR YEARS AFTER THE COMPLETION OF A MAINTENANCE EXERCISE PROGRAMME IN PEOPLE WITH COPD

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Introduction To determine if quality of life and exercise capacity had been maintained 4 years after the completion of a12-month maintenance exercise programme (MEP) that followed an 8-week pulmonary rehabilitation programme (PRP) in people with COPD.
Methods At the completion of the 12-month MEP, participants had maintained exercise capacity and quality of life and were instructed to continue with unsupervized exercise without further follow-up. Four years later participants were invited to be reassessed with spirometry, two 6-min walk tests (6MWT), St. George's Respiratory Questionnaire (SGRQ) and the Health and Activity Survey (HAAS). Daily Physical Activity (PA) was also measured using the SenseWear Pro 3 armband.
Results Thirty-seven of the 48 (79%) who completed the MEP were reassessed at 4 years (mean (SD): age 70 (8); males 22; BMI 26 (6); smokers 14%). Results compared to the end of the MEP (mean difference (95%CI)) showed a maintenance of SGRQ (2.5 (–4 to 9), $P = 0.43$] with a decline in 6MWT (–56m (86 to 25) $P = 0.001$) and FEV1% predicted (–8 (12 to 4), $P < 0.001$). The HAAS results showed that 64% reported performing regular exercise and 71% that they were physically active. For 22 participants (60%) who wore the armband the daily step count and time spent at or above a moderate level of physical activity (≥3 METS) was (mean (SD)) 5,522 steps (3,603) and 65 (62) min per day, respectively.
Conclusion Four years following a PRP plus a12-month MEP people with COPD had maintained quality of life but showed a significant decline in exercise capacity.
Conflict of Interest The authors have no conflict of interest to declare.

TO-015

HEALTH-MENTORING IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) TO REDUCE PSYCHOLOGICAL MORBIDITY

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Introduction Depression and anxiety symptoms contribute significantly to reduced quality of life in COPD. Community nurses facilitated self-management through health-mentoring using a cognitive behavioural approach.
Methods We report psychological domains of an RCT in 30 general practices comparing health-mentoring (HM) and non-directive phone calls (UC) over 12 months. Outcomes assessed at baseline/6/12 months were: Hospital Anxiety and Depression scale (HADS-A, HADS-D), Post-traumatic Stress Disorder Checklist for anxiety (PCL-C), Center for Epidemiologic Studies Depression scale (CES-D). Analysis used linear mixed models with clustering by practice adjusted for age, sex and FEV1.
Results One hundred ninety-two participants: 53% male, 121/71 moderate/severe COPD, mean age 64 (SD 8).

Baseline mean (SD)	(range)	HM ($n = 90$)	UC ($n = 92$)	P value
HADS-Anxiety	(0–21)	6.7 (4.2)	6.9 (4.1)	0.7
HADS-Depression	(0–21)	4.7 (3.1)	5.0 (3.6)	0.4
CES-Depression	(0–60)	12.6 (8.7)	13.1 (8.3)	0.7
PCL-C anxiety general factor	(17–85)	29.6 (11.1)	29.6 (10.5)	0.9

Anxiety and depression was substantial but improved between visits in both groups HADS-A β (95%CI) –0.38 (–0.68 to –0.09), HADS-D –0.26 (–0.54 to 0.01).
Conclusions Health mentoring reduced anxiety and depression in COPD, but not greater than control monthly calls.
Grant Support NHMRC, BI/ALF COPD award, RHH Research Foundation.
Declaration of Interest Statement No conflict.

TO-016

FEASIBILITY OF A RESPIRATORY OUTREACH SERVICE, FACILITATING EARLY DISCHARGE FROM ACUTE CARE FOR PATIENTS WITH PNEUMONIA OR EXACERBATION OF COPD

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Introduction In 2009–2010 respiratory admissions accounted for 7% of NH inpatient admissions, occupying more than 13,000 bed days. The 2009–2010 Health Round Table report identified that the acute care length of stay (LOS) at Northern Health (NH) for pneumonia was 15% longer (LOS = 4.6 days) than the Victorian benchmark (LOS = 4 days). In response, NH established an early discharge intervention, targeting patients admitted with pneumonia or COPD exacerbations. Eligible patients are discharged from acute care on completion of their intravenous antibiotic course and receive a home visit within 24 hours.
Aim The aim of this evaluation is to assess the feasibility, patient outcomes and potential cost savings for the respiratory early discharge intervention.
Methods Data were collected prospectively on service activity and patient outcomes with administrative data used to measure service delivery costs and financial savings achieved by decreasing acute care LOS.
Results Between the first of Dec 2010 and 30th of June 2011, 260 patients were assessed, and 113 (43%) were accepted, resulting in 193 home visits. All received a comprehensive assessment and medication education with chest physiotherapy conducted on 51 occasions. Patients in the early supported discharge intervention had lower LOS compared to usual care (6.35 vs 4.35, 95%CI 1.27 to 2.73, $P < 0.001$). The main impact of the service was on LOS for COPD admissions (usual care 6.46 vs intervention 4.21, 95%CI 1.22 to 3.27, $P < 0.001$).
Conclusion The study has shown it is feasible to establish a respiratory outreach service, decreasing LOS, improving bed access and patient outcomes. The decrease in LOS achieved by this service has contributed to bringing the LOS closer to the Australian exemplar hospitals' benchmark of 4 days.
Conflict of Interest No.

RESPIRATORY INFECTIOUS DISEASES SIG: ORAL SESSION

TO-017

ANTIVIRAL EFFECTS OF ANTIOXIDANTS ON HUMAN RHINOVIRUS

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Aim To investigate whether enrichment of airway epithelial cells with dietary antioxidants will have antiviral effects on rhinovirus (RV)-infected cells.
Methods Human airway epithelial cells (Calu-3) were pre-treated with resveratrol (2 h), vitamin D (18 h), lycopene (24 h) or wortmannin (PI3-kinase inhibitor) (2 h) prior to infection. Calu-3 cells were incubated with RV43 for 1 hr and agitated at room temperature to allow efficient binding of RV. Viral internalization was assessed by confocal microscopy, PI3-kinase activation and cleavage of eIF4GI was determined by Western blot, viral RNA level was assessed by RT-qPCR, viral titer was assessed by $TCID_{50}$/ml, cell viability was assessed by Annexin V-PE and 7-AAD staining and analysed by flow cytometry.
Results A significant reduction in RV43 viral titer was observed in cells pre-treated with resveratrol ($P = 0.0076$), zinc ($P = 0.0011$), vitamin D ($P = 0.0022$) or lycopene ($P = 0.0130$). Antioxidants inhibited RV-induced PI3-kinase activation ($P \leq 0.05$). Inhibition of PI3-kinase by antioxidants also decreased internalization of labeled RV43 into Calu-3 cells. Wortmannin inhibited PI3-kinase activation and subsequent reduction of RV43 titers. Resveratrol and lycopene were found to decrease viral RNA level. The cleavage of eIF4GI which is required during maturation of viral polypeptide was unaffected by antioxidants.
Conclusions Dietary antioxidants reduce major group RV entry into airway epithelial cells via inhibition of PI3-kinase dependent pathway.
Supported FHA was supported by a scholarship from the Ministry of Higher Education, Malaysia.
Conflict of Interest None.

TO-018

IMPAIRED IMMUNE RESPONSE TO INFLUENZA VACCINATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Rationale Clinical guidelines recommend influenza vaccination in chronic obstructive pulmonary disease (COPD), though this is largely based on observational studies and a detailed examination of the immune response to vaccination has not been undertaken to date.
Aims To assess the immunogenicity of influenza vaccination in COPD and the clinical and laboratory factors associated with vaccine responses.
Methods Participants included 21 COPD patients and 14 healthy subjects. Blood was collected before and after trivalent inactivated influenza vaccination. Serum H1N1 influenza-specific antibody titres were measured by haemagglutination inhibition assay, while cellular immune function was assessed using blood mononuclear cells stimulated *in vitro* with vaccine.
Results Antibody titres post-vaccination were significantly lower in COPD patients than in healthy controls ($P = 0.02$), and this was associated with reduced serum IL-21, a cytokine that is important for B cell development and antibody synthesis ($P < 0.01$). *In vitro* functional differences were also observed between COPD patients and healthy controls, with fewer proliferating B cells expressing CD27 ($P = 0.04$) and reduced T-cell IFN-γ synthesis ($P < 0.01$). Multivariate analysis showed that post vaccination antibody titres varied in association with having COPD but not with age or smoking.
Conclusions COPD is associated with an impaired immune response to influenza vaccination. New vaccination strategies may be necessary in COPD in order to provide optimal protection against influenza infection.
Support NHMRC, Princess Alexandra Hospital Foundation.
Nomination None.
Conflict of Interest None.

TO-019

COMPARISONS OF THE SEROLOGICAL IMPACT OF A(H1N1) PDM2009 INFLUENZA IN POPULATION GROUPS OF THE SOUTHERN HEMISPHERE

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*For the Australia, New Zealand and Singapore Pandemic Serosurveillance Study Group**

Introduction Australia, New Zealand and Singapore experienced waves of A(H1N1)pdm2009 influenza during the winter of 2009. Serological studies were performed to estimate population attack rates in this region.
Methods We pooled individual level data from serological studies that used haemagglutination inhibition assays against influenza A/California/ 07/2009 performed in these countries. Pre-, intra- and post-pandemic phases, prior to vaccination, were defined using regional jurisdictions' notification data, with seropositivity defined as a titre of ≥1:40. We determined seropositive proportions for each study region by age group and gender for pre- and post-pandemic phases. Logistic regression was used to assess the effect of age, gender and region on seropositive proportion in pre- and post-pandemic periods.
Results After exclusions, the pooled database consisted of 4414 pre-pandemic assays and 7715 post-pandemic assays. In the pre-pandemic phase, older age groups showed greater seropositive proportions. In the post-pandemic phase in community-based studies, the highest seropositive proportions were seen in school-aged children and more temperate regions. Attack rate estimates ranged from 13·1% in Australia to 19·0% in New Zealand. Pregnancy and residential care were associated with lower post-pandemic seropositivity, while Indigenous Australians and Pacific Peoples of New Zealand had greater post-pandemic seropositivity.
Conclusions Temperate regions, school-aged children, Aboriginal and Torres Strait Islanders and Pacific Peoples of New Zealand may be particularly susceptible to the first wave of a novel influenza strain.
Nomination JRS, Janet Elder Awards.
Conflict of Interest No.

TO-020

MYCOBACTERIUM ABSCESSUS INFECTION AND POTABLE WATER

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M. abscessus is a rapidly growing mycobacteria responsible for progressive pulmonary disease, soft tissue and wound infections, and can contaminate clinical specimens. Considered an environmental pathogen it is not often reported in environmental studies, particularly those of potable water.
Aim To compare the genotype of *M. abscessus* isolates from water to those from human clinical specimens.
Methods From a study of Brisbane potable water (2007–2009), 10 *M. abscessus* isolates were recovered. In addition, a strain was isolated from a rainwater tank, and another from a swimming pool. A random sample of 74 clinical isolates referred to the QLD Mycobacterial Reference Laboratory during the same time period was available for comparison using repPCR strain typing (Diversilab).
Results Drinking water isolates formed two distinct strain patterns (A, B) that shared > 90% similarity. The tankwater isolate (C) shared > 85% similarity with the potable water isolates, but the pool isolate (D) was distinctly different. Fifty-three clinical isolates clustered tightly (>95% similarity) with the Group A potable water isolates, four patients with Group B. Thirteen-patient isolates clustered with the rainwater tank isolate; one patient matched the pool isolate. Three-patient isolates were unrelated to the water isolates. There were no differences between strain types in terms of geographic origin, gender, age or site/type of infection.
Conclusion The high degree of similarity between strains of *M. abscessus* from water and strains causing infection in humans from the same geographic area strengthens the possibility that drinking water may be a source of infection in these patients.
Supported by Gallipoli Medical Research Foundation.
Conflict of Interest No.

TO-021

TUBERCULOSIS CONTACT INVESTIGATIONS IN NSW

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Aim To determine the risk of active tuberculosis (TB) among contacts of patients with TB investigated in NSW TB clinics.
Methods The study population was all persons who were part of a TB contact investigation initiated between January 2000 and December 2009 at six Sydney chest clinics that together manage about 60% of all TB cases in NSW. Cases of active TB among the study population were identified by linking a database containing details for all contacts (the Clinical Surveillance System) and the NSW TB notification database.
Results There were 14,371 TB contacts investigated during the study period. The mean age (SD) of contacts was 32.9 (19.3) years; 55% were female and 44% were Australian born. 1.9% ($n = 273$) of all contacts were diagnosed with TB. Of the contacts with TB, 213 (78 %) were diagnosed at the time of the initial screening; 11 contacts developed TB later than 2 years after the initial screening. The incidence of TB among contacts was 412/100 000 person years (95% CI 365 to 465) during a mean follow-up period of 4.6 years and 1037/100 000 person years (95% CI 917 to 1172) for the first two years of follow-up. The incidence rate for TB in the general population of NSW was 6.5/100 000/year. Hence, the relative risk for TB among close contacts was 63 (independent of TST status) compared to the general population. 4186 (29%) contacts had a Mantoux tuberculin skin test (TST) ≥10 mm, and 548 (4%) received preventive therapy.
Conclusions The proportion of contacts diagnosed with TB and the proportion with a positive TST in NSW is similar to that previously described in the USA and Canada, but few receive treatment for latent TB in NSW. Contacts represent a high risk group for TB.
Supported by International Postgraduate Research Scholarship, University of Sydney.
Conflict of Interest No.

TO-022

COMPARISON OF TUBERCULIN SKIN TEST WITH AN INTERFERON-GAMMA RELEASE ASSAY (IGRA) IN SCREENING FOR LATENT TUBERCULOSIS INFECTION IN A LOW PREVALENCE POPULATION

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Aim To determine whether the Quantiferon TB Gold test (QFT-G) is a more effective screening test for latent tuberculosis infection (LTBI), when compared with the tuberculin skin test (TST), in targeted patients in a low-TB prevalence population in South-East Queensland.
Methods All consenting patients referred to the Queensland Tuberculosis Control Centre for screening evaluation for LTBI were offered standard evaluation (screening questionnaire and clinical review) and TST (where indicated), with the addition a paired QFT-G test.
Results To date, 1200 paired TST and IGRA samples have been collected. TST results have been scored (positive/negative) primarily based on risk assessment but also at specified cut-off levels (5 mm and 10 mm). QFT-G levels have been scored as positive/negative using the recommended TB specific Antigen cut-off level (0.35IU/ml). Three hundred thirty-one (27.6%) TST results, and 151 (12.6%) of QFT-G results, were positive. Concordance between paired TST and QFT-G results was relatively poor with a *Kappa* value of 0.34. In early analysis BCG vaccination status predicted TST result ($P = 0.05$), but BCG status had no significant impact on the QFT-G results. Results varied with chosen cut-offs of TST with reduced positive results at 10 mm, but with relatively poor concordance values at all levels.
Conclusions BCG vaccination may account for a higher number of positive TST results compared to the QFT-G. The role of other contributors is difficult to quantify. Concordance between tests is relatively poor. The study is ongoing, including long-term predictive data evaluation.
Conflict of Interest None.

PRIMARY CARE SIG: ORAL SESSION

TO-023

AN EVALUATION OF THE BREATHE EASY WALK EASY PROGRAMME FOR RURAL AND REMOTE HEALTHCARE PRACTITIONERS

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Introduction This project aimed to evaluate the impact of Breathe Easy Walk Easy (BEWE), an innovative programme designed to develop and support the capacity of rural/remote healthcare practitioners to provide high quality management for people with chronic lung disease.
Methods The BEWE training programme was delivered at two rural/remote sites. Participants attended a 2-day workshop and were provided with online, hard-copy resources and ongoing support. Pre- and post-workshop questionnaires measuring knowledge, skills, confidence and attitudes regarding the management of people with COPD were administered. The provision of pulmonary rehabilitation was documented before, and at 12 months after, the workshop.
Results Questionnaires were completed by 25 participants. Objective knowledge (score out of 19) improved significantly after the workshop (mean difference 7.6 correct answers, 95% CI 5.8 to 9.3). Participants' self-rated confidence and knowledge also increased. At 12 months, pulmonary rehabilitation programmes had been established at both sites and at two affiliated centres.
Conclusions The BEWE programme increased rural/remote healthcare practitioner knowledge and confidence in providing management for patients with chronic lung disease and facilitated the establishment of pulmonary rehabilitation programmes.
Supported by The Australian Lung Foundation.
Conflict of Interest No.

TO-024

ARE INHALED CORTICOSTEROIDS BEING PRESCRIBED FOR RESPIRATORY TRACT INFECTIONS?

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Background Guidelines recommend regular treatment with inhaled corticosteroids (ICS) for asthma and some patients with COPD. However, most people who are dispensed any ICS-containing medications are only dispensed one such medication in any year. We tested the hypothesis that ICS are commonly prescribed for respiratory infections in patients who do not have chronic airways disease.
Methods Data were obtained from the Pharmaceutical Benefits Scheme (PBS) for concessional patients dispensed any respiratory medications during 2008. We assumed that individuals dispensed ICS only once in a year, and no other respiratory medications, were unlikely to have chronic airways disease, and that co-dispensing of oral antibiotics suggested that the ICS were prescribed for patients with symptoms of a respiratory infection. The proportion of people prescribed only one ICS-containing medication (and no other respiratory medications) in a year who were co-dispensed oral antibiotics was calculated.
Results In 2008, 43.6% of the 115 763 patients who were dispensed one-off ICS were co-dispensed oral antibiotics. Co-dispensing was seasonal, with a large peak in winter months. The most commonly co-dispensed ICS formulation for adults was moderate/high dose combination therapy, while lower doses of ICS alone were co-dispensed among children. In this cohort, one-off ICS co-dispensed with oral antibiotics came at a cost of $2.7 million to the Australian Government in 2008.
Conclusions Many people who receive one-off ICS prescriptions do not appear to have airways disease and, as indicated by co-prescribing of antibiotics, may be being inappropriately prescribed this medication for management of respiratory infections. Interventions may be required to improve the quality of prescribing of ICS, and management of respiratory infections, in clinical practice.
Support Australian Institute of Health and Welfare; Australian Government Department of Health and Ageing.
Conflict of Interest Yes.

TO-025

EDUCATIONAL INTERVENTION FOR OLDER PEOPLE WITH ASTHMA: A RANDOMIZED CONTROLLED TRIAL

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Aim To assess the outcomes of older people with asthma after provision of a tailored educational intervention utilizing the Patient Asthma Concerns Tool (PACT) to address patient concerns and unmet needs.
Methods A parallel design, single blind randomized controlled trial comparing asthma education utilizing the PACT versus brochure-only information for asthma patients over age 55 years. Primary outcomes were asthma control including lung function (ACQ) and medication adherence score (ADH). Outcome measures were obtained at baseline, 3 and 12 months.
Results Sixty six participants (50F 16M, mean age 68 ± 8.3 years) were randomized to the intervention group and 58 (40F 18M, mean age 67 ± 6.4 years) to the control.
Significant improvements were observed in the active compared to placebo groups

	Baseline	3-month	12-month
ACQ mean ± SD	1.6 ± 1.0	1.2 ± 0.9	1.1 ± 0.8 ($P = 0.006$)*
ADH mean ± SD	1.5 ± 1.4	0.6 ± 0.8	0.8 ± 0.8 ($P = 0.01$)*

*Repeated measures ANOVA.

Conclusions An educational intervention addressing the concerns and unmet needs of older people with asthma significantly improved asthma control, adherence to preventer medication at 3 months post intervention and this was maintained at 12 months. Participants who received tailored education also used significantly less β2-agonist and were more likely to own an action plan.
Australian New Zealand Clinical Trials Registry ACTRN 12609000639224.
Supported by the Co-operative Research Centre for Asthma and Airways.
Nomination None.
Conflict of Interest No.

TO-026

COMMUNICATION SKILLS FOR DISCUSSING ADHERENCE WITH ASTHMA MEDICATIONS IN PRIMARY CARE

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Background Use of empathic communication techniques such as Motivational Interviewing (MI) can improve patients' motivation and adherence in primary care. Our aim was to investigate general practitioners' (GPs) attitudes to and use of MI.
Methods Fifty-three Sydney-based GPs (mean age 51, mean years practicing 22, 45% female) entering a study to improve asthma control completed baseline questionnaires about attitudes to MI principles, usefulness, frequency of use and confidence in using MI techniques with asthma patients. Chi-square was used to test categorical differences.
Results Ninety-four percent of GPs agreed it is their role to motivate patients to adhere and 72% felt confident in doing so. Only 55% of GPs agreed that they should respect a patient's choice to use medication differently than prescribed. Seventy-two percent thought confronting patients with negative consequences was useful to improve adherence. When discussing adherence, 53% of GPs commonly (often/always) asked patients to nominate their most important asthma problem, but 23% rarely (never/hardly ever) asked for patients' interest in information. More younger GPs rated confronting patients about the consequences of poor adherence as useful (moderately–extremely) than older GPs (79% vs 64% $P = 0.02$). Males more commonly (sometimes/often/always) asked for patients' interest in information than females (90% vs 63% $P = 0.01$).
Discussion GPs report confidence in motivating patients to take asthma medications, but sub-optimally use effective communication techniques. GP education on MI may promote patients' adherence in primary care.
Supported by NHMRC, GlaxoSmithKline (medications).
Nomination None.
Conflict of Interest No.

TO-027

TRANSLATION OF EVIDENCE-BASED ASTHMA INTERVENTIONS

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The Physician Asthma Care Education Program (PACE) is an evidence-based intervention developed in the US to improve paediatric asthma outcomes that has been adapted for use in Australia.
Aim We set out to examine the evaluations of the two programmes, in order to identify similarities and differences in the study populations, intervention components and outcomes.
Methods The RE-AIM framework (Reach, Effectiveness, Adoption, Implementation, and Maintenance) was used to assess the translation of PACE to Australia.
Results REACH: Both targeted a similar population, the US study included more children with persistent disease. EFFECTIVENESS: (i) US participants had significant reductions in symptoms and urgent care use. (ii) Australian patients were significantly more likely to receive a written asthma action plan and appropriate prescriptions for inhaled corticosteroids. US physicians were significantly more likely to prescribe inhaled corticosteroids. ADOPTION: Delivery of the intervention was similar in the US and Australia. IMPLEMENTATION: PACE intervention includes guideline recommended clinical practices, 10 communication and education strategies and clinical case studies. In Australia, we added asthma device demonstration, writing written action plans, and a quiz show. MAINTENANCE: US PACE is available through the National Heart, Lung, Blood, Institute website. Dissemination strategies for PACE Australia are being actively explored.
Conclusion Both produced improvements in physician use of inhaled corticosteroids and greater use of written asthma management plans for patients. According to RE-AIM criteria PACE has been successfully translated to Australia.
Conflict of Interest No.

