

## TSANZ POSTER ABSTRACTS

## ASTHMA &amp; ALLERGY SIG: POSTER SESSION 1

P001

ROLE OF *CD14* METHYLATION IN IGE LEVELS IN 'EAST-WEST' KARELIAN CHILDREN

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**Rationale** DNA methylation, a key epigenetic mechanism that controls gene expression has the potential to modulate gene-environment interactions that are involved in the pathogenesis of complex diseases such as asthma & allergy. The aim of this study is to assess the role of *CD14* methylation in determining the differences in IgE levels used as a surrogate for the high allergy disparity observed in the genetically similar Karelian population east and west of the Finnish-Russian border.

**Methods** Methylation levels of *CD14* gene were determined in 30 children with high and low IgE levels in each of the Finnish-Russian Karelian populations. DNA samples from the 120 individuals were bisulfite-converted and either Sanger-sequenced or pyrosequenced to examine a total of 89 CpG sites. In total, the level of methylation was determined for 25 CpG sites by pyrosequencing.

**Results** High levels of methylation were found in the promoter CpG sites, in contrast to the intragenic CpG island, where the majority of sites were unmethylated. For one of the promoter CpG sites which itself is a single nucleotide polymorphism (SNP) (rs2569191:–1145CT) that is in linkage with a functionally important SNP (rs2569190:–159/–260CT), Russian Karelian children with high IgE were found to have higher levels of methylation (98.1%) than children with low IgE (89.3%,  $p = 0.012$ ). No differences in methylation were detected between Finnish and Russian children.

**Conclusion** Methylation levels in *CD14* cannot explain the disparity in allergy between Finnish and Russian Karelians. However, the higher methylation in Russian children with high IgE indicates a possible role of *CD14* promoter methylation in allergy.

**Supported by:** NHMRC.

**Conflict of Interest** Nil.

P002

## TISSUE-SPECIFIC EXPRESSION OF LEUKOTRIENE B4 RECEPTOR

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**Background** Leukotrienes are pro-inflammatory lipid mediators that play an important role in inflammation, particularly in asthma. Leukotriene-B<sub>4</sub> (LTB<sub>4</sub>) is produced by leukocytes and acts as potent chemoattractant, activator and survival factor. BLT1 is a high affinity, highly specific LTB<sub>4</sub> receptor of which alternative splicing results in three isoforms, with the full-length protein being the only functional form. The two truncated splice variants lack domains that are necessary for LTB<sub>4</sub> receptor binding, acting as regulators/inhibitors of the receptor. This may lead to tissue-specific responses to LTB<sub>4</sub>.

**Aim** Characterize specific expression of functional and non-functional forms of BLT1 in different tissues and cell types involved with asthma pathophysiology.

**Methods** Total mRNA was isolated and gene expression of BLT1 transcripts was assessed by RT-PCR using different primer sets along the BLT1 gene to identify wild-type and splice variant transcripts. Total cellular protein was extracted and Western blotting performed to identify the three BLT1 isoforms.

**Results** Full-length and truncated BLT1 expression is varied in different cell types at both the mRNA and protein level. A novel BLT1 splice variant was identified in HL-60 cells differentiated into neutrophilic phenotype. *In silico* analysis indicates that this new splice variant encodes a non-functional protein. Preliminary results indicate the most abundant transcript to be wild-type. Monocytes and granulocytes also appear to express higher levels of full-length BLT1 as well as the novel splice variant compared to epithelial and smooth muscle cells.

**Conclusions** The variations in BLT1 splice variant expression may be important in the disease state and needs to be further investigated to assess the functional significance of this finding for possible use in novel asthma therapies.

**Nomination** TSANZ Travel Award.

**Conflict of Interest** No.

P003

LYMPHOTOXIN- $\alpha$  POLYMORPHISMS AND LUNG FUNCTION INDICATE GENE-ENVIRONMENT INTERACTIONS IN INUIT

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**Aim** To investigate the genetic effects on lung function and allergic conditions of the 8 asthma candidate genes, in Greenlander Inuit and first generation immigrant Inuit residing in Denmark.