TO-028

ASTHMA CARE TEAMS: CAN INTERPROFESSIONAL LEARNING CHANGE ATTITUDES AND BEHAVIOURS?

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Introduction To investigate the impact of a sociocultural theory (SCT) based interprofessional learning (IPL) intervention on health professional (HP) attitudes and behaviours to asthma care teams.
Method Thirty-three HCPs participated in an interactive problem-based IPL workshop based on the socioculutral theory of learning and the Working Relationships Collaborative Model. The IPL workshop was audio and video recorded, following which data were transcribed, and analysed for individual HCP behaviours and group interactions utilizing a qualitative analysis approach.
Results Individual HCPs differed on entry with regards to interests, confidence, professional concerns, experiences and perspectives. By the end most showed evidence of role transformation to a level of common understanding, displaying trust, respect and interprofessional collaboration.
Discussion This innovative study used SCT as a framework for investigating role transformations during the IPL process. Three distinct roles evolved: team leader, team member and outsider. The extent and rate of individual transformation was influenced by personality, gender, past experiences, professional socialization and stereotypes. Future work should explore the sustainability and impact of 'transformation' on long-term collaborative behaviours in practice.
Conclusion The patterns of connections suggested that participants have open asthma networks, lacking interprofessional collaboration whereby patients are placed in a position of power and freedom to achieve optimal asthma control independently.
Conflict of Interest No.

OLIV SIG: ORAL SESSION 1

TO-029

AN AUSTRALIAN TERTIARY REFERRAL CENTRE EXPERIENCE OF THE MANAGEMENT OF CTEPH

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Objective To report the outcome of pulmonary endarterectomy (PEA) surgery performed for chronic thromboembolic pulmonary hypertension (CTEPH) at a single tertiary centre.
Method Prospective study of 35 patients with surgically amenable CTEPH undergoing PEA between September 2004–2010. Functional data; NYHA class, 6MWD, haemodynamic data (echocardiography, RHC and cardiac MRI), morbidity and mortality were collected.
Results Following PEA, significant improvements in NYHA class (2.9 ± 0.7 vs 1.3 ± 0.5, $P < 0.0001$), RVSP (77.4 ± 24.8 mm Hg vs 44.6 ± 24.3 mm Hg, $P = 0.0003$), 6MWD (438.0 ± 97.9 m vs 520.2 ± 81.4 m, $P = 0.0005$), Borg score (4.2 ± 1.9 vs 2.8 ± 1.4, $P = 0.0123$), mPAP(42 ± 15.1 mm Hg vs 24 ± 8.8 mm Hg, $P < 0.0001$), and cardiac MRI indices (RVEDV 213.8 ± 49.2 mls vs 148.1 ± 34.5 mls, $P < 0.0001$; RVESV 130.1 ± 41.9 mls vs 78.8 ± 25.6 mls, $P < 0.0001$). Mean coronary bypass time 258.77 ± 26.16 min, clamp time 110.96 ± 35.26 min, rewarming time 81.76 ± 27.02 min, and mean circulatory arrest time of 43.83 ± 18.78 min. Mean ventilation time 4.7 ± 7.93 days (range 0.2–32.7), mean intensive care unit stay 7.22 ± 8.71 days (range 1.1–33.8). Complications included slow respiratory wean (25.7%), pericardial effusion (11.4%), persistent pulmonary hypertension (17.1%), reperfusion lung injury (20%). One year mortality was 11.4%.
Conclusion PEA can be performed safely with relatively low mortality.
Conflict of Interest Nil.
Supported Nil.
Nomination Nil.

TO-030

THE RELATIONSHIP BETWEEN PULMONARY HYPERTENSION AND PULMONARY ARTERIAL REMODELLING IN COPD IS LOBE DEPENDENT

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Introduction Pulmonary hypertension (PHT) is common in patients with severe chronic obstructive pulmonary disease (COPD). We sought to determine whether PHT severity was associated with pulmonary arterial remodelling in severe COPD.
Methods Histological morphology of pulmonary arteries was performed on explants from 44 COPD lung transplant patients. Muscular pulmonary arteries from upper and lower lobe locations were classified as small (0.10–0.15 mm), medium (0.15–0.20 mm) or large (0.20–0.25 mm) in diameter. Pulmonary arterial remodelling was measured as the ratio of pulmonary arterial wall thickness to vessel diameter (R_{WV}). PHT was diagnosed from pre-transplant echocardiography and severity categorized by right ventricular systolic pressure (RVSP) as no PHT (RVSP < 35 mm Hg), mild PHT (35 ≤ RVSP < 45 mm Hg) or moderate-severe PHT (RVSP ≥ 45 mm Hg). Repeated measures multivariate analysis of variance was performed for lung lobe location, vessel size and PHT severity.
Results 1366 vessels were analysed. Overall, R_{WV} (mean ± SE) varied according to arterial size (large: 0.141 ± 0.007, medium: 0.153 ± 0.007, small: 0.167 ± 0.006; $P < 0.001$) and lobe location (lower: 0.146 ± 0.006, upper: 0.161 ± 0.006; $P < 0.001$) but not PHT severity (P = ns). There was an interaction effect between lobe location and PHT severity, such that subjects with no PHT had a smaller R_{WV} in the lower lobes compared with the upper lobes ($P < 0.001$) but R_{WV} did change for the other PHT categories across lobe location. In the lower lobes, moderate-severe PHT subjects had a greater R_{WV} compared with the no PHT category ($P < 0.05$).
Conclusions Pulmonary arterial remodelling in severe COPD is greater in the upper lobes and in smaller arteries. The relationship between PHT and arterial remodelling is present in the lower lobes but not in the upper lobes.
Supported by National Health & Medical Research Council Scholarship
Conflict of Interest No.

TO-031

GENE DELIVERY OF BONE MORPHOGENETIC PROTEIN RECEPTOR TYPE 2 AMELIORATES PAH VIA CHANGES IN SMAD SIGNALLING

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Down-regulation of the bone morphogenetic protein receptor type 2 (BMPR2) is causally linked to heritable, idiopathic and secondary forms of PAH. BMPR2 Smad1/5/8 signalling has been shown to be diminished, with increased activation of TGF-βR Smad2/3 signalling. We have previously ameliorated PAH following BMPR2 targeted gene delivery, showing an increase in BMPR2 with a decrease in TGF-β expression. We now investigate the effect of the targeted gene delivery on Smad1/5/8 and Smad2/3 signalling pathways, hypothesizing that the amelioration of PAH is due to a switch from Smad2/3 to Smad1/5/8 signalling.
Methods Human Microvascular Endothelial Cells (HMVEC) were transduced with adenoviral BMPR2, stimulated with BMPs 24–48 h post infection then analysed. Adenoviral BMPR2 gene delivery was targeted to the pulmonary vascular endothelium in the monocrotaline (MCT) rat model of PAH.
Results At 48 h transduced HMVEC showed a 7-fold increase in pSmad1/5/8, 10-fold increase in Smad5 and 7-fold increase in BMPR2 expression via western blot analysis. Conversely there was a 3-fold decrease in p-Smad3 expression. Similar results were found at 24 h. Unexpectedly, we demonstrated an association between BMPR2 and Smad5 and verified this via co-immunoprecipitation. Extracted lungs from hypertensive rats given BMPR2 did not show a change in Smad1/5/8 protein expression, however did show a 71% reduction of Smad3 expression compared to MCT control.
Conclusion These results indicate that BMPR2 treatment alters Smad signalling. This mechanism may underpin the therapeutic impact on PAH we have seen with BMPR2 gene delivery.
Supported by NHMRC.
Conflicts of Interest No.

TO-032

ABNORMAL PULMONARY ARTERY STIFFNESS IN PULMONARY ARTERIAL HYPERTENSION: IN VIVO STUDY WITH INTRAVASCULAR ULTRASOUND

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Background There is increasing recognition that both resistance and compliance contribute to right ventricular (RV) afterload in pulmonary arterial hypertension (PAH). However, changes in the stiffness properties of the proximal elastic pulmonary arteries (PA) and the contribution of this to RV afterload have not been well studied. Furthermore, the effect of PAH-specific therapy on proximal PA stiffness is unknown.
Methods Using intravascular ultrasound (IVUS) and simultaneous right heart catheterization, 20 pulmonary segments in eight PAH subjects and 12 pulmonary segments in eight controls were studied to determine their compliance, distensibility, pressure-strain modulus and stiffness index β. PAH subjects underwent repeat IVUS examinations after 6 months of bosentan therapy.
Results At baseline, PAH subjects demonstrated greater stiffness in all measured indices compared to controls; compliance (1.50 ± 0.11 × 10–2 mm2/mm Hg vs 4.49 ± 0.43 × 10–2 mm2/mm Hg, $P < 0.0001$), distensibility (0.32 ± 0.03 %/mm Hg vs 1.18 ± 0.13 %/mm Hg, $P < 0.0001$), pressure-strain modulus (720 ± 64 mm Hg vs 198 ± 19 mm Hg, $P < 0.001$), and stiffness index β (15.0 ± 1.4 vs 11.0 ± 0.7, $P = 0.046$). Strong inverse exponential relationships existed between mean pulmonary artery pressure and compliance (r2 = 0.815, $P < 0.0001$), and also between mean PAP and distensibility (r2 = 0.790, $P = 0.002$). Bosentan therapy for 6 months was not associated with significant changes in PA stiffness.
Conclusion Increased stiffness occurs in the proximal elastic PAs in patients with PAH, and may be an important contributor to the pathogenesis of RV failure in this condition.
Supported by NHMRC and Actelion Pharmaceuticals.
Conflict of Interest No.

TO-033

IDENTIFYING AND QUANTIFYING PROGNOSTIC FACTORS IN SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE USING A TIME-VARYING COVARIATE SURVIVAL MODEL

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Introduction Total extent of disease on high-resolution CT (HRCT) lung at baseline, predicts prognosis in SSc-ILD. We sought to determine factors that predict mortality in SSc-ILD using a time-varying covariate survival model.
Method SSc patients and their data, including HRCTs and PFTs were identified through the Australian Scleroderma Cohort Study (ASCS). HRCTs were scored as previously reported. The outcome was deterioration defined as need for home oxygen, or death. Predictors of outcome, including HRCT grade, PFTs, demographic and disease-related variables were identified and quantified using a time-varying Cox proportional hazards regression model.
Results In multivariable time-dependent Cox regression analysis using 1178 time-points in 161 patients followed for mean (SD) of 4.9 (3.9) years, FVC (dL) (HR = 0.78, (95% CI; 0.65 to 0.92), $P = 0.003$) and DLCO (ml/min/mmHg) (HR 0.74, (0.58 to 0.96), $P = 0.02$) at each time-point were independently predictive of outcome, as was gender (female sex HR = 0.05, (0.01 to 0.28), $P = 0.001$). In contrast, extent of disease on serial HRCTs performed during follow-up was not significantly associated with outcome ($P = 0.5$).
Conclusions We have shown that while extent of lung disease on HRCT at baseline is strongly predictive of deterioration and death in SSc-ILD, serial HRCTs performed over time add no prognostic information. In contrast, serial FVC and DLCO are significantly predictive of outcome and offer prognostic information in follow-up of patients with SSc-ILD.
Conflict of Interest No.

TO-034

IMPAIRED CHRONOTROPIC RESPONSE TO EXERCISE PREDICTS SHORTER SURVIVAL IN INTERSTITIAL LUNG DISEASE

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Aim Reduced chronotropic response to maximal exercise has been associated with poor survival in normal subjects. This study investigated the relationships between chronotropic response to functional exercise testing, exercise capacity and survival in interstitial lung disease (ILD).
Methods Eligible participants had ILD, were ambulant and free of heart failure and beta blocker therapy. Chronotropic response (CR) during the 6-min walk test was defined as peak heart rate (HR) minus resting HR. Survival was recorded at four years.
Results Sixty-two participants (40 idiopathic pulmonary fibrosis) were included, with mean (SD) diffusing capacity for carbon monoxide (DLCO) 50(18)% predicted and 6-min walk distance (6MWD) 377(127) metres. Smaller CR to exercise was associated with reduced 6MWD ($r = 0.65$, $P < 0.001$), reduced DLCO ($r = 0.48$, $p < 0.001$) and greater pulmonary hypertension ($r = –0.42$, $P = 0.002$). Impaired CR to exercise and peak oxygen uptake explained 75% of the variance in 6MWD ($P < 0.001$ for model). A CR < 20 beats per minute and pulmonary artery pressure were independent predictors of survival at 4 years ($P = 0.001$).
Conclusions Impaired CR to submaximal exercise is associated with reduced 6MWD and reduced survival in ILD, independent of physical fitness and pulmonary hypertension. Investigation of the mechanisms underlying attenuated HR response to exercise in ILD is warranted.
Supported by Nil.
Nomination Physiotherapy Prize.
Conflict of Interest No.

COCHRANE & EVIDENCE BASED MEDICINE SESSION

TO-035

TRAINING HEALTH PROFESSIONALS IN SMOKING CESSATION: A COCHRANE SYSTEMATIC REVIEW

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Aim To determine the efficacy of training health professionals in the delivery of smoking cessation interventions to patients, and additional effects of trial characteristics e.g., content, delivery method and intensity.
Methods The Cochrane Tobacco Addiction Group's register, electronic databases and bibliographies of studies were searched. Randomized controlled trials of at least 6 months duration, with an intervention of training healthcare professionals in smoking cessation were included.
Results Thirteen of 12 studies were meta-analysed. A statistically and clinically significant effect was produced in favour of the intervention for smoking point prevalence (odds ratio 1.40, 95% CI 1.09 to 1.80, $P = 0.008$). Healthcare professionals who received training were more likely to perform smoking cessation tasks than untrained controls, including: asking patients to set quit dates ($P < 0.0001$), making follow-up appointments ($P < 0.00001$), counselling of smokers ($P < 0.0001$) provision of self-help material ($P < 0.0001$) and prescription of quit dates ($P < 0.00001$). No evidence of an effect was observed for provision of nicotine gum/replacement therapy.
Conclusion Training health professionals to provide smoking cessation interventions had a measurable effect on smoking point prevalence and professional performance. New studies are needed to investigate multi-component interventions that incorporate newer pharmacotherapies or other smoking cessation aids alongside physician training, to determine if any additional benefit in long term abstinence can be obtained.
Support Nil.
Nomination Nil.
Conflict of Interest No.

TO-036

COMMUNITY INTERVENTIONS FOR THE PREVENTION OF SMOKING IN YOUNG PEOPLE: A COCHRANE SYSTEMATIC REVIEW

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Aim To determine the effectiveness of multi-component community-based interventions in influencing smoking behaviour, which includes preventing the uptake of smoking in young people.
Methods We conducted a search of the Cochrane Tobacco Addiction Group Specialised Register with additional searches of online clinical trial registries in August 2010. Inclusion criteria were randomized controlled and controlled clinical trials that had the primary aim of influencing the uptake of smoking in young people through multi-component community interventions, compared to no intervention or to single component or school-based programmes only.
Results Twenty-five studies met the inclusion criteria. One study reported a reduction in short-term (<12 months) smoking prevalence ($P < 0.001$), while nine studies detected significant long-term effects. Two studies reported significantly lower smoking rates in the control population while the remaining 13 studies showed no significant difference between groups. Common to the effective campaigns were incorporation of school-based intervention delivery, parental involvement, intervention duration > 12 months and theoretical model based on the 'social influences' or 'social learning theory'.
Conclusion There is some evidence that community-based interventions can be effective in preventing the update of smoking in young people. However, the studies that contributed to this evidence base have some methodological flaws. Rigorous trials that incorporate the latest social media and communication tools the youth uses, including Internet communication through FaceBook and telecommunication such as Twitter, are now required.
Support Nil.
Nomination Nil.
Conflict of Interest No.

TO-037

PERIPHERAL VENOUS AND ARTERIAL BLOOD GAS ANALYSIS IN ADULTS: ARE THEY COMPARABLE? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background Peripheral venous blood gas analysis is increasingly being used as a substitute for the standard method of arterial blood sampling to diagnose hypercapnia and acidosis prior to the initiation of treatment, however, their comparability is not clearly established.
Aim To determine if the pH, pCO2 and pO2 obtained from peripheral venous blood gas (pVBG) analysis are comparable to arterial blood gas analysis (ABG).
Methods A systematic review of relevant case-control or consecutive series that compared peripheral venous versus arterial blood gas estimations. Studies were reviewed for methodological quality and sources of heterogeneity using predefined criteria and the comparability of the pVBG to the ABG for pH, pCO2 and pO2 was assessed using the Bland-Altman method.
Results A total of 15 studies that included 1848 patients were identified as meeting the inclusion criteria. There was little difference between the pH obtained from the pVBG and the ABG, with the arterial pH typically 0.037 higher than the venous (SD = 0.018 with 95% CI 0.002–0.073). There was fair agreement between the pCO2, typically the arterial pCO2 would be 4.2 mm Hg less than the venous (SD = 3.4 mm Hg with 95% CI −10.8 mm Hg to +2.4 mm Hg). The pO2 demonstrated very poor agreement between venous and arterial derived samples (SD = 67.21 mm Hg and 95% CI from −71.98 to +191.5 mm Hg).
Conclusions The peripheral venous blood gas analysis appears useful for the diagnosis of acid-base abnormalities in adults but cannot replace arterial blood gas analysis for the diagnosis of ventilatory failure.
Conflict of Interest No.

TO-038

A COCHRANE SYSTEMATIC REVIEW – ANTICHOLINERGIC THERAPY FOR ACUTE ASTHMA IN CHILDREN

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Introduction Inhaled anticholinergics are a treatment option for severe asthma. By comparing the efficacy of anticholinergics as a single agent with other single agents and combined therapy, we aimed to establish the role of anticholinergics as monotherapy in the treatment of children aged > 2 years with acute asthma.
Methods A search was undertaken in accordance with Cochrane methodology, including the Cochrane Central Register of Controlled Trials (which includes the Cochrane Airways Group Specialised Trials Register) and clinical trial registers. Inclusion criteria were any randomized controlled trials (RCTs), where only inhaled anticholinergics were given compared with placebo or any other drug or drug combinations for children over the age of 2 years with acute asthma.
Results Three hundred forty-eight abstracts were reviewed but only six trials met the inclusion criteria. Meta-analysis from four trials on 171 children revealed that children who received anticholinergics alone were significantly more likely to have treatment failure compared to those who received β_2-agonists (OR 2.27; 95% CI 1.08 to 4.75). Also, data from four trials on 173 children showed treatment failure on anticholinergics alone was more likely than when anticholinergics were combined with β_2-agonists (OR 2.65; 95% CI 1.2 to 5.88).
Conclusions In children over the age of 2 years with acute asthma exacerbations, inhaled anticholinergics as single agent bronchodilators were less efficacious than β_2-agonists. Inhaled anticholinergics were also less efficacious than inhaled anticholinergics combined with β_2-agonists. Inhaled anticholinergic drugs are not appropriate for use as a single agent in children with acute asthma exacerbations.
Supported by Australian CAG scholarship for L Teoh, NHMRC for AB Chang.
Conflict of Interest No.

TO-039

OUTCOMES OF CONTACT INVESTIGATION FOR TUBERCULOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction Contacts of tuberculosis patients are at high-risk group for developing the disease. Investigation of contacts may enhance the early detection of tuberculosis and reduce transmission. Decisions about whether to commit resources to contact investigation should be informed by evidence of effectiveness. We aimed to quantify the yield of contact investigation in various settings.
Methods We performed a systematic review and meta-analysis of studies reporting the outcomes of tuberculosis contact investigation. We calculated the prevalence of latent tuberculosis infection and of tuberculosis as well as the annual incidence of disease during the 5 years after contacts were exposed to an index case using an exact binomial method. Subgroup analyses were also performed.
Results There were 212 studies that met the inclusion criteria and were published before 1 October 2011. Among the 109 studies conducted among contacts in low and middle-income settings, the weighted mean prevalence of previously undiagnosed tuberculosis was 3.1% (95% CI 2.3–4.2). Bacteriologically confirmed disease was present in 0.9% (95% CI 0.6–1.3). Latent tuberculosis infection was present in 45.9% (95% CI 41.3–50.6). The prevalence of TB among contacts of patients with multi-drug resistant and extensively drug resistant tuberculosis (X/MDR-TB) disease was 5.5% (95% CI 2.5–11.7). In 74 studies in high-income settings, the prevalence of TB was 1.0% (95% CI 0.7–1.4) among all contacts and 3.5% (95% CI 2.3–5.3) among household contacts. The prevalence of latent infection was 26.3% (95% CI 22.1–30.9) in high-income countries.
Conclusions While observational studies show that contacts have a higher risk of developing tuberculosis than the general population, further research is needed to establish the effect of contact investigations on the epidemiology of the disease.
Supported by National Health and Medical Research Council.
Conflict of Interest No.

TO-040

WATER-BASED EXERCISE TRAINING FOR COPD: A COCHRANE REVIEW

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Background Water-based exercise training in people with COPD may be an alternative to land-based exercise training especially for people who have physical co-morbidities that may limit weight-bearing exercise. This Cochrane review sought to determine whether water-based exercise training is safe and effective in COPD.
Methods The Cochrane Airways Group specialized register was searched using an exhaustive list of terms to identify randomized or quasi-randomized controlled trials of water-based exercise training of at least 4 weeks duration compared to no exercise training or any other form of active exercise training. Bibliographies of all potentially relevant retrieved studies were searched for further trials. The primary outcome measures were exercise capacity and quality of life.
Results Five studies involving 218 subjects met inclusion criteria, three of which were published as abstracts. Meta-analysis was limited by significant risks of bias in the majority of studies, heterogeneity in outcome measures and lack of reporting of primary outcome measure data. There was minimal evidence of any adverse events occurring during water-based exercise training.
Conclusion Water-based exercise training appears to be safe for people with COPD. However, this review was unable to support or refute the effectiveness of water-based exercise training for improving exercise capacity or quality of life in people with COPD. Future high-quality randomized controlled trials are required.
Supported by Australian Cochrane Airways Group Network Scholarship.
Conflict of Interest The authors conducted one of the studies included in this review.
Nomination Physiotherapy Prize.

INTERVENTIONAL PULMONOLOGY & BRONCHOLOGY SIG: ORAL SESSION

TO-041

AUSTRALASIAN BRONCHOSCOPIC TRAINING AND MAINTENANCE OF COMPETENCY ARE INCONSISTENT WITH GUIDELINE RECOMMENDATIONS

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Introduction The Australasian practise and training of bronchoscopy is not standardized and has not previously been reported. We examined adherence to previously published Australian guidelines for flexible bronchoscopy.
Methods All adult physician and trainee members of the Thoracic Society of Australia New Zealand (TSANZ) were e-mailed a web link to an online survey. Survey responses were benchmarked against TSANZ guidelines.
Results The response rate was 42% (217 out of a total of 517 specialists and trainees). Response rate amongs trainees was higher at s78% (46 of 59). Forty-nine percent respondents performed *less* than the guideline-recommended ideal 50 procedures per year. Sixty percent of trainees are unlikely to achieve the guideline-recommended 200 supervized bronchoscopies.
Conclusions Significant gaps between bronchoscopy guidelines and practice of bronchoscopy in Australasia exist. Trainees may not be completing sufficient procedure volumes to *achieve* competency and a majority of consultant bronchoscopists may not be *maintaining* proficiency. We suggest that the TSANZ position paper should be reviewed and updated. Alternatives to the current volume-based approach to achieving and maintaining of competence should be considered.
Reference
1 Wood-Baker R, Burdon J. McGregor A *et al.* Fibre-optic bronchoscopy in adults: a position paper of The Thoracic Society of Australia and New Zealand Internal Medicine Journal 2001; 31: 479–87.
Conflict of Interest None to declare.

TO-042

TRANSBRONCHIAL LYMPH NODE ASPIRATION TRAINING AND MAINTENANCE OF COMPETENCY ARE INCONSISTENT WITH GUIDELINE RECOMMENDANTIONS

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Introduction The Australasian practice and training of conventional transbronchial needle aspiration (TBNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is not standardized and has not previously been reported. We examined adherence to previously published international guidelines.
Methods All adult physician and trainee members of the Thoracic Society of Australia New Zealand (TSANZ) were e-mailed a web link to an online survey. Survey responses were benchmarked against relevant international guidelines[1,2].
Results The response rate was 42% (217 out of a total of 517 specialists and trainees). Response rate among trainees was higher at 78% (46 of 59). Less than 20% of trainees receive adequate training in transbronchial lymph node aspiration. The majority of consultant physicians performing such techniques are not performing sufficient numbers to maintain competency as per guideline recommendations.
Conclusion Significant gaps exist between TBNA guidelines and the practice of TBNA in Australasia. Trainees may not be completing sufficient procedure volumes to *achieve* competency and a majority of consultant bronchoscopists may not be *maintaining* proficiency. We suggest that the TSANZ position paper should be reviewed and updated. Alternatives to the current volume-based approach to achieving and maintaining of competence should be considered.
References
1 Bolliger CT, Mathur PN Becker S *et al.* ERS/ATS statement on interventional pulmonology Eur Respir J 2002; 19: 356–33.
2 Ernst A, Gerard A, Silvestri GA, Johnstone D. Interventional Pulmonary Procedures: Guidelines from the American College of Chest Physicians Chest 2003; 123:1693–1717.
Conflict of Interest None to declare.

TO-043

OBJECTIVE SKILL ASSESSMENT USING LOW AND HIGH FIDELITY SIMULATORS AFTER HANDS ON BRONCHOSCOPY TRAINING

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Aim To test the feasibility of incorporating objective testing of bronchoscopy skills following hands on training courses.
Methods Two courses were run a 4-day Advanced EBUS skills course and a 1-day introductory training course for first year trainees starting bronchoscopy training. Simulated training was with video bronchoscopes and dedicated EBUS TBNA and guide sheath (Koken) models, Accutouch high fidelity EBUS TBNA simulator, Dexter and Bronchoboy training models. Post course testing used the following 100 point objective testing instruments[1]: Bronchus STAT (for basic bronchoscopy), EBUS STAT (for EBUS TBNA), and a modified Bronchus STAT for EBUS Guide sheath testing. Timed scope navigation test was done on a Dexter.
Results There were 23 attendees for the EBUS course and five for the introductory course. All skills were testable on the models, in particular the endobronchial biopsy, brush and TBNA skills were possible on the Accutouch. Approximate hands-on testing times for the STAT tests were 20 min. Dexter testing took 3–8 min. Mean results for EBUS STAT and Guide sheath STAT were 83.4(SD7.8) and 81.3(6.8). For Bronchus STAT mean results were 89.2(1.1). All of these results were in the high Intermediate range, with results > 90 indicating Advanced skill. Dexter testing of a navigation route was 2.8 (1.5) min in the advanced group and 3.4(1.0) in the introductory group, P = NS. Independent course rating by attendees for the EBUS group on a 7-point likert scale was 6.6 (0.6), and all introductory attendees rated the course 5/5.
Conclusions Objective testing after training courses was easily achieved. All course attendees rated well compared to published scales. Good dexterity scores were achieved by the novice group. Such testing was well accepted by attendees and may have overall increased course satisfaction.
1. Colt HG Surg Endosc 2011; 25: 207–16.
Supported by Olympus Australia.
Nomination Nil.
Conflict of Interest Nil.

TO-044

SOUTH AUSTRALIAN PLEURAL PROCEDURES SURVEY

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Introduction When do trainees gain experience in pleural procedures? Who teaches the trainees? How many procedures should be performed to be deemed competent?
Methods An online questionnaire was sent to all advanced trainees in respiratory medicine in South Australia in 2010.
Results Eight out of nine (89%) of trainees responded; two (22%) were Australian graduates, six (78%) from overseas. Overseas graduates had performed a mean 38.4 pleural taps, 31.6 seldinger and 8.4 large bore chest drains prior to entering Australia. Australian trainees had performed a mean 12.2 pleural taps and one chest drain before advanced training. Advanced trainees had performed a mean 29.71 pleural taps, 19.51 seldinger and 8.16 large bore chest drains, and 3.3 closed pleural biopsies. 60.8% of these procedures were taught by a more senior registrar, 18.1 % by a consultant physician, 7.25% by a peer doctor, 4.6% in a skills lab, 2.78% by an ED physician and 6.55% self taught. All trainees self rated as competent to perform all pleural procedures unsupervised, except closed pleural biopsy. Trainees thought performing 26.6 pleural taps, 31.88 seldinger drains, 15.88 large drains and 9.38 closed pleural biopsies would demonstrate procedural competency.
Discussion SA overseas trainees have significant procedural experience prior to Australian training. Local graduates have minimal procedural experience prior to advanced training. The respiratory STC recommends 20 chest drains and 20 closed pleural biopsies during advanced training. SA trainees had performed adequate numbers of chest drains and too few closed pleural biopsies by these standards.
Conclusion Overseas graduates are experienced in pleural procedures before advanced training, Australian graduates gain experience during advanced training. SA trainees have good pleural procedural experience, and their opinions should be used to inform STC recommendations
Conflict of Interest The author is an advanced trainee from South Australia.

TO-045

AN AUDIT OF WARD-BASED CHEST-TUBE INSERTION AT A TERTIARY TEACHING HOSPITAL

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Aim To review the adherence of ward-based chest tube insertion at the Royal Melbourne Hospital (RMH) to consensus guidelines.
Method Patients who underwent chest tube placement between 1/9/2010 –28/2/2011 were identified by a key word search of the radiology database at RMH. Patients who underwent tube insertion in Emergency, Intensive Care, Theatre and Radiology were excluded. A retrospective chart review was performed to identify indications, method of insertion, tube bore, experience of the operator, utilization of ultrasound guidance, complications and pathology investigations requested. Practice and outcomes were benchmarked against the British Thoracic Society consensus guidelines published in 2010 prior to the audit period.
Results Twenty-nine cases were identified. Of these, 25 had histories available. From the histories examined, chest tubes where generally inserted where indicated. Only 44% had written consent, 56% had adequate documentation, 64% were inserted in-hours, 35% used a small-bore tube, 52% had appropriate investigation of pleural fluid as recommended by the guidelines and 44% used ultrasound guidance. The complication rate was about 10%.
Conclusion Chest-tube insertion at RMH was poorly adherent to consensus guidelines. Key concerns focused on lack of consent, documentation, standardization and inadequate use of ultrasound. Consequently, a two-stage quality improvement project was implemented and practice will be subject to re-audit.
Conflict of Interest No.

TO-046

THORACIC ULTRASOUND IN ACUTE RESPIRATORY PATIENTS: THE '*C3PO'* PROTOCOL

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Introduction Chest ultrasound has excellent test characteristics for diagnosing alveolar and interstitial lung syndromes as well as pleural disease. We examined the utility of lung ultrasound when integrated into the routine care of patients admitted to a respiratory high dependency unit.
Methods Patients admitted in-hours to the respiratory HDU of our university teaching hospital underwent bedside thoracic ultrasound by one of five clinicians within 24 h of admission. A standardized protocol was applied with the acronym '**C3PO**', documenting the presence of '**C**omets', **C**onsolidation, **C**VP elevation, **P**leural effusion or '**O**' (zero findings suggestive of pulmonary embolus or pure ventilatory failure). This was compared with the clinical assessment and available radiology. Clinicians were asked if the ultrasound results influenced their confidence of the primary diagnosis or changed subsequent management.
Results Fifty patients were assessed over 6 months. Ultrasound assessment took an average of 18 min. The clinical diagnoses included: chronic obstructive pulmonary disease (COPD), right heart failure, left heart failure, bi-ventricular failure, interstitial lung disease, pleural effusion and pneumonia. Chest ultrasound increased diagnostic confidence in 44%. New or additional diagnoses were made in 28%. Ultrasound changed clinical management in 30%.
Conclusions When incorporated into the routine assessment of patients admitted to respiratory high dependency, structured chest ultrasound is both feasible and clinically useful.
Conflict of Interest MH convenes a Chest Ultrasound Course which receives sponsorship from Sonosite, Astra Zeneca and Cook Medical.

COPD SIG AND RESPIRATORY INFECTIOUS DISEASES SIG: COMBINED ORAL SESSION

TO-047

INCREASED REACTIVE OXYGEN SPECIES IN MACROPHAGES INFECTED WITH RHINOVIRUS AND NON-TYPEABLE *H. INFLUENZAE*

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Introduction Exacerbations of chronic obstructive pulmonary disease are most commonly caused by infection either bacterial or viral. Frequently patients have combined bacterial and viral infections and the most common combination is with rhinovirus (RV) and nontypeable *Haemophilus influenzae* (NTHi). This combination of RV/NTHi is associated with more inflammation and more severe exacerbations. Reactive oxygen species (ROS) have been recognized to have a key role in the pathogenesis of COPD. Our aim in this study was to assess the effect of NTHi and combined RV/NTHi infection on macrophage ROS production in COPD.
Methods Macrophages were obtained from the bronchoalveolar lavage from human subjects. Macrophages were cultured and infected with: (i) NTHi; or (ii) a combination of RV/NTHi; or (iii), uninfected as control cells. The measurement of ROS was performed using flow cytometry to assess the cleavage of the fluorescent dye dihydrorhodamine.
Results Eleven subjects have been assessed so far. Results are expressed as the intensity in measured fluorescence. There was a progressive increase in macrophage ROS production from (i) control (median value of 233); (ii), NTHi (median value of 350) to the (iii) combined RV/NTHi infection (median value of 596). The median value of the RV/NTHi was significantly higher than control ($P = 0.05$).
Conclusions Preliminary results have demonstrated that combined rhinovirus/nontypeable *Haemophilus influenzae* infection produces a significant upregulation in reactive oxygen species production by macrophages. This may be an important mechanism in exacerbations of COPD.
Conflict of Interest No.

TO-048

A RETROSPECTIVE MICROBIOLOGICAL AUDIT OF COPD INPATIENTS AT A REGIONAL UNIVERSITY TEACHING HOSPITAL

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Aim To delineate the sputum bacteriology found in inpatients with an infective exacerbation of COPD (IECOPD) at a regional university teaching hospital and to suggest empiric antibiotic therapy.
Method A retrospective audit was undertaken over 14 months of all admissions under the Respiratory unit at Royal Hobart Hospital with an acute exacerbation of COPD (AECOPD). We reviewed spirometry, age, sputum results, antibiotic choice and inpatient mortality. The hospital wide sensitivities of H.*influenzae* and M.*catarrhalis* were also assessed.
Results Tow hundred two AECOPD inpatients were included with 66.8% classed as an IECOPD. The mean age was 69 years, mean predicted FEV1 39.7% and inpatient mortality 5.4%. A potentially pathogenic microorganism (PPM) was isolated in 67.9% of valid samples from patients with an IECOPD. The most common microbes isolated were: H.*influenzae* (40.4%), P.*aeruginosa* (21.1%), M.*catarrhalis* (10.5%), E.*coli* (7%), S.*maltophilia* (5.3%), S.*pneumoniae* (5.3%), less common were S.*aureus*, Citrobacter, and Achromobacter (10.5%). H.*influenzae* amoxycillin resistance was 30.4% which was the similar to the hospital-wide prevalence of 22.2% ($P = 0.38$). Sixty-eight percent of all PPM's isolated in IECOPD were resistant to amoxycillin, compared to 36% resistance with amoxy-clavulanic acid. Doxycycline could potentially be an appropriate empiric choice, but PPM sensitivity was not routinely preformed. We were unable to assess correlation between antibiotic choice and outcomes.
Conclusion H.*influenzae* was the most common organism followed by P.*auerginosa* and M.*catarrhalis*. With an amoxycillin resistance rate above 25% among H.*influenzae* and an overall PPM resistance rate of 67.7%, we concluded that amoxycillin should not be used empirically in our IECOPD cohort.
Conflict of Interest No.

TO-049

PATTERNS (2007–2009) OF RESPIRATORY VIRUSES ISOLATED FROM ACUTE EXACERBATIONS OF AIRWAYS DISEASE

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Respiratory virus infections are important triggers of acute asthma and COPD. If antiviral strategies are to be considered to reduce the frequency or severity of acute airways disease then it is important to know the patterns of virus infection over time.
Aim To characterize the viruses associated with acute exacerbations of asthma and COPD. With a further aim to sequence and identify the rhinovirus species present.
Methods From March 2007 to September 2009 (2.5 years) we recruited adult subjects admitted to hospital with acute exacerbations of asthma or COPD. Spontaneous sputum and/or throat/nasal swabs were collected from 200 subjects. Samples were assayed by real-time PCR for six respiratory viruses; rhinovirus (RV), respiratory syncytial virus types A and B (RSV), non-SARS coronavirus (CoV), enterovirus (EV), human metapneumovirus (hMPV) and influenza virus types A and B (Flu). RV positive samples were then sequenced.
Results Viruses were detected in 88 subjects (37%). Of these virus positive samples 35 (40%) were RV, 18 (20%) RSV, 12 (14%) CoV, 9 (10%) EV, 8 (9%) hMPV and 6 (7%) Flu. The lowest virus detection occurred in summer. Peak RV detection occurred in autumn, but was evident in all seasons. Of the 33 RV-positive samples sequenced, 22 (67%) belong to RV species A (HRV A), 5 (15%) RV species B (HRV B) and 6 (18%) to the newly identified RV species C (HRV C).
Conclusion HRV A is the most prevalent virus associated with acute asthma and COPD and is evident all year round. Autumn and winter are peak times for virus induced exacerbation, with winter having the most diverse. RSV and flu are present in winter and early spring.
Supported by NHMRC Australia, Biota Australia.
Nomination Respiratory Infectious Diseases.
Conflict of Interest None.

ANN WOOLCOCK YOUNG INVESTIGATOR AWARD SESSION

TO-050

EPITHELIAL DERIVED LIPIDS RESULT IN RHINOVIRUS INDUCED B_2 ADRENOCEPTOR DESENSITIZATION

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Rationale Rhinovirus (RV)-infected epithelial cells produce unidentified mediators which cause β_2 adrenoceptor desensitization on airway smooth muscle cells (ASM), which may explain why β_2 agonists have reduced efficacy during exacerbations. Our study investigated which mediator from RV infected epithelial cells was responsible for the desensitization of the β_2 adrenoceptor on ASM.
Methods Conditioned medium was generated from epithelial cells infected with RV-16 for 24 h and used to treat ASM. After 72 h cyclic AMP (cAMP) levels were measured using a functional assay kit. Conditioned medium was prepared prior to treatment: (i) To remove proteins, conditioned medium was incubated with trypsin for 24 h and stopped with bovine serine albumin; (ii) To inhibit prostaglandin production, conditioned medium was generated in the presence of indomethacin (10^{-6}M); (iii) To determine the size fraction of the active factor/s, conditioned medium was centrifuged through molecular weight cut off filters: 100kDa, 50kDa, 30kDa, 10kDa and then 3kDa.
Results RV-16 produced conditioned medium which caused ASM β_2 adrenoceptor desensitization ($n = 8$, $P < 0.05$). Protein digested conditioned medium still caused β_2 adrenoceptor desensitization ($n = 6$, $P < 0.05$). Fractionation of the conditioned medium revealed that the responsible mediator was smaller than 3kDa ($n = 6$). RV conditioned medium produced in the presence of indomethacin did not cause β_2 adrenoceptor desensitization in ASM ($n = 6$).
Conclusion Our results indicate that RV-infected epithelial cells produce prostaglandins which either alone or in combination can induce desensitization of the β_2 adrenoceptor in ASM. These RV induced lipids may explain why virally induced exacerbations are more difficult to treat with β_2 agonists.
Supported by NHMRC.
Nomination Ann Woolcock Young Investigator Award.
Conflict of Interest No.

TO-051

DEFICIENT ANTIVIRAL RESPONSES TO INFLUENZA IN PRIMARY BRONCHIAL EPITHELIAL CELLS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim People with chronic obstructive pulmonary disease (COPD) are more susceptible to influenza infection leading to acute exacerbations with excess mortality. The mechanisms underlying this observation in COPD however are unknown. Our aim was to assess the antiviral responses in primary bronchial epithelial cells (pBECs) from COPD and healthy control subjects to influenza infection.
Methods Primary BECs from healthy non-smoking volunteers and subjects with COPD were infected with human influenza A/H3N2, A/H1N1, and a low pathogenic avian influenza A/H11N9 at MOI of 5. Influenza haemagglutinin (HA), RIG-I, interferon (IFN)-β, and IFN-λ1 protein was measured by western blotting. Viral replication was measured by plaque assay.
Results Influenza viruses replicated more efficiently in COPD pBECs. The viruses entered COPD pBECs more efficiently than healthy control cells, and this was dependent on PI3 kinase, which showed increased expression in COPD. COPD pBECs also showed impaired IFN responses to infection. RIG-I, the primary viral RNA sensor and initiator of IFN responses, was minimally expressed in COPD cells, and this correlated with reduced IFN-β and IFN-λ1 release compared to healthy control cells.
Conclusion COPD pBECs have increased susceptibility to influenza viral entry, and have inherent deficiencies in innate antiviral responses, which in combination lead to more severe infection.
Supported by National Health and Medical Research Council.
Nomination Ann Woolcock Young Investigator Award.
Conflict of Interest None.

TO-052

ARSENIC EXPOSURE VIA DRINKING WATER ADVERSLY AFFECTS LUNG HEALTH

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Introduction The contamination of drinking water with arsenic is a global health problem. Early life exposure to arsenic increases the risk of lower respiratory tract infections during infancy and increases the risk of mortality from bronchiectasis in adulthood. We aimed to characterize the effect of arsenic exposure via drinking water on lung development and responses to early life viral infection.
Methods C57BL/6 mice were exposed to 100 μg/L arsenic in prenatal and postnatal life with or without influenza infection. Somatic growth, lung structure, lung function and airway hyperresponsiveness were measured using stereology, plethysmography and the forced oscillation technique. Differential gene expression was determined by microarray and confirmed with qRT-PCR.
Results Mice exposed to arsenic in early life were smaller, had smaller lungs and impaired lung function. Early life exposure to arsenic altered the expression of genes that function in innate immunity (Lplunc1, Reg3γ), lung morphogenesis (Sox2) and airway mucous regulation (mClca3, Muc5b). Upregulation of mClca3 corresponded to mucous cell metaplasia. Adult mice that were exposed to arsenic early in life had increased airway smooth muscle and airways that were hyperresponsive to methacholine, while mice exposed to arsenic for the same period of time in adulthood were not affected. Arsenic exposure increased the acute inflammatory response to early life influenza infection and had additive effects on long term lung function impairment and airway hyperresponsiveness.
Conclusions Arsenic is a potent developmental toxicant that adversely affects the lung by altering lung structure, mucous expression, innate immunity, responses to bronchoconstricting agents and exacerbating respiratory viral infection.
Support NHMRC #634420.
Nomination Ann Woolcock Young Investigator Award.
Conflict of Interest No.

TO-053

CHEST CT DIRECTLY REFLECTS PROGRESSIVE LUNG DISEASE IN INFANTS AND YOUNG CHILDREN WITH CYSTIC FIBROSIS

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Background The lack of suitable clinical endpoints has been an obstacle to clinical trials in infants with cystic fibrosis (CF). Chest CT has been proposed as an endpoint in this population. This study aimed to examine interval changes in CT-detected structural disease in infants and young children with CF and determine factors associated with development, persistence and progression of disease.
Methods Four hundred forty-four annual assessments from 143 children with CF age ≤6 years were analysed as 301 scan pairs 1 year apart. Limited slice volume controlled inspiratory and expiratory chest CT was performed under general anaesthesia, followed by bronchoalveolar lavage (BAL) to assess infection and inflammation. A simplified CF-CT score assessed presence and extent of bronchiectasis and air trapping. Age-adjusted logistic and linear regression models determined associations between risk factors and development, persistence and progression of structural changes, with generalized estimating equations to account for multiple measures.
Results Rates of development, persistent and progressive bronchiectasis were 53%, 74% and 63%, and for air trapping 54%, 81%, 46%. Associations were seen between interval changes and acquisition of pulmonary infection and worsening neutrophilic inflammation, with progression associated with CFTR genotype.
Discussion CT reflects persistent structural changes, and detects disease progression, with longitudinal changes associated with factors of known patho-biological importance. This indicates that chest CT directly reflects progressive lung disease and is a suitable endpoint for patient management and clinical trials.
Supported by CFFT, NHMRC, UWA, ACFRT, CFWA.
Conflict of Interest No.
Nomination Ann Woolcock Young Investigator Award.