**Methods** Nineteen single nucleotide polymorphisms (SNPs) in the 8 genes have been genotyped from 625 Greenlander Inuit and 680 Danish Inuit. Regression analyses were employed to investigate genetic associations in the population.

**Results** We found in Greenlander Inuit that individuals with homozygous CC in *lymphotoxin- $\alpha$*  (*LT- $\alpha$* ) SNP rs1041981 had significantly increased lung function (mean FEV<sub>1</sub> 3.22 l, 95% CI 3.07 to 3.38 l; mean FVC 4.12 l, 95% CI 3.93 to 4.31 l), compared with homozygous AA individuals (mean FEV<sub>1</sub> 2.92 l, 95% CI 2.76 to 3.08 l,  $P = 0.048$ ; mean FVC 3.65 l, CI 3.44 to 3.85 l,  $P = 0.011$ ). Likewise, individuals homozygous TT for *LT- $\alpha$*  SNP rs909253 had significantly increased FVC (mean 3.23 l, 95% CI 3.07 to 3.39 l) compared with homozygous CC individuals (mean 2.94 l, 95% CI 2.78 to 3.10 l,  $P = 0.013$ ). However, we did not find similar relationships in Danish Inuit. For SNPs in the other 7 genes, we did not identify a significant association with lung function.

**Conclusion** *LT- $\alpha$*  polymorphisms of rs1041981 and rs909253 were significantly associated with lung function in Greenlander Inuit but not in the Danish Inuit. As the two populations have a similar genetic background, with no evidence for population stratification on allele frequencies, this suggested a genotype interaction with an environmental factor present in Denmark and not active in Greenland.

**Conflict of Interest** No.

P004

## MICROARRAY ANALYSIS OF THE EPITHELIUM FOLLOWING ALLERGEN CHALLENGE IN A SHEEP MODEL OF ASTHMA

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Aberrant signalling by the epithelium is believed to contribute to both the development and progression of asthma. By sampling the epithelium at a number of time points post house dust mite (HDM) exposure, we were able to analyze the temporal changes in epithelial gene expression in a sheep model of asthma.

**Methods** Merino-cross lambs with high HDM-specific serum IgE levels received weekly intra-lung challenges with HDM allergen. The left caudal lobe received HDM challenges while the right caudal lobe was left untreated. Bronchial epithelium brushings were collected at week 17 of the trial: 1, 2 and 7 days post-HDM challenge. Microarray analysis was performed on  $n = 4$ .

**Results** Approximately 1000 genes were differentially expressed at 1, 2 or 7 days following HDM challenge compared with the control segment ( $p < 0.05$ ). Proliferation and cell cycle associated genes were upregulated at day 1, but not at other time points. Notably at day 2 was the increased expression of cKIT compared with all other time points. The expression of tight-junction and associated genes, and genes relating to vasculature development were differentially expressed across all three time points compared with the control segment. Pathway enrichment software identified a number of related genes, such as those in the TGF- $\beta$  superfamily, that are currently poorly characterized in asthma and may warrant further study in this model.

**Conclusions** The observed similarities in gene expression between the current study and the human disease, demonstrates the utility of the sheep model in studying the asthmatic epithelium remodelling.

**Conflict of Interest** None.

P005

**PLACENTAL MICRORNA EXPRESSION IN PREGNANCIES COMPLICATED BY ASTHMA AND ASTHMA EXACERBATIONS**

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**Background** MicroRNAs (miRs) are non-coding small RNAs that act as important post-transcriptional regulators of gene expression. We have previously identified sex specific differences in placental gene expression associated with strategies for optimal growth and fetal survival in the presence of maternal asthma. The aim of the present study was to determine if there are any differences in placental miRs between male and female placentae in the presence of asthma and asthma exacerbation.

**Methods** RNA was extracted from male (n = 6) and female (n = 6) placenta from pregnancies complicated by asthma and miR analysis was conducted. miRGEN database was used to identify miR predicted targets. Ingenuity Pathways Analysis (IPA) software was used to identify functional networks.