TO-054

FLUTICASONE PROPIONATE ATTENUATES EPITHELIAL MESENCHYMAL TRANSITION (EMT) IN COPD

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Introduction We have previously published[1] that the airway reticular basement membrane (Rbm) in smokers and especially COPD is highly fragmented with 'clefts' containing cells staining for the proteolytic enzyme matrix-metalloproteinase-9 (MMP-9) and fibroblast protein, S100A4. These cells are also present in the basal epithelium (BE). Such changes are 'classic' phenotypic markers of EMT. Our knowledge about the effects of inhaled corticosteroids (ICS) on such airway remodelling changes in the large airways in this disease is very limited. We have now assessed the effects of ICS on remodelling in bronchial biopsies (BB) from COPD patients in a randomized controlled study.
Methods Double-blind, randomized, placebo-controlled study assessing the effects of inhaled fluticasone propionate (FP) on EMT in 34 COPD patients. BB were stained for the markers of EMT, S100A4 and MMP-9 and the marker of epithelial activation, epidermal growth factor receptor (EGFR). Computer-assisted image analysis was used to quantify the structural changes in the Rbm and expression of markers. The slides were counted by an observer blinded to subject and phenotype. We used non-parametric statistics.
Results Rbm 'fragmentation' markedly improved with ICS, with a significant change compared to placebo ($P < 0.03$). There were also significant reductions in S100A4 ($P < 0.004$), MMP-9 ($P < 0.02$) and EGFR ($P < 0.03$) staining in both basal epithelial cells and in the 'clefts' comparing ICS with placebo.
Conclusions This is the first study reporting an anti-EMT effect of FP in COPD airways.
Reference
1. Sohal SS *et al*. Respirology 2010; (15): 930–38.
Supported by NHMRC project grant 490023.
Nomination Ann Woolcock Young Investigator Award.
Conflict of Interest No.

TO-055

HETEROGENEOUS PERIPHERAL AIRWAY NARROWING MEASURED BY THE FORCED OSCILLATION TECHNIQUE PREDICTS POOR ASTHMA CONTROL

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Introduction Respiratory system reactance (Xrs) as measured by the forced oscillation technique is sensitive to heterogeneous peripheral airway narrowing, which is a key characteristic of pulmonary dysfunction in asthma. In the current study, we test the hypotheses that heterogeneous narrowing measured by Xrs is a key contributor to asthma symptoms and sensitively identifies 'not well-controlled' asthma.
Aim To investigate the relationship between Xrs and asthma control.
Methods In 22 subjects with asthma, Xrs and FEV_1 were obtained after bronchodilator administration. Xrs was measured between TLC and RV; to quantify the degree of heterogeneous narrowing that persists above closing volume, Xrs was taken immediately above this critical volume (Xrs_{crit}) prior to the precipitous decline in Xrs with airway closure. Asthma control was assessed via the Asthma Control Questionnaire score excluding the FEV_1 parameter (ACQ6). Not well-controlled asthma was defined as ACQ6 > 1.0.
Results ACQ6 was strongly associated with Xrs_{crit} ($R^2 = 0.43$, $P < 0.001$), but not with FEV_1 ($R^2 = 0.14$, $P = 0.1$). Receiver operator characteristic analysis demonstrated that Xrs_{crit} was an excellent predictor of not well-controlled asthma (area under curve = 0.94, $P < 0.001$); a threshold of $Xrs_{crit} = -1.2$ accurately predicted asthma control status in 19/22 subjects.
Conclusion Heterogeneous airway narrowing measured via Xrs is an important contributor to the perception of asthma symptoms and control. Further, the assessment of heterogeneous airway narrowing using Xrs may provide a powerful new tool to identify not well-controlled asthma.
Supported by NHMRC, CRCAA.
Nomination Ann Woolcock Young Investigator Award.
Conflict of Interest No.

ASTHMA & ALLERGY SIG: ORAL SESSION 2

TO-056

RESISTIN-LIKE MOLECULE BETA IN BRONCHIAL EPITHELIUM INCREASES WITH ASTHMA SEVERITY AND AIRWAY CHALLENGES

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Resistin like molecule beta (RELM-β) is a member of the adipokine protein family and is known to be a necessary and sufficient stimulus for airway remodelling in animal models of asthma, but its role in human disease has not been fully investigated.
Aims We examined the hypothesis that RELM-β expression would be increased with increasing asthma severity and further increase following acute bronchoconstrictor challenges.
Methods Bronchial biopsies from healthy subjects ($n = 13$) and patients with mild ($n = 36$) and severe asthma ($n = 22$) were immunostained for RELM-β, as were airway biopsies obtained in mild asthmatics before and 4 days after repeated inhalation challenges with either allergen, methacholine or methacholine preceded by salbutamol as a control ($n = 12$ each group). Bronchial brushings were also evaluated for RELM-β mRNA.
Results RELM-β immunoreactivity, which co-localized to airway epithelial cells, increased with disease severity; healthy volunteers, median epithelial percentage area 1.89%, mild asthma 3.49% and severe asthma 5.89% ($P < 0.001$ between groups). RELM-β immunoreactivity significantly and inversely correlated in asthma with percentage predicted FEV1 ($P < 0.002$). Acute changes in immunoexpression were evident after repeated inhalation challenge with allergen (median 2.15% to 4.35 % ($P = 0.01$)) and methacholine (4.21% to 6.16% ($P = 0.01$)) but did not change in the salbutamol/methacholine challenge group. Epithelial RELM-β gene expression, although present, was not altered in asthma.
Conclusions These findings suggest that RELM-β may play an important role not only in animal models of airway remodelling, but also in human airway pathology.
Supported by Medical Research Council (UK).
Conflict of Interest No.

TO-057

BRONCHIAL SEGMENTS FROM ASTHMATIC SUBJECTS ARE HYPERRESPONSIVE BUT RETAIN A NORMAL BRONCHODILATORY RESPONSE TO DEEP INSPIRATION

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Background In asthma a reduced bronchodilatory response to deep inspiration (DI) may be associated with airway hyperresponsiveness (AHR).
Aim To determine if a reduced bronchodilatory response to DI and AHR arise from a specific abnormality of the airway wall.
Methods Bronchial segments were obtained from subjects undergoing lung resection and who had doctor-diagnosed asthma (n = 4) or no history of asthma (n = 7). Airway narrowing (% lumen volume) to cumulative acetylcholine and bronchodilation to DI (% reversal in narrowing) were measured in a servo-controlled syringe pump and organ bath system.
Results Maximal airway narrowing was increased ($P = 0.022$) in the asthmatic (49.6 ± 5.6%) compared with the non-asthmatic group (30.1 ± 4.3%). There was no difference in airway sensitivity. When compared at the same acetylcholine dose there was a strong trend for reduced bronchodilation to DI in the asthmatic group (NS, $P = 0.051$) which was attributed to increased bronchoconstriction prior to DI. At comparable levels of airway narrowing, there was no difference in the bronchodilatory response to DI between groups.
Conclusions Bronchi from asthmatic subjects are hyperresponsive but retain a normal bronchodilatory response to DI at comparable levels of narrowing. We suggest that abnormal bronchodilation to DI in asthma is unrelated to AHR.
Supported by NHMRC (513921 & 513842).
Conflict of Interest No.

TO-058

ASTHMA AND WHEEZE ARE ASSOCIATED WITH REDUCED VITAMIN D LEVELS IN A POPULATION COHORT

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Background Although some evidence suggests a relationship between reduced levels of 25-hydroxyvitamin D (VitD) and respiratory infections, asthma, allergic diseases and impaired lung function, only two studies have been reported from large adult population samples and findings were not consistent. The aim of this study was to determine the relationship between vitamin D levels and respiratory disorders including asthma, wheeze and atopy in participants at stage 3 of the North West Adelaide Health Study (NWAHS), a representative population sample.
Methods Clinic assessment ($n = 2487$) included spirometry, measurement of height, weight, skin prick testing and questionnaires assessed doctor diagnosed asthma, respiratory symptoms in the past 3 months (Chronic Lung Disease Index), smoking and sociodemographics. Asthma was identified by self-report or bronchodilator reversibility of 12% and 200ml. Respiratory outcomes were assessed in relation to quintiles of Vit D (< 47, 47–59, 60–71, 72–87, ≥88 nmol/L).
Results The prevalence of asthma and wheeze was 18.1% ($n = 447$) and 30.3% ($n = 727$). Compared to the highest quintile of Vit D, there was an increased prevalence of asthma (19.7% vs 13.6%, OR, 95% CI:1.6, 1.1–2.3), wheeze (36.8% vs 28.0%, OR:1.4, 1.1–1.9) and moderate–severe symptoms (11.0% vs 4.6%, OR: 3.0, 1.7–5.4) in the lowest Vit D quintile and atopy prevalence decreased (60.5% vs 70.0%, OR: 0.6, 0.5–0.8) These persisted in multivariable analyses adjusted for age, sex, smoking, body mass index, household income. The relationship between Vit D and wheeze was modified by smoking status, but otherwise associations of Vit D, asthma and wheeze were not modified by atopy, age or smoking.
Conclusion Vit D supplementation trials have been suggested to improve respiratory health, however longitudinal studies are required to further investigate these relationships.
Support Adelaide University, SA Department of Health.
Conflict of Interest No.

TO-059

VITAMIN D DEFICIENCY CAUSES DEFICITS IN LUNG FUNCTION BUT DOES NOT ALTER AIRWAY SMOOTH MUSCLE MASS

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Introduction Studies in children with asthma have revealed that reduced levels of vitamin D are associated with reduced lung function, airway remodelling and poor asthma control. The aim of this study was to determine if Vitamin D deficiency alters lung function resulting in airway hyperresponsiveness (AHR) and/or causes alterations in ASM mass.
Methods A physiologically relevant mouse model of Vitamin D deficiency was developed by raising BALB/c mice on Vitamin D-deficient or -replete diet. Studies were carried out on offspring from deficient and replete mice of both sexes at 8 weeks of age. Lung function and thoracic gas volume (TGV) were measured by the forced oscillation technique (FOT) and plethysmography, respectively. AHR was assessed by measuring lung function responses to increasing doses of inhaled methacholine. Formalin-fixed lungs embedded in paraffin were cut into 5 μm thick sections. Sections were stained with Masson's Trichrome for ASM measurement.
Results Vitamin D-deficient females had a smaller TGV compared to replete controls ($P < 0.05$). At 20 cm H_2O transrespiratory pressure, Vitamin D-deficient mice had a smaller lung volume compared to controls (females, $P = 0.024$; males, $P = 0.028$). There were no significant differences in airway resistance, however tissue damping was higher for vitamin D-deficient mice (females, $P = 0.03$; males, $P = 0.006$). The dose of methacholine required to cause a doubling in airway resistance was lower in female Vitamin D-deficient mice. ASM mass was not significantly altered.
Conclusions Vitamin D deficiency can lead to alterations in lung function and an increased sensitivity to bronchoconstricting agents but does not alter ASM mass.
Conflict of Interest No.

TO-060

ASTHMA IS ASSOCIATED WITH MULTIPLE DEFICIENCIES IN ANTI-VIRAL TYPE I INTERFERON SIGNALLING PATHWAYS

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Rationale Rhinovirus (RV) infections are a major cause of asthma exacerbations. Circulating immune cells from asthmatics have a decreased capacity to produce anti-viral interferons (IFNs) such as IFNα and IFNβ, though a detailed analysis of the molecular events responsible has not been undertaken.
Aims To compare the molecular pathways controlling IFNα/β synthesis in asthmatic and healthy subjects.
Methods Blood mononuclear cells were isolated from 18 healthy donors and 18 asthmatics of moderate disease severity, and cultured with RV for 24 h. Components of the Toll-like receptor (TLR), IFN regulatory and NFκβ pathways were compared at the mRNA and protein level.
Results Compared to RV-stimulated cells from healthy donors, cells from asthmatics exhibited significantly lower expression of IFNβ ($P < 0.0001$), interferon regulatory factors IRF1 ($P < 0.001$) and IRF7 ($P = 0.03$), the interferon stimulated genes MxA and OAS (both $P < 0.01$), and reduced secretion of IFNα protein ($P = 0.005$). Induction of IKKα, p65, p52 and p50 and Toll-like receptor 7 (TLR7) was also reduced in asthma, whereas TLR8 and IRF5 expression were similar in both groups, and RelB and cRel were not induced by RV. These observations could not be attributed to alterations in the numbers of dendritic cell subsets or their baseline expression of TLR7.
Conclusions Multiple deficiencies in innate interferon signalling pathways were identified in asthma. Aberrant function of TLR7 and/or IFN regulatory proteins is likely to be fundamental to the abnormal anti-viral immunity observed in asthma.
Supported by: NHMRC, Asthma Foundation of Queensland.
Nomination None.
Conflict of Interest None.

TO-061

EFFICACY OF ANTIBIOTIC-BASED THERAPEUTIC STRATEGIES FOR THE TREATMENT OF INFECTION-INDUCED, STEROID-RESISTANT ALLERGIC AIRWAYS DISEASE

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Background Steroid-resistant asthma is an important clinical problem and effective therapies are urgently required. Macrolides have benefit in the treatment of steroid-resistant forms of asthma, however, whether the effects of treatment are due to anti-inflammatory or antibiotic properties of this class of drugs remains unknown.
Aim To determine and compare the efficacy of macrolide versus β-lactam therapy in treating experimental infection-induced, steroid-resistant allergic airways disease (AAD) in order to delineate the anti-inflammatory versus antibiotic effects of macrolides.
Methods Using mouse models of *Chlamydia* lung infection and ovalbumin-induced AAD we have shown that infection induces airways hyperresponsiveness (AHR) and inflammation in AAD that is resistant to steroid treatment. In the current study the effectiveness of clarithromycin versus amoxicillin for treating *Chlamydia*-induced, steroid-resistant AAD was assessed.
Results Clarithromycin treatment suppressed both AHR and airways inflammation in *Chlamydia*-induced, steroid-resistant AAD. Significantly, treatment also suppressed AHR and inflammation in uninfected, allergic groups, thus demonstrating a strong anti-inflammatory effect. By contrast amoxicillin treatment had no effect on AHR or inflammation in either infected or uninfected groups with AAD but did restore steroid sensitivity in *Chlamydia*-induced AAD.
Conclusion These findings suggest that macrolide treatment may have anti-inflammatory effects on responses in the asthmatic lung in the absence of infection. The mechanisms of action of the anti-inflammatory properties of macrolide therapy will now be assessed, which may inform novel therapeutic targets for steroid-resistant asthma.
Supported by Asthma Foundation NSW, NHMRC.
Conflict of Interest No.

PULMONARY PHYSIOLOGY & SLEEP SIG: ORAL SESSION

TO-062

CHANGES IN VENTILATORY CONTROL SENSITIVITY WITH AGEING IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction Although mechanisms for the age-related increase in obstructive sleep apnea (OSA) are not completely understood, it may be attributed to a hypersensitive ventilatory control feedback loop (described by a high loop gain; LG). We aimed to determine whether LG is different in elderly subjects with OSA compared to younger matched OSA subjects.
Methods Eleven young (20–40 years) and 11 older (> 60 years) BMI and gender matched OSA patients underwent two nights of polysomnography to measure the LG and AHI respectively. LG was determined using multiple 3-min 'CPAP pressure drops' to disturb the ventilatory control system. Measurements of plant gain (change in end-tidal CO_2 for a corresponding change in ventilation) and controller gain (ventilatory sensitivity to CO_2) were also calculated; plant gain was given by the reciprocal of the slope of the metabolic hyperbola during sleep, and controller gain was defined as (LG)/(plant gain).
Results Compared to younger individuals with OSA, older adults had a lower LG (5.0 ± 0.7 vs 3.1 ± 0.5; $P < 0.05$). Further analysis shows that this reduction was primarily driven by a reduction in controller gain (0.7 ± 0.1 vs 0.4 ± 0.1 L/min/mm Hg; $P < 0.05$), as plant gain remained unchanged (7.5 ± 0.5 vs 9.0 ± 0.7 mm Hg/L/min). AHI did not differ between groups (44.6 ± 10.0 vs 37.9 ± 8.6 events/h).
Conclusions Our data suggest that in OSA subjects, the sensitivity of the ventilatory control system decreases with ageing, which is similar to findings in subjects without OSA. Thus, changes in ventilatory control sensitivity do not explain the increased prevalence of OSA in the elderly. Future research is needed to examine how ageing alters other factors known to cause OSA.
Supported by NIH grants (5R01HL048531–16, 1R01HL090897–01A2)
Presenting as the 2010 TSANZ Allen & Hanburys Respiratory Research Fellow.
Conflict of Interest Yes.

TO-063

PATHOPHYSIOLOGICAL PHENOTYPIC TRAITS IN OBSTRUCTIVE SLEEP APNOEA: TARGETS FOR NOVEL TREATMENT APPROACHES

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Aim OSA pathophysiology is multifactorial and likely varies substantially between patients. The purpose of this study was to measure and characterize the relative contribution of four key pathophysiological traits in a large cohort of OSA patients. The ultimate aim is to develop targeted treatment approaches in individual patients.
Methods Patients were studied overnight on three occasions, ~1 week apart. Initially, OSA severity (AHI) was determined via PSG. During subsequent visits, patients were studied supine on therapeutic CPAP. On one night, transient CPAP reductions were used to induce varying degrees of airway collapse for measurement of Pcrit (estimated mask pressure where flow ceases), muscle responsiveness (genioglossus EMG vs negative epiglottic pressure) and the arousal threshold (nadir epiglottic pressure prior to arousal). Steady-state loop gain was measured on a separate night.
Results To date, we have enrolled 69 OSA patients and obtained data in 58 (AHI 11–112 events/h). Non-REM values for the four key traits measured in the first 35 patients analysed thus far, varied substantially between patients. Pcrit ranged from –5 to 5 (0 ± 3)cmH_2O, muscle responsiveness from 0 to 2.1(0.32 ± 0.47)%max EMG per –cmH_2O epiglottic pressure, arousal threshold from –8 to –28 (–15 ± 6)cmH_2O and steady state loop gain from 0.8 to 11.7 (4.3 ± 2.6)dimensionless. A substantial proportion (59%) had negative Pcrit values (< 0cmH_2O) and loop gain was higher in patients with negative versus positive Pcrit values (5.3 ± 2.6 vs 2.7 ± 0.8, $P = 0.02$).
Conclusions While Pcrit/anatomy remains an important determinant, a significant proportion of patients have negative Pcrit values suggesting that other traits (e.g. loop gain) importantly contribute to the presence of OSA within this group. Thus, strategies to manipulate the other pathophysiological traits may be therapeutically advantageous for a substantial proportion of carefully selected patients.
Supported by NHMRC, American Heart Association and NIH.
Nomination JRS Early Career Development Award.
Conflict of Interest Yes.

TO-064

SMALL AIRWAY FUNCTION PREDICTS FUTURE ASTHMA CONTROL AFTER INHALED CORTICOSTEROID TITRATION

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Background The physiological determinants of asthma symptom control are poorly understood. We sought to explore the range of physiological abnormalities at baseline that may predict future asthma control following ICS dose adjustment.
Methods Adult asthmatics had the Asthma Control Questionnaire (ACQ) and lung function measured at baseline and after 8 weeks. Tests included spirometry, plethysmography, sputum cell count, exhaled nitric oxide (F_ENO), mannitol bronchial challenge, respiratory system mechanics and the multiple breath nitrogen washout to derive the parameters Scond and Sacin as measures ventilation heterogeneity. Poorly controlled subjects (ACQ > 1.5) doubled the ICS dose and well-controlled subjects (ACQ < 1.5) quartered the ICS dose during the study. The primary outcome was the change in the symptom-only five-item ACQ (deltaACQ-5). A deltaACQ-5 > 0.5 is clinically significant. Spearman correlations, forward stepwise linear regressions and receiver operator curve analyses were performed.
Results In 20 poorly controlled subjects, ACQ-5 improved (1.76 to 1.16, $P = 0.04$). Baseline F_ENO ($r = -0.55$, $P = 0.01$) and Second ($r = –0.64$, $p = 0.002$) correlated with deltaACQ-5 but Scond was the only independent predictor ($r^2 = 0.34$, $P = 0.007$). In 41 well-controlled subjects, ACQ-5 worsened (0.46 to 0.80, $P < 0.001$) and 29% had a deltaACQ-5 > 0.5. Baseline Sacin correlated with deltaACQ-5 ($r = 0.40$, $P = 0.009$) and worsening Sacin predicted a deltaACQ-5 > 0.5 (ROC = 0.78, $P = 0.0003$).
Conclusions Ventilation heterogeneity at baseline predicts symptomatic response following a change in ICS dose. Abnormal small airway function at baseline predicts loss of symptom control during ICS down-titration.
Support Cooperative Research Centre (CRC) for Asthma and Airways
Conflicts of Interest None.