**Results** Seventy five miRs were differentially expressed between male and female placentae (P < 0.05). Maternal asthma exacerbation was associated with 24 differentially expressed miRs in female placenta compared with males. This included miR-203 and miR-223 which has been associated with chronic inflammatory diseases and cytokine response. Pathway analysis identified networks involved in glucocorticoids receptor signalling, cytokine signalling, apoptosis, cellular growth and differentiation.

**Conclusions** There are differentially expressed miRs in male and female placenta in pregnancies complicated by asthma and also in an event of an exacerbation, which target genes involved in cytokine expression and other immune pathways in the placenta. This may be related to the differential gene regulatory mechanisms initiated by males and females in-utero for growth and survival.

**Supported by** Florey Medical Research Foundation.

**Nomination** No.

**Conflict of Interest** No.

P007

**EPIGENETIC ALTERATIONS IN INFANTS ASSOCIATED WITH MATERNAL ASTHMA DURING PREGNANCY**

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Maternal asthma is a risk factor for the development of childhood asthma. Epigenetic changes, such as DNA methylation, refer to heritable changes in gene expression that occur without direct modification of the DNA sequence, and represent genomic adaptation to environmental exposures.

**Aim** To investigate changes in DNA methylation of infants from mothers with and without asthma during pregnancy.

**Methods** Peripheral blood was collected from 12 month old infants born to women with (n = 25) and without (n = 15) asthma. DNA was extracted, bisulfite converted, and hybridized to Illumina's Infinium Methylation27 arrays. CpG loci in autosomal genes were classified as differentially methylated at 99% level (p < 0.01, DiffScore > 22).

**Results** There were 159 CpG loci that were significantly differentially methylated in infants due to maternal asthma. Of these, 12 CpG loci (11 genes) had a change in methylation of 10% or higher. Seven genes (*C14orf152*, *MGC3207*, *PIWIL1*, *CHFR*, *DEFA1*, *MRPL28*, *STK6*) had increased methylation and 4 genes (*NAP1L5*, *MAPK8IP3*, *ACAT2*, *FLJ32569*) had decreased methylation. Methylation of *MAPK8IP3* was significantly negatively correlated with maternal blood eosinophils (r = -0.38; p = 0.022), maternal eNO (r = -0.44; p = 0.005), and maternal serum total IgE (r = -0.39, p = 0.015). Methylation of *STK6* negatively correlated with maternal haemoglobin (r = -0.43; p = 0.008), as well as the infants height (r = -0.51; p < 0.001) and weight (r = -0.36; p = 0.021).

**Conclusions** Changes in the DNA methylation of peripheral blood of 12 month old infants are associated with maternal asthma during pregnancy.

**Supported by** TSANZ Grant in Aid for Paediatric Respiratory Research.

**Conflict of Interest** Nil.

P006

**MICRORNA INHIBITION IN NEONATAL CHLAMYDIA LUNG INFECTION PREVENTS INFECTION-INDUCED LUNG PATHOLOGY IN LATER LIFE**

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**Background** Early-life respiratory infections lead to chronic respiratory disease and *Chlamydia* infections are commonly linked with neonatal pneumonia, permanent deficits in pulmonary function and the induction of asthma. Using mouse models of neonatal, infant and adult *Chlamydia* lung infections we have previously shown that neonatal infections induce airways hyper-responsiveness (AHR) and permanent destruction of parenchymal architecture.

**Aim** To characterize the microRNA expression profile induced in response to early-life *Chlamydia* lung infection and to determine their functional relevance in the induction of infection-induced pathologies through therapeutic inhibition.

**Methods** Using array-based microRNA profiling we identified pathogenically overexpressed microRNAs in neonatal *Chlamydia* lung infection and inhibited their activity *in vivo* using microRNA-specific antagonists.

**Results** We show that five microRNA signatures that are overexpressed in response to neonatal *Chlamydia* lung infection play functional roles in the development of several key pathophysiological outcomes. Therapeutic *in vivo* inhibition of these microRNAs during an ascending infection protect neonatally infected mice from disease features including, but not limited to; pulmonary inflammation (BALF), reduced baseline lung function, AHR and emphysema-like alveolar enlargement.