TO-065

MANIPULATING CEREBRAL BLOOD FLOW AFFECTS CENTRAL SLEEP APNOEA AT HIGH ALTITUDE

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Aim To measure the effects of altering cerebral blood flow (CBF) on central sleep apnoea (CSA) at high altitude.
Methods Twelve normal volunteers aged 30 ± 10 years were studied 6–9 days after arrival at 5050 metres. After control measurements they received ivi Acetazolamide (Acet) 10 mgs/kg or oral Indomethacin (Indo) 100 mgs with placebo controls in a randomized order. Ventilatory Responses (VRs), ABGs, AHI during sleep by PSG and CBF by transcranial Doppler were recorded.
Results CBF rose by 28% with Acet and fell by 23% with Indo. PaCO2 rose from 28 ± 4 to 31 ± 3 mm/mg with Acet ($P < 0.001$), whereas ABGs were unchanged with Indo. VRs were unchanged with Acet but Indo increased HVR by 100% and HCVR by 36%. AHI was halved by Acet (89 to 47/h, $P < 0.001$), but increased 25% with Indo (89 to 112/h, $P < 0.05$).
Conclusions Indomethacin reduced CBF and increased VRs and CSA during the first 3 h of sleep. Whereas Acetazolamide increased CBF but had no effect on VRs and reduced CSA severity. These results highlight the link between CBF and CSA at high altitude.
Supported by Peninsula Sleep Laboratory, University of Otago.
Nomination Nil.
Conflict of Interest Nil.

TO-066

ARTERIALIZED-VENOUS BLOOD GASES ACCURATELY MEASURE $PACO_2$, PH AND BICARBONATE IN PEOPLE WITH HYPERCAPNIA

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Background Arterial blood gases (ABGs) provide reference measures of $PaCO_2$, pH and bicarbonate (HCO_3^-). However, ABGs may be painful, and repeated punctures over a brief period can be traumatic. Arterialized-venous blood gases (AVBGs) can be sampled repeatedly and have been used to provide surrogate measures of arterial PCO_2, pH and HCO_3^-. This technique has not been validated in people with chronic hypercapnia.
Aim To investigate the validity of AVBGs for measuring arterial PCO_2, pH and HCO_3^- in people with stable chronic hypercapnia.
Methods A vein in the hand or arm was cannulated, then arterialized by heating the skin to 42–46°C. Radial arterial puncture was performed on the opposite arm. ABGs and AVBGs were taken simultaneously and analysed within 15 min. Data pairs were compared using Bland Altman analysis.
Results Forty-four paired samples were obtained from patients with stable chronic hypercapnia due to obesity ($n = 27$) or neuromuscular disease ($n = 3$), and from healthy controls ($n = 14$). Mean (SD) age was 47(12) years; $PaCO_2$ 48.6(6.5) mm Hg, range 34 to 64. The mean AVBG-ABG difference for PCO_2 was 0.5 (limits of agreement (LOA) –2.7 to 3.7) mm Hg, for pH –0.007 (LOA –0.023 to 0.008) units and for HCO_3^- –0.2 (LOA –1.76 to 1.29) mmol/L.
Conclusions AVBG measures of PCO_2, pH and HCO_3^- have acceptable agreement with ABG values in people with chronic hypercapnia and therefore can be used as an alternative to ABGs, allowing repeated sampling with minimal trauma.
Conflict of Interest Nil.

TO-067

CARDIO-SYMPATHETIC ACTIVATION IS REDUCED IN CHILDREN WITH DOWN SYNDROME AND SLEEP DISORDERED BREATHING

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Aim As children with Down Syndrome (DS) have a reduced cardiovascular response to spontaneous arousal from sleep, we hypothesized that, compared with typically developing (TD) children with SDB, children with DS would have a reduced cardiovascular response and delayed reoxygenation after obstructive respiratory events, and also reduced sympathetic drive evidenced by reduced overnight urinary catecholamines.
Methods Sixty-four children (2–17 years) referred for investigation of SDB (32 DS; 32 TD) matched for age and obstructive apnoea/hypopnoea index underwent overnight polysomnography with 12 h urine collection. Beat-by-beat heart rate (HR) was analysed during obstructive events and compared between groups. Time for oxygen resaturation post event and urinary catecholamine concentrations were also compared between groups.
Results Children with DS had significantly reduced HR changes from late to post event during NREM compared to TD children (Mean ± SEM, DS: 21.4 ± 1.8%, TD: 26.6 ± 1.6%, $P < 0.05$). Time to resaturation post event was significantly increased in the DS group ($P < 0.05$ for both NREM and REM sleep). Children with DS had significantly reduced overnight urinary noradrenaline ($P < 0.01$), adrenaline ($P < 0.05$) and dopamine levels ($P < 0.01$) compared with TD children.
Conclusion Children with DS and SDB exhibit a compromised acute cardiorespiratory response and dampened sympathetic response to SDB compared with TD children with SDB. These data may reflect autonomic dysfunction in children with DS that may place this group at increased risk for cardiovascular complications, namely pulmonary hypertension.
Supported by TSANZ/Allen & Hanburys Research Fellowship, NHMRC and the Windermere Foundation.
Conflict of Interest No.

PAEDIATRIC SIG: ORAL SESSION

TO-068

A MULTICENTRE RETROSPECTIVE STUDY OF MANAGEMENT OF SPONTANEOUS PNEUMOTHORAX IN EMERGENCY DEPARTMENTS

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Aim Paediatric spontaneous pneumothorax (SP) management is limited by a lack of evidence and paediatric specific guidelines. Adult guidelines recommend aspiration as 1st line intervention, if required, for primary SP (PSP) and intercostal chest catheter (ICC) for secondary SP (SSP).
Methods Retrospective analysis of SP presenting to nine paediatric emergency departments (ED) across Australia and New Zealand over an eight year period since BTS guideline publication (2002–2010)., excluding traumatic pneumothoraces. PSP and SSP management were compared.
Results 221 episodes of SP in 162 children occurred over the study period.

	PSP, n = 144		SSP, n = 76	
	1st episode	Recurrent*	1st episode	Recurrent*
Number (Male)	97 (72, 74%)	48	40 (28, 70%)	36
Mean (SD) age (yrs)	14.4 (3.6)		12.2 (5.7)	
Initial conservative	61 (63%)	27 (56%)	25 (63%)	12 (33%)
Conservative success	49/61 (80%)§	14/27 (52%)	14/25 (56%)	6/12 (50%)
Aspiration	14 (14%)	7 (9%)	5 (13%)	1 (3%)
Aspiration success	7/14 (50%)	4/7 (57%)	2/5 (40%)	1/1 (100%)
ICC insertion	41 (42%)	30 (63%)	24 (60%)	29 (81%)
Discharged from ED	24/95 (25%)	6 (13%)	6/39 (15%)	5/35 (14%)

*Recurrent may include >1 presentation/subject. §$p < 0.05$ vs. 1st SSP.

Conclusions In this largest paediatric SP series, current ED management does not differentiate between PSP and SSP. ICC insertion is the most common initial intervention for both, despite current BTS guidelines. SP recurrence is common. Further research is required to determine optimal paediatric management when conservative treatment is not inappropriate.
Conflict of Interest: No

TO-069

ADAPTIVE IMMUNITY TO NON-TYPEABLE *H. INFLUENZAE* IN CHILDREN WITH NON-CF BRONCHIECTASIS

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Introduction Non-typeable *H. influenzae* (NTHi) is the most common bacterial infection associated with non-CF bronchiectasis in children and adults. In adults with bronchiectasis, chronic NTHi infection may be associated with a T helper type 2 (Th2) immune response[1] however, there are no data describing the NTHi-specific immune response in children. The aim of this study was to characterize the NTHi-specific immune response in children with non-CF bronchiectasis.
Method Peripheral blood mononuclear cells from Indigenous and non-Indigenous children with bronchiectasis and healthy controls were cultured with NTHi whole cell antigen (10^6 and 10^5 cfu/ml) for 72 h. Cytokines (IFNγ, IL-5, IL-13) were quantified from culture supernatants using time-resolved fluorometry.
Results Children with bronchiectasis had elevated levels of Th2 and lower levels of Th1 cytokines in response to 106 NTHi. This effect was also seen at 105 cfu/ml.

NTHi 10^6 cfu/ml	IFNg pg/ml median (IQR)	IL-13 pg/ml median (IQR)	IL-5 pg/ml median (IQR)
Bronchiectasis ($n = 39$)	1768 (87–30,030)	71 (0–2838)	26 (0–2069)
Healthy control ($n = 40$)	8590 (623–70,906)	43 (0–623)	0 (0–181)
p	< 0.001	0.011	< 0.001

Conclusion Data suggest that children with bronchiectasis have Th2 type immune response in response to NTHi whilst healthy children have a Th1 type immune response. Assessment of the full cohort, including impact of a pneumococcal *H. influenzae* protein D conjugate vaccine, is currently underway.
1 King P *et al.* 2003; Am J Respir Crit Care Med 167: 587–92.
Supported by Financial Markets Foundation for children; JU and AC are supported by NHMRC Practitioner Fellowships.
Conflict of Interest No.

TO-070

LUNG FUNCTION ABNORMALITIES IN EXTREMELY PRETERM, EXTREMELY LOW BIRTH WEIGHT SURVIVORS AT 18 YEARS COMPARED WITH TERM, NORMAL BIRTH WEIGHT CONTROLS

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Aim To determine the respiratory function of extremely preterm (EPT; gestational age/GA < 28 weeks), extremely low birth weight (ELBW; birth weight/BW < 1000 g) survivors at 18 years of age compared with term controls.
Methods 18-year follow-up of participants born either EPT/ELBW in 1991–1992 in the state of Victoria and randomly selected term, NBW controls (C). Spirometry, plethysmography, airways resistance (sRaw), diffusing capacity and multiple-breath-washout were measured according to standard guidelines.
Results: The EPT/ELBW (All) had impaired lung function especially variables reflecting flow, and airways resistance. Those with BPD had greater impairments in lung function. Data are mean (SD), unless otherwise stated.

	BPD	No BPD	Controls (C)			95% CI
Variable	$n = 62$	$n = 72$	All $n = 134$	$n = 140$	95% CI All-C	BPD-C
GA wk	26.2	25.6	25.9	39.1	–	–
BW g	783	855	820	3412	–	–
$zFEV_1$	–1.17 (1.50)	–0.70 (1.05)	–0.91 (1.30)	0.19 (1.17)	–1.40, –0.81^	–1.74, –0.97*
zFVC	–0.41 (1.53)	–0.39 (1.06)	–0.40 (1.29)	0.15 (1.24)	–0.85, –0.25+	–0.96, –0.16^
zFEF	–1.47 (1.37)	–0.83 (1.17)	–1.13 (1.30)	0.05 (0.99)	–1.45, –0.90^	–1.86, –1.18*
sRaw (kPa*s)	1.69 (0.51)	1.42 (0.31)	1.55 (0.44)	1.34 (0.29)	0.12, 0.30^	0.24, 0.47*

t-tests *$P < 0.0001$; +$P \leq 0.001$; ^$p \leq 0.01$; z = z-score; pp = percentage predicted

Conclusions EPT/ELBW survivors had lower lung function than their NBW peers in late adolescence. Those who had BPD had the greatest impairment in their lung function. The impaired lung function is obstructive in nature.
Support Dora Lush Priority Scholarship NHMRC #607440; NHMRC #491246.
Conflict of Interest No.

TO-071

IMPAIRED LUNG HEALTH IN CHILDREN BORN PRETERM IS RELATED TO SEVERITY OF NEONATAL LUNG DISEASE

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Long-term impacts of preterm birth and bronchopulmonary dysplasia (BPD) are unclear. We assessed lung function, neonatal factors, chest computed tomography (CT) and symptoms in preterm children with and without BPD.
Methods Children born at term (n = 44) and ≤32 weeks gestational age (n = 61 BPD, n = 35 non-BPD) performed forced oscillation, static lung volumes, spirometry and gas transfer (DLCO) at 9–11 years of age. Preterm children performed chest CT (n = 87) and ISAAC questionnaires (n = 95).
Results Children with BPD had impaired respiratory resistance (R_{rs}) and reactance (X_{rs}), reduced FEV_1 and $FEF_{25–75\%}$ compared to non-BPD and term controls (one-way ANOVA; post hoc comparisons $p < 0.05$). Neonatal duration of supplemental O_2 and mechanical ventilation, were associated with impaired lung function. Abnormal CT was recorded in 82/87 (94%) children with increased prevalence correlated with reduced spirometry and DLCO/VA (t-test; $p < 0.03$). Recent wheeze (n = 56; 59%) and symptoms on exertion (n = 50; 52%) were associated with impaired R_{rs} ($P = 0.04$) and X_{rs} ($P = 0.02$), and reduced FEV_1/FVC ($P = 0.02$) and $FEF_{25–75\%}$ ($P = 0.05$).
Conclusions Children born ≤32w GA with BPD have worse lung function compared to preterm children without BPD. Structural lung damage and recent respiratory symptoms are common in preterm children and associated with poor lung function outcomes, indicating the need for ongoing respiratory follow-up of preterm infants.
Supported by NH&MRC, Raine Foundation and PMH Foundation.
Key Words children, preterm, bronchopulmonary dysplasia, lung function.
Conflict of Interest None.

TO-072

FASTER ASSESSMENTS OF LUNG CLEARANCE INDEX ARE FEASIBLE IN CYSTIC FIBROSIS WITHOUT COMPROMISING SENSITIVITY

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Aim To investigate the feasibility of adult-based recommendations in children and whether test duration could be shortened to two acceptable MBW tests. Lung clearance index (LCI) measured by multiple breath washout (MBW) offers improved sensitivity, compared to spirometry, in detecting cystic fibrosis (CF) related lung disease. Current guidelines, which require three technically acceptable MBW tests with FRC values within 10%, limit widespread clinical utility due to the time required.
Methods Retrospective analysis of MBW data was performed in both healthy control (n = 90) and CF subjects (n = 108) across infancy, pre-school and school age. Suitability and feasibility of using adult guidelines for FRC repeatability in children were investigated. To assess the validity of performing only two MBW tests, agreement of mean LCI values (LCI_{2tests} vs LCI_{3tests}) and sensitivity to detect abnormal peripheral airway function (LCI_{2tests} vs LCI_{3tests}) were compared.
Results FRC co-efficient of variation (CoV) and disease category (CF vs health) were significant predictors of LCI CoV in children ($P < 0.001$ and $P = 0.002$, respectively). LCI CoV was significantly lower in those with FRC values within 10% (mean 4.7 vs 8.7%, $P < 0.001$), however, this criterion was only achieved by 103/198 (52%) subjects. There was no significant difference in mean LCI derived from three or first two tests: mean (95% CI) $LCI_{Diff(3-2)}$:0.024 (–0.01,0.57) in healthy controls; 0.069 (0.004,0.134) in CF subjects. Sensitivity was not compromised: LCI_{3tests} was abnormal in 65/108 (60%) CF subjects vs 64/108 (59%) for LCI_{2tests}.
Conclusions FRC repeatability does influence and improve LCI repeatability in paediatric subjects, however application of adult FRC quality control was only feasible in half of paediatric subjects. MBW testing can be shortened to two technically acceptable tests without significantly affecting mean LCI or LCI sensitivity.
Conflict of Interest No.

TO-073

LIMITATIONS OF CURRENTLY AVAILABLE REFERENCE EQUATIONS FOR PEAK AEROBIC CAPACITY IN CHILDREN WITH CYSTIC FIBROSIS

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Peak oxygen uptake (VO2) declines over time in cystic fibrosis (CF) and once it drops below 80% predicted, long-term survival declines. Prompt identification of children who demonstrate poor peak VO2 is important but challenging in the paediatric setting due to the differing results of currently available reference equations.
Methods Children attending the CF outpatient clinic performed a maximal treadmill exercise test (Bruce Protocol). Peak measures of VO2 in L/min were normalized to percent predicted results for reference equations used for the interpretation of exercise testing in children [1–4].
Results Eighty-one children, 6–18 years of age were included in the analysis. Depending on the prediction equation used, the number of children with a peak VO2 below 80% varied (6 – Cooper *et al.* 1984; 17; Godfrey *et al*. 1971*;* 19; Bruce *et al*. 1973; Drinkwater *et al*. 1975*)*.
Conclusion Paediatric centres face challenges in the interpretation of peak VO2 in children with CF.
Conflicts of Interest No.
References
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4 Drinkwater, BL, Horvath SM, Wells CL, Aerobic power of females, ages 10 to 68. J Gerontol 1975; 30(4): 385–94.

TOBACCO & RELATED SUBSTANCES SIG: ORAL SESSION

TO-074

CIGARETTE SMOKE INDUCES A DISTINCT FIBROTIC SIGNATURE IN BRONCHIAL EPITHELIAL CELLS IN COMPARISON TO TGFB

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Rationale We have previously shown cigarette smoke extract (CSE) directly induces the production of the extracellular matrix proteins fibronectin and perlecan in human lung fibroblasts (Krimmer *et al.* AJRCMB 2011). The proteins were also induced by transforming growth factor β (TGFβ); however the signal transduction pathways activated by CSE were different to those used by TGFβ.
Aim To compare fibrosis related genes upregulated by TGFβ or CSE in primary human bronchial epithelial (HBE) cells.
Methods HBE cells were grown to confluence in bronchial epithelial growth medium in the absence or presence of 5 ng/ml of TGFβ1 or 5% CSE. Total RNA lysates were collected after 72 h. The expression of fibrosis related genes was measured by real time PCR. In total we examined 85 fibrosis related genes. A cut off of a minimum of 1.5 fold induction was used to indicate upregulation of a gene.
Results TGFβ upregulated 49 different fibrosis associated genes, CSE upregulated only 16, and of all the upregulated genes, four were uniquely upregulated by CSE (catenin β1, extracellular matrix protein 1, and TIMP 1 and 2). As expected, TGFβ upregulated a variety of ECM proteins (e.g. collagen I, IV–VIII, fibronectin); integrins (e.g. integrin α2, α4–6), and degradative enzymes (e.g. matrix metalloproteinase (MMP) 1–3, 9–16). In contrast, CSE upregulated only two collagens (XI and XIV) and MMP9.
Conclusion As CSE selectively upregulated a subset of TGF-β induced genes, elucidation of the specific mechanisms involved is likely to give novel insight into the pathophysiology of COPD.
Supported by NH&MRC
Nomination **TSANZ Travel Grant to the 2012 ASM and Janet Elder International Travel Awards**
Conflict of Interest No.

TO-075

PLATELET ACTIVATING FACTOR RECEPTOR (PAFR) EXPRESSION INCREASES IN AIRWAYS OF CURRENT SMOKERS

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Introduction Cigarette smoking increases the risk of pulmonary pneumococcal disease, but the mechanism is unclear. We have shown that inhalable particulate matter (PM) stimulates pneumococcal adhesion to human lower airway cells[1]. Increased pneumococcal adhesion is associated with increased invasiveness of bacteria. Oxidative stress mediates the adhesive response of airway epithelial cells, and platelet activating factor receptor (PAFR) is a receptor co-opted by pneumococci to facilitate PM-stimulated adhesion. The aim of the study was to investigate the expression of PAFR in the airways of normal controls (NC) and smokers with normal lung function (NS) in vivo.
Methods Endobronchial biopsies from 16 NS and 11 normal controls (NC) were immuno-stained using anti-PAFR monoclonal antibody. PAFR expression was assessed as percentage of epithelium stained for PAFR over total basement membrane length by using computer-assisted image analysis. The slides were counted by an observer blinded to subject and phenotype.
Results Percentage of epithelial staining for PAFR was increased significantly in NS compared to NC [Chi-Square = 30.3, (median (range), 0 % (0–4.8) versus 0 % (0–0), $P < 0.001$].
Conclusions This is the first description of increased in vivo expression of PAFR in the epithelium of NS compared to NC. Our data suggest that enhanced PAFR expression may be the mechanism of increased vulnerability of smokers to pneumococcal infection.
Reference
1 Mushtaq N *et al.* Allergy Clin Immunol 2011;(127): 1236–42.
Supported by NHMRC project grant 490023.
Conflict of Interest No.

TO-076

KNOWLEDGE ABOUT AND ATTITUDES TOWARDS SMOKING CESSATION IN FINAL YEAR PHARMACY STUDENTS

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Introduction and Aim With the emerging and promising role of pharmacists in implementing smoking cessation services, a tool to assess baseline knowledge and address gaps is urgently needed. Our study aims at exploring pharmacy students' knowledge, attitudes and training needs about smoking cessation.
Methods As no previous smoking cessation knowledge questionnaires exist, a review of the literature informed the development of such a questionnaire (Smoking Cessation Attitudes and Knowledge (SCAK)). Face and content validity were assessed by a smoking cessation expert (RB). The questionnaire was administered to fourth year pharmacy students at the University of Sydney, smoking cessation educators and clinicians. Data analysis was performed using the Predictive Analytics SoftWare (PASW Statistics 18).
Results Responses from 250 pharmacy final year students were obtained. The mean total knowledge score was 20.3/32 (63.4%) and the attitude score was 15.3/18 (84.85%). Majority of the students reported positive attitudes towards general smoking and smoking cessation concepts.
Discussion The SCAK identified clear areas of information gap in future pharmacy practitioners. High scores on the attitude scale indicate a high level of interest in acquiring further education and professional training to improve current knowledge and practice standards.
Conflict of Interest None.

TO-077

SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS IS DECREASED IN HEALTHY SMOKERS AND CURRENT SMOKER COPD SUBJECTS

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Background The soluble receptor for advanced glycation end-products (sRAGE) functions as decoy receptor for ligands of membrane bound RAGE, attenuating the downstream inflammatory responses. Recent studies have observed significantly reduced levels of sRAGE systemically and in the airway in COPD, however the relationship between smoking status and BAL sRAGE levels in COPD has not been investigated.
Method We investigated sRAGE in BAL from COPD subjects (26 current and 21 ex-smokers), 18 healthy smokers and 27 never-smoker controls. Correlations between sRAGE, disease severity and smoking history were performed using Spearman's rank correlation.
Results sRAGE levels were significantly decreased in healthy smokers and current-smoker COPD subjects compared with never-smoker controls (sRAGE pg/mL: controls: 1851 ± 219; healthy smokers: 634 ± 157; current smoker COPD: 937 ± 224; ex-smoker COPD: 1164 ± 253). There were no significant differences in sRAGE levels in ex-smoker COPD subjects versus never-smoker controls. There was a significant relationship between FEV_1 and sRAGE levels (r 0.295, p = 0.005) and a significant inverse relationship between smoking Pk/y and sRAGE levels (r –0.317, $P = 0.002$). **Conclusions** Our findings suggest that decreased levels of BAL sRAGE are associated with smoking status, rather than COPD disease per se.
Supported by NHMRC.
Conflict of Interest No.

COPD SIG: ORAL SESSION 2

TO-078

THE LONGITUDINAL DETERMINANTS OF DECLINE IN OBSTRUCTIVE AIRWAY DISEASES

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Longitudinal examination of the characteristics of older people with asthma/COPD overlap will further improve our understanding of these conditions and identify the role of systemic inflammation (SI) in these disorders. We hypothesized that overlap and SI are associated with the greatest decline in FEV_1 and health status.
Aim To determine the association between lung function decline and other clinical outcomes over time.
Methods A prospective cohort study with 4-year follow-up. Subjects (> 55 years) with asthma, COPD and overlap, underwent assessments of spirometry, QoL (SGRQ), and biomarkers (CRP and sputum cell counts) at baseline and 4 years.
Results Eighty-four (84%) participants were contacted, (41) 41% were reassessed and 15 (15%) had died. The mean (SD) age at follow-up was 72.2 (6.8) years and 37% were male. COPD, asthma and overlap diagnosis was 57.5%, 7.5% and 35% respectively. The mean difference in FEV_1 was –.08mls (0.3). 6MWD decreased by 42 (44) m and there was a 2.2 (11.4) unit decrement in SGRQ. These outcomes did not differ by diagnosis. Those with baseline SI (CRP > 3 mg/L) had the greatest decline in SGRQ (diff 5.7 (2.4) V –2.2 (2.5); $P = 0.03$), but there was no difference in lung function decline. Mean baseline FEV_1% predicted (41.6 (12.3) V 59.5 (18); $P = 0.0007$), 6MWD (319 (100) V 440 (97); $P = 0.0001$) and SGRQ (55 (16) V 42 (17.7); $P = 0.009$) was worse in the group that died compared to survivors.
Conclusions Overlap asthma/COPD is not associated with increased functional decline. SI is associated with declining QoL, suggesting a need to target treatment to low grade SI. Overall there was only slight health status and functional decline over 4 years, however the 15% that died had the greatest baseline impairment.
Supported by NHMRC for the visit 1 data.
Nomination Janet Elder Travel Award.
Conflict of Interest No.

TO-079

TAI CHI IMPROVES WALKING CAPACITY, BALANCE, QUADRICEPS STRENGTH AND QUALITY OF LIFE IN PEOPLE WITH COPD

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Aim To determine whether short-form Sun-style Tai Chi was effective in improving walking capacity, balance, quadriceps strength and quality of life in people with COPD compared to usual medical care.
Methods This was a randomized controlled trial with assessor blinding. Participants with a medical diagnosis of COPD were recruited at Concord Hospital, Sydney. After confirmation of eligibility, participants were randomly allocated to either the Tai Chi Group 9TCG) or the Control Group (CG) (no exercise training). The TCG trained for twice weekly for 12 weeks. Walking capacity, balance, quadriceps strength and quality of life were measured at baseline and study completion.
Results Of 42 participants (mean (SD) age 73 (8) years, FEV_1% 59 (16)% predicted), 38 completed the study (19 in TCG and 19 in CG). Compared to control, Tai Chi significantly increased incremental shuttle walk distance (mean difference 55 m, 95% CI 31 to 80) and endurance shuttle walk time (384 s, 95% CI 186 to 510); reduced medial-lateral body sway in semi-tandem stand (–12.4 cm, 95% CI –21 to –3); increased quadriceps strength in both leg (right: 24 Newtons, 95% CI 14.5 to 33.5 and left: 17.8 Newtons, 95% CI 6 to 29); and increased total score on the chronic respiratory disease questionnaire (11 points, 95% CI 4 to 18).
Conclusion Short-form Sun-style Tai Chi was significantly more effective than no exercise training in improving walking capacity, balance, quadriceps strength and quality of life in people with COPD. Such findings provide compelling evidence for the use of Tai Chi as an alternative to current training modalities in people with COPD.
Supported by PRF seeding grant and Ian Collier Memorial Scholarship.
Nomination The Janet Elder Travel Awards; Physiotherapy Prize.
Conflict of Interest No.

TO-080

CBT REDUCES RATINGS OF BREATHING DIFFICULTY IN RESPONSE TO EXTERNAL RESISTIVE LOADS IN PEOPLE WITH COPD

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Introduction There is evidence that psychological factors contribute to the perception of increased difficulty of breathing in patients with COPD, and increase morbidity. We tested the hypothesis that cognitive behaviour therapy (CBT) decreases ratings of breathing difficulty in response to resistive load testing in patients with COPD.
Methods From a group of patients with COPD, 15 were randomized to have a brief course of specifically targeted CBT and nine to routine care. After 6 months patients were tested with an inspiratory resistive load-testing protocol.
Results Six months after randomization we measured the perceived dyspnoea in response to a series of inspiratory loads from 5–40 cm H_20/L/sec and compared the results to the same measurements prior to randomization. The average reduction in load rating was 16% for the CBT group and 0% for the routine care group ($P = 0.02$).
Conclusions COPD patients who received a brief CBT intervention showed decreased ratings of breathing difficulty in response to external resistive loads. This decrease persisted for 6 months, a result that suggests that CBT may have a place in the treatment of people with COPD.
Conflict of Interest No.

TO-081

A RETROSPECTIVE VALIDATION OF THE BAP-65 SEVERITY SCORE FOR AN AECOPD IN AN AUSTRALIAN REGIONAL UNIVERSITY TEACHING HOSPITAL

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Background The BAP-65 severity score has been retrospectively validated by Shorr *et al.* in admissions with an acute exacerbation of COPD (AECOPD). This simple score is made up of four components (**B**lood urea > 8.9 mmol/L, **A**ltered consciousness, **P**ulse rate > 109 and age > **65**) and predicted inpatient mortality, mechanical ventilation and length of stay.
Aim To validate BAP-65 as a severity score in an Australian cohort.
Method A retrospective audit was undertaken of all admissions under the Respiratory unit at the Royal Hobart Hospital with an AECOPD over 14 months. Collected data included: urea, conscious state, pulse rate, age, inpatient mortality, length of stay and the use of invasive or non-invasive ventilation. Patient data and outcomes were compared to the Shorr *et al.* cohort by chi-squared tests. A Cochran-Armitage trend test was used to assess for correlation between BAP-65 score and outcome.
Results Two hundred two inpatients were included. The distribution of patients across the BAP-65 score was similar (χ^2 $P = 0.38$), as was the average age (69 years +/– 9.77). Our cohort was intubated less frequently (2.48% vs 9.2%, χ^2 $P = 0.02$). We found no correlation between intubation or length of stay and BAP-65 score. Overall mortality was similar between cohorts (5.45% χ^2 $P = 0.50$) and varied linearly with an escalating score ($P = 0.0015$). The use of non-invasive ventilation appeared to vary linearly, though this was non-significant ($P = 0.054$).
Conclusion We retrospectively validated the BAP-65 in an Australian cohort, with BAP-65 score correlating with mortality. BAP-65 might also predict non-invasive ventilation use.
Conflict of Interest No.

TO-082

AN EVIDENCE-BASED CHECKLIST FOR ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim To establish current practice in managing acute exacerbations of chronic obstructive pulmonary disease (AECOPD) at The Prince Charles Hospital (TPCH), and to develop a checklist promoting evidence-based recommendations.
Methods Focus groups, statewide stakeholder consultation and a literature review were used to develop a one page AECOPD Inpatient Checklist based on the COPDX Plan guidelines. A chart audit collecting demographic, process of care and patient outcome data for AECOPD admissions was conducted in pre-checklist (2010) and checklist-implementation (2011) phases.
Results One hundred ten admissions were audited in pre-checklist ($n = 42$) and checklist-implementation ($n = 68$) groups, with checklist use in 35 (51%) admissions. Rates for COPDX Plan recommendations were high overall for patient assessment (admission chest x-ray 100%) and initial treatment (inhaled bronchodilator 100%, systemic corticosteroids 79%, antibiotic therapy 91%). Rates were lower for inpatient consideration of longer-term issues such as referral to pulmonary rehabilitation (36%). Checklist use was associated with significantly increased rates of arterial blood gas analysis (86% vs 61%, $P = 0.02$), sputum microbiology testing (83% vs 58%, $P = 0.02$) and influenza vaccination assessment (71% vs 51%, $P = 0.04$) compared with admissions without checklist use. Median length of stay did not change significantly with checklist use.
Conclusions This study quantified management of AECOPD at a Queensland tertiary facility, with reference to national guidelines. Checklist use was associated with increased rates of several recommended strategies. There is opportunity to improve aspects of inpatient care and to refine methods of guideline dissemination.
Supported by The University of Queensland MBBS Honours Program.
Conflict of Interest No.

TO-083

BONE DENSIOMETRY UTILIZATION IN COPD OUTPATIENTS AND PREVALENCE OF OSTEOPENIA AND OSTEOPOROSIS

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Aim Patients with COPD share a number of risk factors for osteoporosis, but screening with bone densiometry (BMD) is not routinely recommended. This study aimed to determine the proportion of patients undergoing BMD in the COPD outpatient clinic of a tertiary institution, and the prevalence of osteopenia and osteoporosis.
Methods A retrospective audit was carried out of the first 98 patients in our centre's COPD outpatient database, still attending COPD clinic follow-up between January 2009 and October 2010. Demographics, medication, healthcare utilization and physiological data were collected, as were results of any BMD scans performed.
Results Ninety-eight patients were evaluated: mean (sd) age 69.6 (9.7) years, FEV1 43.3 (14.0) % predicted, BMI 26.4 (7.3), $n = 52$ male. BMD scan results were able to be retrieved in 24 patients (24.5%), requested by a registrar ($n = 2$), specialist ($n = 13$) or GP ($n = 9$). There was no significant difference in mean age, FEV1 or BMI between patients who did or did not have BMD scans. In the 24 patients with BMD scan data, mean (SD) T score at the spine was –1.32 (1.06), and at the hip was –1.54 (1.2); 6 (25%) patients had osteoporosis and 14 (58.3%) had osteopenia. Bisphosphonate use was recorded in the records for $n = 10$ patients ($n = 6$ with BMD data, $n = 4$ without) and Vitamin D supplementation in $n = 16$ patients ($n = 5$ with BMD data, $n = 11$ without).
Conclusions This audit suggests that ordering of BMD scans in the COPD outpatient clinic is haphazard and not based on disease severity. Osteopenia or osteoporosis is frequently found in COPD patients when BMD scans are performed. While acknowledging the limitations of retrospective audit, pharmacological strategies to maintain bone health appear to be very underutilized in these high-risk COPD patients. Data collection is continuing.
Supported by A+ trust, Auckland District Health Board.
Conflict of Interest No.

TO-085

MIRNAS REGULATE BACTERIAL INFECTION IN LUNGS

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Aim Lung pathogens such as non-typeable Haemophilus Influenzae (NTHi) are able to activate different TLR signalling pathways and inflammatory cytokines, which are important in inflammatory responses and bacterial clearance. Here we investigated the roles of miRNA in regulating these processes.
Methods BALB/c mice were challenged with a low infectious dose of NTHi. miRNAs that were differentially expressed in the airways were identified by microarray and quantified by Taqman PCR. Expression of specific miRNAs were inhibited using miRNA inhibitors (antagomirs) compared to scrambled control to determine the effect of miRNA on cellular infiltrates, bacterial clearance and inflammation during lung infection.
Results Interestingly further knockdown of a specific miRNA that was downregulated by infection followed by infection showed altered bacterial clearance from the lungs. Cell counts on BALF showed a marked increase in cellular infiltrate in particular neutrophils in the antagomir treated group compared to the scrambled control. These effects occurred within 24 h of infection.
Conclusions MiRNA knockdown may play a protective role against bacterial replication and suppressing cellular inflammation. Inhibiting this specific miRNA in vitro model using primary lung macrophages and neutrophils isolated from naive mice showed an increased bacterial uptake into the cells and also decreased bacterial load in supernatants. Our study suggests that miRNA may play important roles in regulating bacterial clearance.
Supported by NHMRC & CRC asthma.
Nomination TSANZ Travel Awards.
Conflict of Interest No.

CELL BIOLOGY & IMMUNOLOGY SIG: ORAL SESSION

TO-084

PLASMINOGEN EVOKES EXTRACELLULAR MATRIX REMODELLING BY HUMAN AIRWAY FIBROBLASTS

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Aim In asthma, the conversion of serum-derived plasminogen (Plg) into plasmin, a serine protease, is implicated in airway inflammation and extracellular matrix (ECM) remodelling. In cultures of human airway fibroblasts (HAFs) derived from asthmatic and non-asthmatic donors, we have compared Plg conversion into plasmin and the subsequent effects of plasmin on ECM remodelling.
Methods 3D collagen gel plugs seeded with human airway fibroblasts (HAF) were incubated with Plg (27 nM). Plg-activator (PA) and plasmin enzyme activity, changes in gene expression and the percentage decrease in gel plug diameter were measured.
Results Plasminogen stimulated the contraction of HAF gels, over a 72 h incubation period ($P < 0.01$, n = 15). Plasminogen-stimulated contraction was preceded by an increase in plasmin activity in the supernatant ($P < 0.001$, $n = 13$), indicating a potential role for both PAs and plasmin. Moreover, Plg also stimulated increases in tissue type-PA (tPA) gene expression and PA enzyme activity, that correlated with gel contraction responses. The serine protease inhibitor, aprotinin (10 KIU·mL^{-1}), which inhibits PA and plasmin activity, attenuated gel contraction stimulated by either Plg ($P < 0.05$, $n = 7$) or exogenous plasmin (100 mU·mL^{-1}) ($P < 0.05$, $n = 5$). The more specific plasmin inhibitor, α2-antiplasmin, also attenuated gel contraction induced by plasmin. HAF cultures derived from asthmatic donors expressed lower basal levels of tPA and contracted less in response to Plg than those derived from non-asthmatic donors.
Conclusion Our findings raise the possibility that local conversion of plasminogen into plasmin by airway fibroblasts contributes to ECM remodelling and expands the evidence supporting a role of plasminogen in asthma.
Supported by NHMRC.
Conflict of Interest No.

TO-086

NOX1 OXIDASE PROTECTS AGAINST INFLUENZA A VIRUS-INDUCED LUNG INFLAMMATION

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Introduction We have recently shown that the Nox2 isoform of the NADPH oxidase family of superoxide-generating enzymes promotes influenza A virus-induced lung injury and airways inflammation. However, airway epithelial cells and lung endothelial cells also express the Nox1 isoform of NADPH oxidase placing this enzyme at key sites to regulate influenza A virus-induced lung inflammation. Thus, the aim of this study was to investigate the role of Nox1 oxidase in influenza A virus-induced lung inflammation.
Methods Male WT and Nox1-deficient mice (i.e. Nox1$^{-/y}$) were infected with 1x10^4 PFU of the moderately virulent influenza A virus HKx31 (H3N2). Viral titre, airways inflammation, bodyweight, oxidative stress, lung histopathology, cytokine/chemokine expression in whole lung and T lymphocyte subsets (CD8$^+$, CD4$^+$ and CD25$^+$CD4$^+$FoxP3$^+$) were assessed 3 and 7 days post infection.
Results HKx31 virus infection of Nox1$^{-/y}$ mice resulted in a significantly greater: loss of bodyweight (~30%); BALF neutrophilia; peri-bronchial, perivascular and alveolar inflammation; BALF inflammatory cell superoxide production and peribronchial, epithelial and endothelial oxidative stress; and expression of pro-inflammatory cytokines including CCl2, CCl3, CXCl2, IL-1β, IL-6 and TNF-α when compared to WT mice. Expression of the anti-inflammatory cytokine IL-10 was lower in Nox1$^{-/y}$ mice. Lung viral titers, and the degree of airways infiltration of active (i.e. CD69$^+$ and CD44$^+$) CD8$^+$ and CD4$^+$ T lymphocytes, and of Tregs were similar between influenza-infected WT and Nox1$^{-/y}$ mice.
Conclusions These data indicate that Nox1 oxidase protects against influenza A virus infection in mice and that there are differential roles of Nox1 versus Nox2 oxidases in the regulation of inflammation caused by influenza A viruses.
Conflict of Interest No.

TO-087

INTERLEUKIN-33-DRIVEN ACTIVATION OF ALVEOLAR MACROPHAGES

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Introduction Allergic asthma is associated with alternative activation of alveolar macrophages (AM). Recently, we showed that in an experimental acute exacerbation of asthma, activated AM can stimulate pulmonary $CD4^+$ T cells. In parallel, there is upregulated airway epithelial expression of interleukin (IL)-33. In this study, we investigated whether IL-33 could stimulate AM previously polarized towards an alternatively activated phenotype.
Methods AM recovered by lavage from BALB/c mice, or cells of the mouse AM line designated MH-S, were cultured in the presence of IL-4 and IL-13, then stimulated with IL-33. mRNA expression was assessed by quantitative real-time PCR and cytokine secretion was measured using a multiplex immunoassay. In further experiments, we assessed the effect of treatment with dexamethasone or the phosphodiesterase inhibitor pentoxifylline on IL-33-stimulated MH-S cells.
Results Treatment of lavage AM with IL-4 and IL-13 followed by IL-33 increased expression of markers of alternative activation such as Arginase-1 and Ym-1, as well as of various pro-inflammatory cytokines. MH-S cells expressed much lower levels of alternative activation markers, which were not enhanced by stimulation with IL-33. However, treatment of MH-S cells with IL-33 strongly stimulated expression of pro-inflammatory cytokines including TNF-α, IL-1β, IL-6, IL-12p40 and G-CSF, whether or not the cells had been pre-treated with IL-4 and IL-13. IL-33-induced cytokine expression was markedly inhibited by dexamethasone, whereas pentoxifylline selectively inhibited transcription of mRNA for TNF-α.
Conclusions MH-S cells could provide a useful *in vitro* model in which to test the effects of other anti-inflammatory drugs for their ability to suppress activation of macrophages, as well as to elucidate their mechanism of action.
Supported by NHMRC.
Conflict of Interest No.

OLIV SIG: ORAL SESSION 2

TO-088

IDENTIFYING RECIPIENTS WITH DELAYED RECOVERY IN EXERCISE CAPACITY AFTER LUNG TRANSPLANTATION

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Aim To determine if pre-operative factors can identify lung transplant recipients who have delayed recovery in exercise capacity and to determine if these recipients catch their peers during the first 12 months post-transplant.
Methods All lung transplant recipients at a single institution between December 2006 and September 2011 were assessed. Exercise capacity was assessed by 6-min walking distance (6MWD), with delayed recovery defined as a recipient who decreased ≥15% (large Cohen's Effect Size (0.8SD)) in 6MWD at2 weeks post-transplant when compared to their pre-transplant level. Pre-operative factors assessed were age, sex, FEV_1%, body mass index, percentage of predicted 6MWD and quadriceps strength; with peri-operative factors including primary graft dysfunction, mechanical ventilation time and intensive care days (ICU). All recipients completed exercise rehabilitation both pre- and post-transplantation.
Results Seventy-six (68 bilateral lung, 5 single lung; mean (SD) age 43(13) years) recipients were studied. Twenty-six percent (20/76) of recipients experienced an initial decline (≥15%) in their 6MWD. In a multiple logistic regression, only longer ICU days (Exp (B) 1.240(1.090–1.410) $P = 0.001$) identified which recipients were more likely to have delayed recovery in 6MWD. No other factor contributed to the model. The delay in recovery of 6MWD persisted at six (mean (SD) 6MWD 493(137)m vs 576 (104)m; $P = 0.027$) and 12 months (500 (99) m vs 582 (77) m; $P = 0.013$) post-transplant.
Conclusions Prolonged ICU stay leads to reduced exercise capacity throughout the first post-transplant year. This subgroup of patients should be targeted for intensive exercise rehabilitation in order to optimize transplant outcomes.
Supported by Nil.
Conflict of Interest No.

TO-089

PHENOTYPING INFILTRATING T LYMPHOCYTES WITHIN THE LUNG ALLOGRAFT

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Lymphocytic bronchiolitis (LB) is the strongest risk factor for lung allograft loss due to obliterative bronchiolitis, however it is poorly assessed by the current biopsy-based techniques. We hypothesized that phenotyping and quantifying infiltrating lymphocyte populations using flow cytometry would provide a better assessment of LB.
Methods Post-transplant small airway brushings were analysed by flow cytometry. The median (interquartile range) number of nucleated cells expressing CD3, CD4, CD8, CD103 (expressed on intraepithelial lymphocytes) and granzyme B was determined.
Results Brushings were obtained from 30 patients 23.0 (6.2–60.1) months post-transplant. The level of infiltrating $CD4^+$ cells was significantly higher in patients undergoing routine surveillance (0.82, 0.45–1.51) compared to those being assessed for a decline in lung function (0.42, 0.21–0.58, $P = 0.04$). Patients with a decline in lung function also had four-fold higher levels of $CD8^+CD103^-$granzymeB$^+$ cells compared to those undergoing routine surveillance (1.12 (0.81–2.19) vs 0.28 (0.17–0.48), $P = 0.031$). There was no association between time post-transplant and any cellular subtype.
Conclusions Reduced lung function post-transplant is associated with an influx of activated cytotoxic T cells into the small airways. Flow cytometric evaluation of these lymphocyte populations appears to be a valuable addition to the current lung allograft assessment, and current studies are underway to better understand the inverse relationship between $CD4^+$ T cells and activated cytotoxic T cells in allograft dysfunction.
Supported by Roche Organ Transplant Research Fund.
Conflict of Interest No.

TO-090

DOWNREGULATION OF CD28 AND UPREGULATION OF 4–1BB ON PERIPHERAL BLOOD PRO-INFLAMMATORY CD8+ T CELLS IS ASSOCIATED WITH BOS

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Background We have previously shown that bronchiolitis obliterans syndrome (BOS) is associated with lack of immunosuppression of T-cell pro-inflammatory cytokines and increased T-cell granzyme B particularly by peripheral blood CD8+ T cells. Repeated antigen-driven proliferation downregulates T-cell CD28. We hypothesized CD28 downregulation and upregulation of alternate co-stimulatory molecules on CD8+ T cells may be associated with BOS.
Method CD28, alternate co-stimulatory molecules and granzymeB expression and cytokine profiles on CD4 and CD8 T-cell subsets from stable patients, patients with evidence of BOS and healthy controls was determined using flow cytometry.
Results There was a significant increase in the percentage of CD8/28null versus CD4/28null T-cells producing granzyme B, IFNγ, TNFα and IL-2 in BOS compared with stable patients. Downregulation of CD28 was associated with an upregulation of 4–1BB (CD137) on both CD4 and CD8 T-cell subsets. There was a significant correlation between increased CD28null T-cells producing IFNγ, TNFα and IL-2 and time post transplant.
Conclusions BOS is associated with downregulation of CD28 and upregulation of 4–1BB on peripheral blood pro-inflammatory T cells, particularly CD8+ T cells. Therapeutic targeting of T-cell 4–1BB expression and monitoring response using these assays may help manage patients with BOS where current treatments are ineffective and following progress is limited to lung function.
Supported by NHMRC.
Conflict of Interest None.
Nomination Nil.