**Conclusions** Our findings suggest that the inhibition of specific microRNA signatures during a viable neonatal *Chlamydia* lung infection can have protective effects against the development of several key infection-induced pathophysiological outcomes in later life.

**Supported by** NHMRC & CRCAA.

**Nomination** TSANZ Travel Award.

**Conflict of Interest** No.

P008

**EARLY LIFE EXPOSURE TO ENVIRONMENTAL PARTICULATES PREDISPOSES TO DEVELOPMENT OF ASTHMATIC INFLAMMATION**

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**Introduction** Epidemiological studies suggest that childhood exposure to environmental particulates increases the risk of development of asthma. We sought to investigate the ability of ambient environmental particulates to contribute to sensitization via the airways, and thus to the pathogenesis of childhood asthma.

**Methods** We devised a novel model in which weanling BALB/c mice were exposed to ambient particulate pollutants and ovalbumin for sensitization via the respiratory tract, followed by chronic inhalational challenge with a low mass concentration of the antigen. We examined whether these particulates caused oxidant injury and activation of airway epithelial cells (AEC) *in vitro*. We also assessed the potential benefit of minimizing oxidative stress to AEC during sensitization and challenge, by dietary intervention.

**Results** Asthmatic inflammation developed only in animals which received particulates at the same time as respiratory sensitization, and were then chronically challenged with allergen. Ambient particulates induced oxidative stress and pro-inflammatory/pro-Th2 cytokine production by AEC, both *in vitro*, and *in vivo*. Early-life dietary supplementation with anti-oxidants did not prevent the development of an asthmatic inflammatory response.

**Conclusions** Injury to airway epithelium by ambient environmental particulates in early life promotes development of asthmatic inflammation in sensitized and antigen-challenged mice.

**Supported by** National Health & Medical Research Council of Australia.

**Nomination** Janet Elder International Travel Award.

**Conflict of Interest** No.

P009

### MACROLIDES SUPPRESS KEY FEATURES OF EXPERIMENTAL STEROID-SENSITIVE AND STEROID-RESISTANT ASTHMA

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**Background** Steroid-resistant asthma is an important clinical problem and effective therapies are urgently required. Macrolides have been shown to be efficacious in the treatment of steroid-resistant forms of asthma. However, how these immunomodulatory antibiotics induce their effects is not known.

**Aim** To determine and compare the efficacy of macrolide vs  $\beta$ -lactam therapy in suppressing allergic and inflammatory responses in experimental steroid-sensitive and steroid-resistant asthma.

**Methods** Using mouse models of *Chlamydia* and *Haemophilus* lung infection and ovalbumin-induced allergic airway disease (AAD) we have previously shown that both infections induce airways hyper-responsiveness (AHR) and neutrophilic inflammation in AAD that is resistant to steroid treatment. In the current study the effects of clarithromycin vs amoxicillin on immune responses in Th2-associated, steroid-sensitive eosinophilic and Th1/Th17-associated infection-induced, steroid-resistant neutrophilic AAD was assessed.

**Results** We show that clarithromycin, but not amoxicillin, treatment reduces AHR and inflammation in both steroid-sensitive and steroid-resistant AAD. Furthermore, clarithromycin is capable of reducing a number of Th1, Th2 and Th17-associated immune factors. Significantly, treatment reduced Th2-associated factors in steroid-sensitive AAD and Th1/Th17-associated factors in infected-induced, steroid-resistant AAD.

**Conclusion** These findings suggest that macrolide treatment can have broad anti-inflammatory effects on immune responses in the asthmatic lung and that the specific immune responses that are suppressed may be dependent on the responses that predominate during disease.

**Supported by** Asthma Foundation NSW, NHMRC.

**Conflict of Interest** No.

WITHDRAWN

P011

P010

### CCL7 (MCP-3) MEDIATES RHINOVIRUS-INDUCED LUNG INFLAMMATION AND EXACERBATION OF ALLERGIC AIRWAY DISEASE

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**Background** We identified CCL7 as one of the most upregulated transcripts in gene expression profiling of lungs from mice infected with Rhinovirus (RV) 1B.