TO-091

PULMONARY THROMBOEMBOLIC DISEASE IS ASSOCIATED WITH DONOR SPECIFIC ANTIBODIES AFTER LUNG TRANSPLANTATION

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Aim To determine the incidence of clinically significant pulmonary emboli (PE) and deep vein thrombosis (DVT) in lung transplant recipients with circulating donor specific antibodies (DSA).
Method Single centre retrospective review of 83 consecutive lung transplant patients transplanted January 2009–July 2011. The presence of DVT or PE was determined following clinical suspicion of pulmonary thromboembolic (PTE) disease with duplex ultrasonography, computed tomography pulmonary angiography (CTPA) or ventilation/perfusion (VQ) scanning. Circulating DSA was determined by LUMINEX (LabScreen single antigen assay) when antibody mediated rejection (AMR) was suspected.
Results Fifteen out of eighty-three (18%) patients had confirmed PTE (PE $n = 6$, DVT $n = 5$, PE and DVT $n = 4$). Sixty-nine out of eighty-three patients had LUMINEX testing post transplant in whom circulating DSA (MFI > 1000) were detected in 39 (%) during the study period. Twelve out of fifteen patients with PTE had DSA screening within 4 months of their event, which was positive in eight (67%). Within 4 months of PTE 6/7 (86%) patients with PE and 5/9 (56%) of patients with DVT were found to have a positive DSA result. Eight out of thirty-nine (21%) patients with a positive DSA had a PTE event versus 4/30 (13%) with a negative DSA.
Conclusion Lung transplant recipients with circulating DSA appear to have an increased incidence of PTE disease which raises both pathogenic and therapeutic considerations.
Conflict of Interest None.

TO-092

AZITHROMYCIN DECREASES EXACERBATIONS IN NON-CYSTIC FIBROSIS BRONCHIECTASIS

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Aims To determine the effect of azithromycin in patients with non-cystic fibrosis bronchiectasis.
Methods In a randomized, double-blind trial, we randomly assigned 141 patients with bronchiectasis to receive azithromycin (500 mg three times a week) or placebo for 6 months. Patients were followed for an additional 6 months.
Results The annual rate of event-based exacerbations for the 6-month treatment period was 0.59 in the azithromycin group and 1.57 in the placebo group, corresponding to a 62% reduction in the rate of exacerbations with azithromycin (rate ratio, 0.38: $P < 0.001$). For the 12-month period, the annual rate of exacerbations was 1.58 in the azithromycin group and 2.73 in the placebo group (rate ratio, 0.58: $P < 0.001$). Azithromycin, as compared with placebo, also increased the time to the first event-based exacerbation in the first 6 months (104 days vs 21 days; hazard ratio, 0.34; $P < 0.001$) and the time to the first exacerbation in 12 months (239 days vs 85 days; hazard ratio, 0.44: $P < 0.001$). The CRP level was lower in the azithromycin group at 6 months ($P < 0.01$). Symptom-based exacerbation frequency, change in FEV1, SGRQ, 6-minute walk distance, and sputum neutrophils were not significantly different between the azithromycin and placebo groups. Gastrointestinal adverse effects were more common in the azithromycin group ($P < 0.01$).
Conclusions Azithromycin decreased the frequency of event-based exacerbations and increased the time to first exacerbation in patients with non-cystic fibrosis bronchiectasis. A treatment effect on exacerbations was present 6 months after completion of treatment.
Supported by Health Research Council of New Zealand.
Conflict of Interest None.

TO-093

EXERCISE TRAINING IS BENEFICIAL IN NON-CF BRONCHIECTASIS—A MULTI-CENTRE, RANDOMIZED CONTROLLED TRIAL

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Aim To determine whether exercise training improves exercise capacity and quality of life (QOL) in people with non-cystic fibrosis (CF) bronchiectasis.
Methods Participants with non-CF bronchiectasis with a modified Medical Research Council (MMRC) dyspnoea score ≥1 were randomly allocated to receive 8 weeks of supervised exercise training or twice weekly telephone support. Exercise capacity, using the incremental shuttle walk distance (ISWD) and 6-minute walk distance (6MWD), and QOL were measured by a blinded assessor at baseline and following the intervention.
Results Eighty-five participants, aged (mean (SD)) 64 (13) years, FEV_1 74 (22)% predicted and median MMRC score of 1 (IQR 3) were included. Of those in the exercise training group ($n = 42$), 35 (83%) completed the programme. There was a greater magnitude of change in the ISWD (mean difference 62 m, 95% CI 24 to 101 m) and the 6MWD (mean difference 41 m, 95% CI 19 to 63 m) in the exercise training group compared to the control group. Exercise training significantly reduced dyspnoea ($P = 0.009$) and fatigue ($P = 0.01$) but there was no difference in cough-related QOL or mood between groups.
Conclusions Exercise training in non-CF bronchiectasis improves exercise capacity and symptoms of dyspnoea and fatigue. Ongoing follow up will assess changes in these effects over time.
Support Institute for Breathing and Sleep, Sir Charles Gairdner Research Fund, The Alfred Allied Health Research Foundation.
Nominations Physiotherapy Prize.
Conflict of Interest No.

LUNG CANCER SIG: ORAL SESSION

TO-094

PRESENTATION OF PATIENTS WITH LUNG CANCER IN AUCKLAND, NEW ZEALAND: NO IMPROVEMENT 4 YEARS ON

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Aim To compare the results of an audit of patients diagnosed with lung cancer in 2008 in the Auckland area with the findings of a similar audit in 2004, in order to determine if improvements have been made
Methods Cases in 2008 were identified from the New Zealand Cancer Registry and databases of participating primary care organizations within the Auckland and Lakes regions. Patient, tumour and management details were collected from the primary and secondary care medical records. The similar 2004 Auckland audit has been described previously.
Results Distribution of age, gender, ethnicity and tumour type was very similar between the two (slightly different) study populations. In both studies, 85% of patients had a pathological diagnosis of lung cancer made. Comparing 2008 with 2004, the entry route into secondary care was via an acute admission (either self referral or via GP) in 43% vs 37% of cases and via a GP referral to respiratory clinic in 31% vs 28% of cases. Median (IQR) time from presentation to secondary care to diagnosis was 22 (10; 45) days in 2008 and 22 (11; 42) days in 2004. The time remained shorter for cases presenting via ED: 13 (8; 27) days in 2008 and 14 (8;33) days in 2004 and remained longer for Stage I/II cases (39 vs 35 days) than stage III (23 vs 26 days) and IV (14 vs 16 days) cases. Thoracic MDM discussion occurred in 56% of cases in 2008, and 28% of cases in 2004.
Conclusions Apart from a large improvement in the proportion of cases presented at a TMDM, there was no improvement in the presentation pathway, stage at or timeliness of diagnosis of lung cancer in Auckland. The publication and dissemination of the 2004 audit results alone did not lead to improvement in any of these areas. Specific strategies are needed to achieve improvement.
Supported by Health Research Council of New Zealand.
Conflict of Interest No.

TO-095

VOLUME DOUBLING TIME OF NON-SMALL CELL LUNG CANCER: RELATIONSHIPS TO TUMOUR AND PATIENT CHARACTERISTICS

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Aim To correlate patient and tumour characteristics with volume doubling times (VDT) and growth rates (GR) of primary non-small cell lung cancers (NSCLC).
Methods Resected tumours were retrospectively identified from our database. Those which underwent two similar CT scans separated by ≥25 days were selected. Tumour volume was measured manually and using volumetric software. VDT was calculated using the Schwartz equation and GR was defined as 1/VDT. VDT and GR were correlated to patient and tumour characteristics.
Results Forty-six NSCLC (36 adenocarcinomas (AC), six squamous cell (SCC), two large cell and two carcinoids) in 46 patients underwent 109 eligible scans between 2003 and 2011. Median time (range) between scans was 112 days (26–491). Median (range) VDT and GR were 191 days (–9435–2256) and 0.0038 (–0.0086–0.0186) respectively. AC GR (median = 0.0034) was significantly slower than for SCC (0.0103, $P = 0.037$). Nine AC had VDTs > 400 days, three of which (VDT 0 = 450, 597 and 2256) were associated with distant metastasis. GR (median) of AC in smokers (0.0052) was faster than in never-smokers (0.0014, $P = 0.02$). GR was not related to symptoms at diagnosis ($P = 0.16$). A trend to faster GR with larger tumour size was observed, consistent with the exponential model of lung cancer growth.
Conclusions We found NSCLC growth rate to be highly variable and related to histological subtype and smoking history, but not the presence of symptoms at diagnosis. Apparently indolent AC (VDT > 400 days) can metastasize. Significant growth may be detected in as little as 2 months in NSCLC in smokers. This has implications for the assessment of indeterminate pulmonary nodules.
Supported by The Australian Lung Foundation Post-Graduate Grant-in-Aid for Lung Cancer Research 2011.
Conflict of Interest No.

TO-096

FREQUENCY OF NSCLC EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) MUTATIONS IN AN AUSTRALIAN TESTING PROGRAMME

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Introduction The response to inhibitors of the EGFR tyrosine kinase can be predicted by the presence of specific EGFR mutations in Non-Small Cell Lung Cancer (NSCLC). The frequency and pattern of such mutations in Australia is unknown.
Methods In October 2010, AstraZeneca initiated a programme to gather data on EGFR mutation testing outcomes in Australia. Participating laboratories were funded for test costs in return for provision of results. For participating patients, the test charge was fully carried by the programme. Mutation testing was performed using Sanger sequencing. No clinical or personal details were gathered.
Results Five hundred sixty-nine samples were submitted for analysis. Ninety eight (17%) were not evaluable due to absent or inadequate tumour tissue, poor quality or inadequate DNA. In 471 evaluable samples, 96 mutations were detected in 89 samples (18.9%). Thirty-nine samples (8.3%) exhibited exon 19 deletions and 25 (5.3%) the L858R point mutation in exon 21; the most common activating mutations. Exon 20 mutations were seen in 14 samples (3.0%). Three samples showed T790M mutation associated with resistance to EGFR-TKI; one as an isolated abnormality, one with a sensitizing exon 19 deletion and one with a G719S point mutation.
Conclusions Acknowledging the influence of pre-selection of patients in this programme, there was a significant incidence of activating EGFR mutations. EGFR mutation testing is feasible in Australia and can be used to guide initial treatment of patients with advanced NSCLC. Sample quality is important in maximizing test yield.
Conflict of Interest PC and JL are employees of AstraZeneca. BS and MP have participated in advisory boards, and JB has received honoraria from AstraZeneca.

TO-097

FIBROBLAST GROWTH FACTOR-9 IS UPREGULATED AND MAY BE INVOLVED IN MESOTHELIOMA DISEASE PATHOBIOLOGY

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Introduction Malignant mesothelioma (MM) is the cancer of the mesothelium that has no cure. Hence identifying molecules in the pathobiology of MM is needed to develop new therapies and biomarkers.
Methods and Results Our Affymetrix microarray data on 22 prospectively collected human thoracoscopic pleural tissue biopsies showed that fibroblast growth factor-9 (FGF-9) was the leading novel candidate gene with a median overexpression of 17 fold in MM over metastatic pleural carcinomas and benign pleuritis. Our Oxford and Perth cohorts totalling to 1000 pleural fluids showed that pleural fluid FGF-9 levels in MM patients, as measured by ELISA, were significantly higher than in metastatic pleural cancers and benign pleuritis, $P < 0.05$ for both. FGF-9 plays an important role in the pathobiology of MM. Using WST-1 assay, exogenous FGF-9 induces dose-dependent proliferation of both human and murine MM cells. Balb/c mice were inoculated with FGF-9 shRNA knockdown murine MM cells subcutaneously and animal weights and tumour sizes were monitored over time. Tumour growth was significantly retarded in mice inoculated with FGF-9 shRNA knockdown MM cells compared to the scrambled vector MM cells ($P < 0.001$).
Conclusion In summary, MM produces high levels of FGF-9 which potently induces MM cell proliferation and knockdown of FGF-9 retards tumour growth *in vivo.*
Supported by Cancer Council Research Grant.
Conflict of Interest No.

TO-098

DEREGULATED INTERLEUKIN-6 SIGNALLING SUPPRESSES LUNG TUMOURIGENESIS IN MICE INDUCED BY TOBBACO CARCINOGENS

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Aim Serum levels of the potent immunomodulatory cytokine interleukin (IL)-6 are elevated in smokers, and are higher still in those with lung cancer, the leading cause of cancer death worldwide. However, the precise role that IL-6 plays in the pathogenesis of lung cancer remains to be elucidated. Nicotine-derived Nitrosamine Ketone (NNK) is a potent tobacco carcinogen and reliably induces lung tumours in mice. The aim of our study was to examine the effect of deregulated IL-6 signalling on NNK-induced lung carcinogenesis.
Methods We have utilized the $gp130^{F/F}$ mouse which carries a knock-in mutation in gp130, the critical co-receptor for the IL-6 cytokine family, leading to deregulated IL-6 signalling. Specifically, these mice display hyperactivation of the latent transcription factor Stat3 via gp130 in the absence of gp130-mediated PI3K/Akt and Mapk signalling. The $gp130^{F/F}$ and control $gp130^{+/+}$ (wild-type) mice at 6 weeks of age were injected with NNK or PBS and observed over 16 weeks prior to the evaluation of lung tumourigenesis at the cellular (immunohistochemistry, histology) and molecular (immunoblotting, qrtPCR) levels.
Results While no spontaneous lung tumours were observed in either PBS-treated $gp130^{+/+}$ or $gp130^{F/F}$ mice, in response to NNK the absolute number of lung lesions in $gp130^{F/F}$ mice (3.81 ± 0.84;mean ± SEM) was markedly reduced compared to $gp130^{+/+}$ (6.43 ± 1.72) mice. In addition, we also observed a significant reduction in the size of lesions in $gp130^{F/F}$ compared to $gp130^{+/+}$ mice (1.00 ± 0.05 mm vs 0.69 ± 0.05; $P < 0.0001$). Notably, the number and size of lesions in the lungs of NNK-treated $gp130^{F/F}$:$Stat3^{-/+}$ mice displaying genetically reduced Stat3 hyperactivation were comparable to $gp130^{F/F}$ mice.
Conclusions Our data suggest that IL-6/gp130-mediated activation of the PI3K/Akt and/or Mapk pathways, but not Stat3, plays an important role in promoting NNK-induced lung carcinogenesis.
Supported by NHMRC.
Conflict of Interest No.

TO-099

THE VICTORIAN LUNG CANCER REGISTRY PILOT: PURSUING QUALITY IN QUANTITY

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Rationale In Victoria lung cancer is the fourth most common cancer type and the leading cause of cancer mortality. A pressing need therefore exists to understand regional structure, process and outcome in lung cancer care; to drive improvement in quality of care; to inform translational research; and inform health care planning. This project aims to develop and pilot a population-based lung cancer clinical quality registry.
Methods Review of literature and evidence-based national/international clinical practice guidelines was undertaken by an expert working group to define an epidemiologically sound data set constructed to enable the capture of nominated structural, process and outcome indicators. Recruitment via an 'opt-off' system with follow up captured 3 and 12 months after initial diagnosis using validated symptom and quality of life assessments.
Results Ethics approval was received for an initial pilot site in June 2011 and data collection commenced July 2011. Data extractions have provided 24 patients for inclusion in the registry. Institutional sites have been identified and a web enabled data collection tool is in development and data linkage options are being explored.
Conclusion Lung cancer registries have proven capacity for improving outcomes in lung cancer. The development of rapid case ascertainment and 'opt off' recruitment strategies appear viable and should ensure broad recruitment from eligible patients diagnosed with lung cancer in Victoria.
Supported by Victorian Cancer Agency.
Conflict of Interest No.

TO-101

DIAGNOSIS OF SILICOSIS AND LUNG CANCER IN WESTERN AUSTRALIAN GOLDMINERS

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Aim This study aimed to determine whether silicosis diagnosed on x-ray or clinically accounted for the excess lung cancer seen in WA goldminers.
Methods Cumulative exposures to respirable silica were derived based on over 550 dust particle counts taken from mines in WA during the 1950s combined with expert dust exposure rankings for over 400 jobs. Chest x-rays were scored according to the ILO Classification of the Pneumoconioses by 3 trained readers and the median score taken. Mortality and cancer incidence were assessed by linking to the WA Death and Cancer Registries, the National Death Index and the National Cancer Clearing House. The association of silica exposure with incidence of lung cancer was estimated before and after adjustment for both radiographic and clinical silicosis using propensity scores for each of these intervening diseases using age-and year-matched conditional logistic regression analyses.
Results There was a strong and consistent effect of estimated exposure to respirable silica on incidence of silicosis, and a much lesser effect on lung cancer. The presence of silicosis was associated with increased lung cancer mortality whether diagnosed only on x-ray or by the compensation board.
Conclusions Silica is widespread throughout the community and although the International Agency for Research on Cancer has specified that it is a carcinogen only from occupational sources, unnecessary exposure should be controlled.
Supported by Cancer Council of Western Australia, Minerals and Energy Research Institute of WA, NHMRC.
Conflict of Interest No.

OELD/POPULATION HEALTH SIG: ORAL SESSION

TO-100

CANCER INCIDENCE IN INDIVIDUALS EXPOSED TO ASBESTOS IN CHILDHOOD

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Background and Aim Asbestos is known to cause malignant mesothelioma (MM) and lung cancer. It has also been associated with various non-respiratory cancers but the data is less clear. The effect early life exposure to asbestos on respiratory and non-respiratory cancers in adulthood is not known. The aim of this study was to investigate the cancer incidence in adults who had been exposed to asbestos as children. **Methods** The Wittenoom Residents' cohort includes over 5000 people who had lived in Wittenoom, a blue asbestos mining town, between 1950 and 1992. Of that cohort 2483 were children (< 16 years old) when living there. Incident cancers are mandatorily notifiable in Western Australia and data-linkage was used to identify cancer incidence in this cohort. Standardized incidence ratios (SIRs) were calculated for selected cancers using WA age- and calendar-period specific rates.
Results One thousand two hundred four females and 1279 males were children at Wittenoom. The median age of arrival was 3.1 years, with 419 (17%) born there or moved there soon after birth. The median duration of residence was 19 months (IQR 7–41 months). The median age in 2009 was 51.5 years (IQR 46.4–57.3 years). Up until the end of 2009 there were 215 cases of cancer in 207 (114 males) individuals. There were 42 MM (28 male) and 8 lung cancers (3 male). For 'all cancers' SIRs were significantly increased for both males and females, with and without respiratory cancers included. SIRs were elevated for a number of individual cancers but only significantly increased for prostate cancer in males (2.47, 95%CI 1.07–3.86).
Conclusion Early exposure to asbestos causes MM and may also increase the risk of non-respiratory cancers in later life.
Conflict of Interest None.

TO-102

CHARACTERIZING THE RESPIRATORY INFLAMMATORY RESPONSE TO GEOGENIC DUSTS

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Aim To determine the respiratory inflammatory response to geogenic PM_{10} (< 10 μm diameter particulate matter).
Methods Samples were collected from two communities associated with open cut iron ore (Newman) and gold mining activities (Kalgoorlie). The PM_{10} fraction was extracted from the top 2 cm of a 1 m^2 plot at each of the sites. Adult BALB/c mice were exposed to 10, 30 or 100 μg of PM_{10} by intranasal instillation (in 50 μL of saline + 0.05% Tween-80). Control mice received 100 μg of polystyrene beads (2.5 μm or 10 μm) or vehicle alone. Mice were euthanased and bronchoalveolar lavage (BAL) fluid was collected for assessment of inflammation and cytokines (MIP-2, IL-6 and IL-1β) 3, 6, 12, 24 or 168 h post exposure. Metal content in the PM_{10} samples was assessed by ICP-MS and preparations were examined under electron microscopy to obtain particles size distributions.
Results The chemical and physical properties of the geogenic particles varied with considerably more Fe and a much wider particle size distribution in the PM_{10} from Newman. Both geogenic particle preparations resulted in dose dependent increases in neutrophils and cytokines (MIP-2 and IL-6) in the BAL. Quantitatively the kinetics of the response was comparable, however, the magnitude of the response was greater in mice exposed to PM_{10} from Newman. The instillation of 2.5 μm polystyrene beads resulted in a significant neutrophilia comparable to the geogenic response; however, the production of pro-inflammatory cytokines was minimal.
Conclusions The unique physical and chemical properties of geogenic particles induce an inflammatory response in the lung. This has important implications for respiratory health in communities exposed to high particulate loads of geogenic origin such as those associated with open cut mining activities.
Supported by CRC for Asthma and Airways.
Conflict of Interest No.

TO-103

INTERACTIONS ARE PRESENT BETWEEN ACTIVE SMOKING AND ASTHMA ON RISK OF LARGE AND SMALL AIRWAYS OBSTRUCTION

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Aim To examine the impact of a history of asthma and/or active smoking on the development of fixed post-bronchodilator airways obstruction, that is, COPD.
Methods Using the population-based Tasmanian Longitudinal Health Study (TAHS) cohort followed since 1968, an asthma-enriched sub-sample was selected consisting of 67% ever reporting asthma symptoms, of whom 36% had current clinical asthma. Pre- and post-bronchodilator flow volume loops were performed. COPD was defined as post-BD FEV_1/FVC ratio less than the statistical lower limit of normal. Multiple linear and logistic regression was used to evaluate the associations and potential interactions, while adjusting for potential confounders.
Results Of those tested, 92% (n = 1277) had complete lifetime asthma and smoking information as well as acceptable spirometry. The mean age was 44.9 years (range 43–47), and 56% were past or current smokers. Compared to non-asthmatics, childhood-onset current asthmatics were at a 5.5 fold increased risk of having COPD (95%CI 2.5–12), similar to the risk of COPD associated with 40 pack-years of smoking (OR 5.6 (3.3–9.6)). Reductions in FEV_1/FVC were greatest in smokers who also had current asthma (–11% (–14,–8)), significantly more than adding individual smoking (–2.7% (–4.4,–1.1)) and asthma effects (childhood –4.3% (–6.4,–2.3)). A similar interaction was seen with forced expiratory flow ($FEF_{25–75}$).
Conclusion Both childhood-onset current asthma and active smoking contribute substantially to having COPD in middle-age. The presence of an asthma-smoking interaction suggests an extra source of lung function loss, and provides another compelling reason for the smoker with current asthma to quit.
Grant Support NHMRC, APA, ALF.
Conflict of Interest No.