**Aim** To characterize the role of CCL7 in RV1B infection and exacerbation of allergic airways disease.

**Methods** Naïve and allergic House dust mite (HDM)-challenged mice were infected with  $1 \times 10^7$  TCID<sub>50</sub> RV1B. Prior to this mice were administered either a CCL7-neutralizing antibody or a species-matched isotype control. Airways hyperreactivity (AHR) was invasively assessed following infection by transpulmonary resistance in response to increasing methacholine challenge (Buxco). Inflammation was assessed by enumeration of bronchoalveolar lavage (BAL) cell populations and fluorescence-activated cell sorting of lung and peribronchial lymph nodes. Chemokine expression in whole lung lysates was quantified by ELISA, and viral replication was assessed by quantitative RT-PCR.

**Results** Inhibition of CCL7 suppressed AHR and neutrophilia in non-allergic RV-infected mice, whereas allergic RV-infected mice showed less eosinophilic recruitment to the lungs compared to isotype controls. CCL7 neutralization did not affect viral replication.

**Conclusions** These data suggest that CCL7 plays a role in orchestrating proinflammatory responses to RV1B.

**Supported by** NHMRC, HMRI, and CRCAA.

**Conflict of Interest** No.

P012

### ROSIGLITAZONE, BUT NOT SALBUTAMOL, OPPOSES CONTRACTION TO DIVERSE AGONISTS IN SMALL AIRWAYS IN MOUSE LUNG SLICES

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**Introduction** Altered reactivity of small airways may contribute to airway hyper-responsiveness and reduced  $\beta_2$ -adrenoceptor sensitivity in severe asthma. It is therefore important to characterize small airway contraction to diverse agonists, such as methacholine (MCh), serotonin (5HT) and endothelin-1 (Et-1), implicated in asthma. These constrictors can then be used to assess the relative efficacies of bronchodilator therapies.

**Aim** To assess the influence of different contractile stimuli on small airway relaxation to  $\beta_2$ -adrenoceptor agonist salbutamol (SAL) and novel bronchodilator rosiglitazone (RGZ).

**Methods** Changes in small airway lumen area were measured in lung slices (150  $\mu$ M) from 6–8 week old male Balb/C mice. After characterizing contraction to MCh, 5HT and Et-1, dilator responses were assessed at varying levels of pre-contraction.

**Results** Et-1 was >12-fold more potent than both MCh and 5HT (Et-1 pEC<sub>50</sub> 8.5  $\pm$  0.1), but elicited similar maximal contraction to MCh (~50% reduction in airway lumen area). In opposing sub-maximal pre-contraction against all constrictors, SAL was more potent than RGZ, but RGZ was more efficacious. Partial relaxation of ~50% with SAL was completely abolished in maximally contracted airways, whilst RGZ was able to partially overcome all levels of pre-contraction.

**Discussion** Et-1 is a potent constrictor of mouse small airways. RGZ was able to oppose contraction to diverse agonists under conditions when  $\beta_2$ -mediated relaxation was markedly impaired. This study emphasizes the need to explore the clinical potential of novel dilators against multiple contractile agonists implicated in human asthma.

**Supported by** The University of Melbourne.

**Conflict of Interest** No.

P013

**VITAMIN D DEFICIENCY PROTECTS AGAINST THE EFFECTS OF CHRONIC HOUSE DUST MITE EXPOSURE**RE FOONG<sup>1,2</sup>, LJ BERRY<sup>1,2</sup>, S GORMAN<sup>1,2</sup>, PH HART<sup>1,2</sup>, GR ZOSKY<sup>1,2</sup><sup>1</sup>Telethon Institute for Child Health Research, and <sup>2</sup>Centre for Child Health Research, University of Western Australia, WA, Australia

**Introduction** Reduced levels of vitamin D are associated with airway hyper-responsiveness (AHR) and increased markers of asthma severity. We aimed to determine whether vitamin D deficiency exacerbates respiratory outcomes in a chronic mouse model of allergic asthma.

**Methods** A physiologically relevant mouse model of vitamin D deficiency was developed by raising BALB/c mice on vitamin D-deficient or -replete diets. Offspring from -deficient and -replete mice of both sexes at 8 weeks of age were intranasally inoculated with house dust mite (HDM) extract (25 µg of protein in 50 µL of saline) or saline as a control 5 days a week for 5 weeks. AHR was assessed by measuring lung function responses to increasing doses of inhaled methacholine 72 h after the last HDM exposure. Bronchoalveolar lavage (BAL) fluid was collected to assess cellular inflammation and cytokine levels.

**Results** Chronic HDM exposure increased baseline airway resistance in female vitamin D-replete mice compared with vitamin D-deficient mice ( $p < 0.05$ ). Similarly, HDM exposure increased the maximum response in tissue elastance and the sensitivity of tissue damping to MCh in vitamin D replete male mice compared to deficient male mice ( $p < 0.05$ ). There were increased eosinophils and transforming growth factor  $\beta$  levels in the BAL of vitamin D-replete HDM-sensitized females ( $p < 0.05$ ), but not males.

**Discussion** Unexpectedly, vitamin D deficiency protects mice against both the inflammatory and physiological impairments induced by chronic HDM exposure.

**Conflict of Interest** No.

P015

**DIFFERENTIAL RESPONSES OF CENTRAL AND PERIPHERAL LUNG FIBROBLASTS TO ACTIVATED MAST CELL PRODUCTS**JM HUGHES<sup>1</sup>, M WAI-SHING<sup>1</sup>, D KRIMMER<sup>2</sup>, BGG OLIVER<sup>2</sup>,CL ARMOUR<sup>2</sup>, H ALKHOURI<sup>1</sup>Respiratory Research Group, <sup>1</sup>Faculty of Pharmacy and <sup>2</sup>Woolcock Institute of Medical Research, The University of Sydney, NSW, Australia

**Background** Activated mast cell numbers are generally increased in the bronchial wall and alveolar parenchyma of people with asthma. Mast cells release a wide variety of cytokines and mediators that may modulate the activities of structural cells such as fibroblasts and contribute to airway remodelling.

**Aim** To examine the effects of human lung mast cell (HLMC) products on the synthetic and proliferative functions of central and peripheral fibroblasts.

**Methods** HLMC were stimulated with IgE/anti-IgE and their supernatants (SN) collected after 2 and 24 h. Serum-depleted fibroblasts obtained from central and peripheral airways were treated with HLMC SN for up to 48 h. Chemokine release and deposition of the extracellular matrix (ECM) proteins were measured using ELISAs and fibroblast DNA synthesis was quantified using bromodeoxyuridine incorporation.

**Results** Both 2 and 24 h HLMC SN significantly increased the synthetic functions of peripheral and central fibroblasts in a concentration-related manner. Release of CXCL8 and IL-6 was increased up to 3.9 and 6.6-fold respectively from peripheral fibroblasts. However, the effects on CXCL8 and IL-6 were even greater in central fibroblasts [up 17.7 and 22.6-fold respectively]. Interestingly, although fibronectin deposition was unchanged, both the 2 and 24 h SN significantly increased collagen IV deposition by central, but not peripheral, fibroblasts up to 1.5-fold, whereas only the 24 h SN increased tenascin-C deposition [1.8-fold] by the central cells. Only the 2 h HLMC SN increased central fibroblast proliferation up to 2.0-fold which was reversed by protease inactivation.

**Conclusions** HLMC products increase lung fibroblast cytokine release and differentially regulate central and peripheral fibroblast proliferation and ECM deposition. Thus HLMC may be key regulators of location-specific inflammation and remodelling especially in the central airways.