TO-104

THE PREVALENCE OF EMPHYSEMA IS SIGNIFICANTLY LESS THAN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Aim In a middle-aged population, to determine the prevalence of obstructive lung diseases (OLD), including classically defined COPD, small airways obstruction (AO), physiological emphysema and hyperinflation in addition to COPD
Methods Using the population-based Tasmanian Longitudinal Health Study (TAHS) cohort followed since 1968, an asthma and chronic cough-enriched sample was selected consisting of 67% ever with asthma, of whom 36% had current clinical asthma. Pre- and post-bronchodilator (BD) flow volume loops, diffusing capacity (D_{LCO}) and lung volumes were performed and analysed using the statistical limits of normal. COPD was defined as post-BD reduced FEV_1/FVC ratio that is not fully reversible; small AO as reduced post-BD forced expiratory flow at low lung volumes ($FEF_{25–75}$) and physiological emphysema as reduced D_{LCO} with either large AO or small AO with normal FVC. Prevalence and 95% confidence intervals (CI) were calculated while adjusting for sampling fractions.
Results All were of Anglo-Celtic ethnicity with a mean age of 44.9 years (range 43–47, n = 1013). 30% were past smokers, and 27% were current smokers (median (interquartile range) 20(10–29) pack–years). The prevalence of COPD was 6.0% (95% CI 4.5–7.5) with no evidence for a gender difference. This was significantly higher than isolated small AO (0.9% (0.3–1.5)), physiological emphysema (1.2% (0.5–1.8)) and hyperinflation with COPD (1.5% (0.7–2.2)).
Conclusion Our prevalence estimates for OLD are generalizable to middle-age populations of European origin. These results are consistent with recent histopathological evidence that AO precedes emphysematous destruction in COPD.
Grant Support NHMRC, APA, ALF.
Conflict of Interest No.

ASTHMA & ALLERGY SIG: ORAL SESSION 3

TO-105

ASTHMA BURDEN REMAINS HIGH: FINDINGS FROM THE ASIA-PACIFIC ASTHMA INSIGHT AND MANAGEMENT SURVEY

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Introduction Poorly treated asthma is a significant socioeconomic burden in the Asia Pacific region. The level of asthma burden and its determinants are poorly understood.
Aim To assess the burden-of-illness via a randomized face to face or telephone survey of asthma patients (pt) from 9 Asia-Pacific countries in 2011.
Methods Eighty-four thousand households across Australia (Aust), China, Hong Kong (HK), India (In), Malaysia (My), Singapore (Sin), S Korea, Taiwan and Thailand (Thai) were screened; ≈3600 households with asthma pt ≥ 12 years identified (Aust: n = 403, mean age 45, F:M 1.8). Survey had 52 questions and eight domains: general health, history/diagnosis, symptoms, exacerbations, burden, management, treatment, and pt attitudes.
Results Significant functional/emotional limits were identified in all countries. In 78% of pts missed work/school in the last year due to asthma, then China 59%, My 52%, Sin 48%, Taiwan 44%, Thai 37%, HK 29%, Aust 24% and S Korea 13%. India and Australia had the most subjects with asthma symptoms on most days (30.8 & 28.3%) and nights (14.9 & 10.2%) in the last month. Asthma control was always overestimated (Aust 78, India 31; all countries 51%). Thirty-five percent of Aust used oral steroids in last year; Forty-three percent concerned re inhaled steroids and 14% felt asthma impacted on control of their life.
Conclusions Asthma burden remains high despite effective treatments and management guidelines. There is substantial variation in asthma burden between countries; and Australia still has a significant number of patients with poor control.
Supported by Merck, Sharp, and Dohme (MSD) Corp.
Awards None sought.
Conflict of Interest None.

TO-106

INTRAVENOUS SALBUTAMOL FOR FIRST PRESENTATION OF ASTHMA: DEFINING THE PHENOTYPE AND COMPARING MANAGEMENT

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Aim To compare and contrast the characteristics and management of children treated with IV salbutamol for their first presentation of wheeze with known asthmatics.
Methods A retrospective audit of all children treated with IV salbutamol at Sydney Children's Hospital between 1 January 2007 and 31 December 2008 was conducted. Children with pre-existing significant cardiopulmonary conditions were excluded. Children were categorized as Newly Diagnosed Wheezers (NDW) if they had never been treated with salbutamol or inhaled corticosteroids, and did not have a doctor diagnosis of asthma.
Results Compared to the 28 NDA children, the 143 Known Asthmatics (KA) were significantly older (mean (SD) 3.80 (2.57) vs 5.33 (3.42) years, $P = 0.03$). There were no significant difference in most of the background risk factors, including family history of atopy (76.7% vs 78.6%), history of eczema (43.3% vs 44.8%), and allergic rhinitis (16.7% vs 23.1%). There was no significant difference between the time when IV salbutamol was started (5.89 (3.85) h vs 6.78 (8.3) h), total duration of IV salbutamol (27.45 (16.09) h vs 30.40 (20.73) h), and the total length of stay in hospital (77.13 (25.60) h vs 86.79 (33.59) h). Interestingly, 26/28 (92.8%) NDW children were discharged home on a controller. Out of the 26 children, 2 (7.1%) were on Montelukast, 24 (85.7%) on Fluticasone, including 5/24 (19.2%) on high dose Fluticasone (> 250 mcg/day), 19/24 (73.1%) on low dose Fluticasone. Two had no controllers commenced.
Conclusions NDW children are no different to KA in their background characteristics and management of their acute asthma presentation. However, the appropriate discharge therapy for NDW remains a management dilemma.
Supported by N/A.
Nomination N/A.
Conflict of Interest None.

TO-107

INCREASED BRONCHODILATOR RESPONSE USING FORCED OSCILLATION TECHNIQUE (FOT) WITH RECENT SYMPTOMS IN YOUNG CHILDREN WITH ASTHMA

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Introduction Use of FOT to assess lung function in young children is increasingly reported in the clinical setting. However, associations between bronchodilator responsiveness (BDR) as assessed by FOT and symptoms in young children with asthma have not been reported. We investigated the relationships between respiratory symptoms and BDR in young children with asthma.
Method Children aged 3 to 6 years with asthma were recruited. FOT (Resistance and reactance at 8 Hz: Rrs8 and Xrs8, respectively) and area under reactance curve (AX) was measured prior to and 15 min following Salbutamol (600 μg) inhalation. The BDR was assessed using the relative changes in Rrs8, Xrs8 and AX. Respiratory symptoms in the month prior to visit were obtained using daily diary card. We used regression analyses to assess the impact of symptoms on the relative BDR in Rrs8, Xrs8 and AX.
RESULTS Pre- and post BD Rrs8 and Xrs8 data were obtained from 83 children and AX in 60 of those children. There were no differences in BDR for Xrs8 with any reported symptoms. In contrast, Rrs8 and AX after BDR was significantly larger ($P < 0.05$) in children reporting wheeze that required relievers in the month prior to FOT testing.
Conclusion In children with asthma increasing symptom incidence requiring reliever use is associated with an increased BDR in Rrs8 and AX. These data suggest that symptoms in early childhood asthma result in alterations in conducting and non-conducting airway function.
Funded by Scholarship funding Ministry of Higher Education United Arab Emirates.
Conflict of Interest No.

TO-108

MODIFICATION OF THE EFFECT OF FLG ON ALLERGIC DISEASE RISK BY MATERNAL SMOKING AND SIBLINGS

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Background Filaggrin (FLG) null alleles have been found to confer an increased risk of childhood atopic dermatitis (AD) and also asthma, but the latter only in children with AD. The aims of this study were to examine the association between FLG and allergic disease in a cohort followed from childhood into middle-age.
Methods TAHS is a longitudinal population-based family study commenced in 1968 with $n = 8583$ children born in 1961, their parents and siblings ($n = 21036$). A postal survey and subsequent clinical visit was conducted of all probands and siblings in middle-age. Information on AD, asthma and hay fever has been collected prospectively. The R501X, 2282del4, R2447X and S3247X FLG null variants were genotyped. Multivariable logistic regression models with robust variance estimates were used to accommodate the possibility of residual correlation within families.
Results The combined carrier frequency of the FLG null mutations was 10.8%. Being a carrier of at least 1 FLG null mutation was associated with a significantly increased risk of childhood flexural eczema OR = 2.94,95%CI 2.14,4.04). There was also an increased risk of childhood asthma in those with the FLG null mutations (1.34, 1.01–1.78) and ever asthma reported in adult life (1.33, 1.02–1.72). In these data maternal smoking and having more than two siblings modify the association between FLG and eczema.
Conclusion FLG null mutations are associated with eczema from childhood into adult life. This relationship is influenced by other modifiable lifestyle factors, which has important implications for clinicians and patients, as it suggests possible preventive strategies.
Grant Support NHMRC.
Conflict of Interest No.

TO-109

ASTHMA CONTROL IS ASSOCIATED WITH BLOOD GRANULOCYTE PATTERNS IN A POPULATION COHORT SAMPLE

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Background Improved clinical phenotyping with simple measures may assist in better targeting of asthma management. Although sputum measures associate with asthma control and assist therapy decisions it is less clear if more easily obtained routine blood tests associate with control. Our aim was to determine the relationship between recent asthma control and blood granulocyte patterns in participants with asthma in the representative population North West Adelaide Health Study (NWAHS).
Methods Clinic assessment ($n = 2487$) included the Asthma Control Questionnaire (ACQ), pre- and post-bronchodilator spirometry, anthropometry, skin prick testing, and self-reported doctor diagnosed asthma, smoking and sociodemographics. In a blood sample Eosinophilia was classified as blood eosinophils (EOS) $\geq 250/mm^3$ and Neutrophilia as neutrophils (NEU) $\geq 5000/mm^3$.
Results In subjects with self-reported asthma ($n = 281$, 11.3%), eosinophilia was present in 42.4% ($n = 118$) and neutrophilia in 30.1% (84). Asthma control was significantly associated with age < 60, university education, higher household income and normal body mass index but not with sex, atopy or smoking status. Well-controlled asthma varied by blood granulocyte patterns, and was identified in the following patterns EOS low/NEU low 77.4%, EOS low/NEU high 43.8%, EOS high/NEU low 40.0%, EOS high/NEU high 32.1%, respectively ($P < 0.001$). In multivariable logistic regression, well-controlled asthma was significantly associated with the EOS low/NEU low pattern (OR 5.23, 95%CI 1.76–15.5).
Conclusion Measures from routine blood tests of granulocytes were strongly associated with recent asthma control. Studies to assess the value of therapy guided by blood testing may be warranted.
Support Adelaide University, SA Department of Health,
Conflict of Interest No.

TO-110

INFLAMMATORY SUBTYPES OF UNCONTROLLED ASTHMA IN AUSTRALIA

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Aim To characterize inflammatory subtypes of uncontrolled asthma in Australia using clinical, physiological and inflammatory data from multiple sites.
Methods Non-smoking adults (n = 210) were assessed for the AMAZES study, a multi-centre RCT evaluating add-on azithromycin for asthma, in five tertiary centres across Australia. Subjects had symptomatic asthma despite maintenance ICS/LABA. They underwent clinical assessment and induced sputum cell counts.
Results Subjects had a mean age of 58 years (range 19–86), high levels of atopy (76%), mild airflow obstruction (mean FEV_1 73% pred.) and uncontrolled symptoms (mean ACQ 1.8), despite a mean total daily ICS dose of 1538 mg. Ex-smokers (36%) had a median of 11 pack years. The inflammatory subtype was classified as eosinophilic (in 40%), neutrophilic (16%), paucigranulocytic (35%) and mixed granulocytic (9%). Neutrophilic asthma ranged from 11–20% of patients across the sites. There was no difference in the proportion of each inflammatory subtype across Australia.
Conclusion Inflammatory subtypes of uncontrolled asthma occur in similar proportions across Australia, with more than 50% of patients exhibiting non-eosinophilic inflammation. There was no significant difference in clinical characteristics between the inflammatory subtypes including total daily ICS dose and smoking history.
Supported by NHMRC.
Conflict of Interest No.

CYSTIC FIBROSIS SIG: ORAL SESSION

TO-111

VIRAL INFECTIONS TRIGGER CF EXACERBATIONS AND WORSEN INFECTION WITH P AERUGINOSA IN ADULTS AND CHILDREN

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Aims This study aimed to assess the prevalence of viral respiratory tract infection in an adult population with cystic fibrosis (CF), and to compare this to children with CF and assess the impact in terms of clinical outcomes and chronic bacterial infection.
Methods Seventeen adults and nine children from CF clinics were recruited. Participants were assessed at baseline and reviewed every 3 months for 1 year. They contacted researchers when they developed an increase in chest or cold symptoms.
Results Participants reported 56 episodes of an increase in chest symptoms or colds, 26 (46%), met the definition of an exacerbation, 17 (65%) of these exacerbations were associated with virus detection. The most common virus isolated was rhinovirus. Virus infection was an independent predictor of exacerbation along with lower FEV1, lower BMI, the presence of *P Aeruginosa* and diabetes. Influenza and a greater fall in FEV1 were associated with an increased risk for hospitalization. While increased frequency of exacerbations and infection with influenza were associated with a greater decline in FEV1 over 12 months.
Conclusions Viral infections are frequent triggers for exacerbations in both adults and children. Strategies need to be considered to reduce their impact.
Supported by Cystic Fibrosis Australia.
Conflict of Interest No.

TO-112

DISTRIBUTION OF VIRULENCE GENES OF *STAPHYLOCOCCUS AUREUS* ISOLATED FROM YOUNG PATIENTS WITH AND WITHOUT CYSTIC FIBROSIS

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Aim To compare the distribution of *S. aureus* virulence genes among isolates from patients with and without CF.
Methods Strains isolated in patients with CF from bronchoalveolar lavage, sputum and throat swabs and non-CF patients collected from a community and hospital surveillance programme were screened for the presence of selected virulence genes by PCR. A panel of 10 genes was chosen used in *S. aureus* identification (*nuc*), bacterial adhesion (*clfA, clfB, cna, ica*), toxin production (*pvl, hla, sek*), virulence gene regulation (*sigB, walK/R*) and cell wall modification (*sceD*). Chi-squared analysis was used to determine if there was a statistical significance ($P < 0.05$) in the presence of virulence factors between CF and non-CF isolates.
Results A total of 155 isolates were tested from 124 paediatric patients. All isolates were confirmed as *S. aureus* by the presence of *nuc* gene. Virulence genes *clfA, clfB, ica, hla, walKR* and *sceD* were commonly found in the majority of isolates. Virulence genes *pvl* and *sek* were absent in the majority of *S. aureus* isolates. Virulence gene *cna* was found to be more prevalent in CF lower airway isolates (31/39, 80%) compared to non-CF isolates (32/82, 39%) ($P < 0.001$).
Conclusion Of the virulence genes tested, the *cna* gene, which encodes a collagen binding protein, was significantly more common in CF *S. aureus* isolates to non-CF *S. aureus* isolates. This factor may play an important role in bacterial adhesion in the CF airway.
Conflict of Interest None.

TO-113

HETEROGENEITY OF SHARED *P. AERUGINOSA* (*PA*) STRAINS ACROSS STATES AND CENTRES IN CYSTIC FIBROSIS

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Background A recent prevalence study of 983 Australian CF patients found > 60% of patients (18 CF centres) had shared *Pa* strains. Although most shared strains involved small clusters and few CF centres, AUST-01 and AUST-02 were highly prevalent. It is unclear if prevalence relates to geographic location and/or local infection control.
Aims (i) To examine strain diversity between centres and regions; and (ii) to study the impact of infection control practices on strain prevalence.
Methods Geographic locations, centre-based infection control practices and molecular surveillance strategies were reviewed.
Results AUST-01 and AUST-02 prevalence ranged from 0–47% and 0–80%, respectively. In some cities rates were markedly different, yet across the country were often similar. Paediatric centres employing strict infection control practices showed lower shared strain rates.
Conclusions Marked heterogeneity in shared strain rates was not entirely explained by CF centre location. The introduction of strict infection control does appear to impact the potential for cross-infection of highly prevalent shared strains.
Support by NHMRC, OHMR, RCH & TPCH Foundation, ACFRT.
Nominations Nil.
Conflict of Interest No.

TO-114

IRON SUPPLEMENTATION AND DEFECTIVE IRON HOMEOSTASIS ARE ASSOCIATED WITH WORSE LUNG FUNCTION IN CYSTIC FIBROSIS (CF)

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Introduction Iron deficiency (ID) in CF is difficult to diagnose due the effects of chronic sepsis on biochemical indicators of iron stores. There is a risk that iron supplementation (IS) in patients are not 'truly' iron deficiency may promote infection by iron requiring bacteria. Soluble Transferrin receptors (STfR) are unaffected by infection. In other chronic diseases a STfR/Log_{10}Ferritin (STfR ratio) > 2 accurately predicts true ID. The iron withholding response to infection is normally coordinated by the regulatory protein, Hepcidin.
Aims To examine the efficacy of STfR ratio in diagnosing true ID in adult CF patients and to examine the relationship between IS, hepcidin, sputum iron content and microbial diversity as well as clinical outcomes.
Methods Blood from adult CF patients was analysed for indices of iron status and haemoglobin. Sputum was collected from IS patients for determination of iron content and microbiology.
Results Eighty-six patients were recruited. Only two patients were ID by STfR ratio. IS patients (15%) had lower FEV_1 % predicted (38% vs 53% $p < 0.05$), and BMI despite similar Hb and STfR ratio (1.3 vs 1.3). When IS patients were excluded, anaemic patients (30%) had lower TS and iron, and higher CRP and SfTR ratio (0.7 vs 1.3, $P < 0.05$), but the SfTR remained in the normal range. Initial hepcidin results suggest a weak correlation with FEV1 during exacerbation ($r^2 = 0.114$, $P < 0.05$).
Conclusion ID in CF is over diagnosed by conventional iron studies. IS patients have lower BMI's and lung function. Hepcidin response may predict outcomes in exacerbating patients. Correlation of iron indices with sputum iron content and microbial diversity is ongoing, as is the impact of withdrawal of IS.
Nomination No.
Conflict of Interest No.

TO-115

EARLY CT-DETECTED BRONCHIECTASIS IN YOUNG CHILDREN WITH CYSTIC FIBROSIS DISPROPORTIONATELY AFFECTS THE RIGHT LUNG

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Background Traditional teaching suggests that cystic fibrosis (CF) structural lung disease preferentially affects the upper lobes. This study aimed to determine whether early structural disease, particularly bronchiectasis, is more common in the upper lobes in young children with CF from a newborn screened population.
Methods Sixty-two children with CF age 1–6 years underwent volumetric chest CT scans while clinically stable. Each lobe was scored for presence and extent of bronchiectasis and mucous plugging (inspiratory scans), and air trapping (expiratory scans). Intraobserver reliability was determined after rescoring 30 scans and calculating kappa coefficients of agreement for presence and intraclass correlation coefficients for extents. Differences in the prevalence and extent of abnormalities between regions were determined using McNemar's test, Wilcoxon's signed-rank test and Cochran's Q test. Relationships between disease components were examined using logistic regression and Goodman-Kruskal's Gamma.
Results Intraobserver reliability was good to very good. Bronchiectasis was more common in the right lung (right 95%, left 68%, $P = 0.003$), while mucous plugging ($P = 0.028$) and air trapping ($P < 0.001$) were more common in lower lobes. Strong relationships were detected between different structural lung disease components.
Discussion Early CF bronchiectasis is more common in the right lung without an upper lobe predominance, contrasting with traditional teaching. If, as previously hypothesized, the observed right lung predominance relates to subclinical aspiration, it may have implications for early life management of infants with CF.
Supported by CFFT, NHMRC, UWA, ACFRT, CFWA.
Conflict of Interest No.

TO-116

SOCIAL PARTICIPATION AND SOCIAL SUPPORT IN ADULT CYSTIC FIBROSIS: IMPORTANT QUALITY OF LIFE DETERMINANTS

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Introduction Treatment advances in Cystic Fibrosis (CF) have ensured that survival in CF has been substantially prolonged such that this disease is now becoming a disease of adulthood. While survival is quantitatively extended it becomes increasingly important to ensure similar qualitative improvement and understanding of the determinants of quality of life (QoL). This study aimed to examine the impact of social participation and social support on QoL in adults with CF.
Methods A cross-sectional, questionnaire-based survey was performed on patients attending the adult CF service, Alfred Hospital, Melbourne Australia between January 2009 and July 2011. Subjects completed the Adult Accomplishment in CF Questionnaire, the SF-36 (generic QoL measure) and the CF-QoL (CF-specific QoL measure).
Results One hundred twenty-six participants completed questionnaires, female (61), mean (SD) age 31.3 (9.1), FEV_1 % predicted 57.4 (23.6) and BMI 21.9 (2.8). Sixty-four percent of subjects were in relationships, 28% were married and 17.5% had children. QoL was enhanced in those who were; a member of a social group or club ($p < 0.01$), in a relationship ($P < 0.05$), in an emotionally and sexually fulfilling relationship ($P < 0.02$) and was enhanced independent of medical variables in those with high participation in sports ($P < 0.02$) and social outings ($P < 0.006$) and those who had someone to rely on ($P < 0.02$).
Conclusions CF patients are living longer and carry significant co-morbidity into adult life. Measures of social participation and social support appear to positively impact QoL in adults with CF. The development and maintenance of sustaining relationships and social engagement may well broadly enhance QoL in adult CF and these findings may support psychosocial inquiry and potential intervention in this chronic disease.
Conflict of Interest No.