**Funded by** NHMRC.

**Conflict of Interest** No.

P016

**DISTRIBUTION OF INCREASED AIRWAY SMOOTH MUSCLE THICKNESS AND AIRWAY INFLAMMATION IN ASTHMA**J ELLIOT<sup>1</sup>, R JONES<sup>1,2</sup>, T MAUAD<sup>3</sup>, M ABRAMSON<sup>4</sup>, K MCKAY<sup>5</sup>, T BAI<sup>6</sup>, F GREEN<sup>7</sup>, A JAMES<sup>1,2</sup><sup>1</sup>West Australian Sleep Disorders Research Institute, Western Australia<sup>2</sup>University of Western Australia, <sup>3</sup>Sao Paulo University, Brazil,<sup>4</sup>Monash University, Melbourne, <sup>5</sup>Children's Hospital at Westmead, Sydney,<sup>6</sup>University of British Columbia, Canada, and <sup>7</sup>University of Calgary, Canada

A study of 10 cases of fatal asthma (Ebina et al. 1993) identified two types of asthma, based on the site of increased airway smooth muscle (ASM) thickness: large airways only (due to hyperplasia), or; both large and small airways (due predominantly to hypertrophy).

**Aim** To determine if this site-specific increase in ASM thickness is reproducible and related to remodelling and inflammation.

**Methods** Post-mortem cases of asthma ( $n = 43$ ) were categorized following morphological and serological examination of the airways, as large only (LO,  $n = 15$ ), small only (SO,  $n = 4$ ) and large/small (LS,  $n = 24$ ) if the mean thickness of the ASM layer in their large or small airways was more than one standard deviation above the mean value observed in control subjects ( $n = 37$ ). ASM cell size and number, airway dimensions and airway inflammation were compared between LS and LO cases and control subjects.

**Results** In LS cases, ASM cell number and volume, thickness of the reticular basement membrane (RBMT), airway wall thickness and eosinophil density, were increased ( $p < 0.05$ ) in large and small airways compared with control subjects. In LO cases ASM cell number, RBMT and eosinophil density were increased ( $p < 0.05$ ) only in large airways compared with control subjects. In addition, neutrophil density was increased ( $p < 0.05$ ) in both large and small airways compared with controls. There were no significant differences in duration, age of onset of asthma or asthma severity between cases.

**Conclusions** Phenotypes of asthma, based on the distribution of increased thickness of ASM layer are reproducible and associated with ASM hyperplasia and hypertrophy, remodelling and eosinophilia. Neutrophilia was observed only in the LO cases, suggesting a distinct phenotype.

**Support** NHMRC Project Grants #618700.

**Nomination** Nil.

**Conflicts** Nil.

P014

**ALLERGEN-INDUCED FUNCTIONAL CHANGES IN SHEEP ALVEOLAR MACROPHAGES**

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**Aim** To investigate the surface marker expression and cytokine production by alveolar macrophages (AMs) collected from 'resting' naïve (pre-challenge AMs), and 'resting' but allergen-exposed lungs (post-challenge AMs) in the house dust mite (HDM) sheep model of asthma.

**Methods** Bronchoalveolar lavage (BAL) samples were collected from HDM-sensitized sheep ( $n = 7$ ) before (pre-challenge AMs) as well as 2 weeks after sheep had been given 4x HDM airway challenges at 3-week intervals (post-challenge AMs). BAL adherent AMs were cultured in the presence of innate stimulators (LPS, Poly I:C, or PAMCys3K) or the cytokines IL-4 or IL-13 for 24 h; IL-6, TNF- $\alpha$  and IL-10 was assessed by ELISA. Additionally, freshly collected BAL AMs were stained with surface markers and analyzed by flow cytometry.

**Results** IL-6 levels were low or undetected in culture supernatants with no discernible differences comparing pre- and post-challenge AMs or responses to the different stimuli *in vitro*. Post-challenge AMs cultured in the presence of LPS showed increased TNF- $\alpha$  production ( $p < 0.05$ ) but decreased IL-10 production ( $p < 0.05$ ) compared to pre-challenge AMs. IL-10 secretion was also lower in post-challenge AMs following stimulation with the TLR-2 agonist PAMCys3K. Conversely, AM cultures containing IL-13 induced higher levels of IL-10 secretion in post- compared to pre-challenge AMs ( $p < 0.05$ ). There were no significant changes in MHC class II, CD1a, CD11a, CD11b, CD11c, CD44 or CD69 expression on pre- compared to post-challenge AMs.

**Conclusions** No phenotypic changes were detected in resting AMs collected from naïve compared to allergen-challenged airways. However, an altered cytokine profile of AMs (pre- vs post-challenge) indicates that there are key changes in the resident AM population following airway allergen challenges in the HDM sheep asthma model.

**Conflict of Interest** No.

## ASTHMA &amp; ALLERGY SIG: POSTER SESSION 2

P019

P017

## CHARACTERISTICS OF UNCONTROLLED ASTHMA IN AUSTRALIA

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**Aim** To compare the characteristics of patients with uncontrolled asthma across multiple urban regions of Australia.

**Methods** Adults (non/ex-smokers) with symptomatic asthma despite maintenance ICS/LABA treatment (n = 248) were assessed for the AMAZES study, a multicentre RCT evaluating the addition of azithromycin in five tertiary centres: John Hunter (JHH), Princess Alexandra (PAH), Royal Adelaide (RAH), Prince Charles (TPCH) and Sir Charles Gairdner (SCGH) Hospitals. Clinical assessment and sputum induction were performed.

**Results** Participants had a mean (SD) age of 58 (13) years, pre  $\beta_2$  FEV<sub>1</sub>% 71.9 (22.4), FEV<sub>1</sub>/FVC 68.4 (12.3) and asthma control questionnaire score 1.82 (0.86) with no significant differences between centres. There were differences in asthma severity with fewer participants at GINA treatment step 4 (p = 0.001) and lower maintenance ICS dose (p = 0.002) from PAH and RAH. Participants from RAH were significantly more sensitive to grass (p = 0.006) and cat hair (p < 0.001) specific allergen, and RAH and SCGH participants more likely to experience hay fever (p < 0.0001). Work was reported as a significant trigger for asthma in JHH participants (p = 0.024), while rhinitis was significantly less of a trigger (p = 0.001). There were no differences in smoking history, sputum phenotype, blood eosinophilia or symptom visual analogue scores between centres.

**Conclusions** Participants with uncontrolled asthma have similar lung function and smoking history but differ in GINA treatment step, specific allergen sensitivity and asthma triggers across Australia.

**Supported by** NHMRC Australia.

**Conflict of Interest** No.

P018

## THE RELATIONSHIP OF AIRWAY SENSITIVITY AND REACTIVITY TO MANNITOL AND THE CLINICAL IMPROVEMENT IN ASTHMA CONTROL

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**Introduction** The Asthma Control Questionnaire (ACQ) is a validated tool for identifying symptomatic benefit to inhaled corticosteroids (ICS). BHR to mannitol (MAN) is a predictor of physiological benefit with ICS. Relationship of the degree of asthma control and airway sensitivity (PD<sub>15</sub>) and reactivity (response dose ratio, RDR) to MAN is unknown.

**Methods** ICS naïve asthmatics were treated for 6 weeks with ICS (200 mcg/day, n = 11 or 1000 mcg/day, n = 11). PD<sub>15</sub>, RDR and ACQ were obtained before and following ICS. PD<sub>15</sub> is the provoking dose of MAN to cause a 15% fall in FEV<sub>1</sub> and RDR is the final % fall in FEV<sub>1</sub> divided by the cumulative dose to cause that fall.

**Results** Before ICS, subjects who were not controlled and had higher ACQ scores (intermediate or uncontrolled score >0.75) had greater airway sensitivity to MAN (74 mg (95% CI 42,131)) than those with ACQ scores indicating control (<0.75) (232 mg (166,324)) (p < 0.001). Following ICS there was a clinically meaningful mean reduction in ACQ of 0.5 (p < 0.001) associated with a reduction of PD<sub>15</sub> from 131 mg (88,195) to 365 mg (268, 500) (p < 0.001) (n = 22), but no difference between ICS doses. However there was no difference in actual ACQ scores between those who had lost their airway sensitivity to MAN (no PD<sub>15</sub>) (0.5 ± 0.5, n = 13) and those in whom it remained (0.4 ± 0.2, n = 9) (p = 0.3). Reduction in ACQ score using ICS was related to the reduction in RDR to MAN (r<sub>p</sub> = 0.73, p < 0.001).

**Conclusion** Control of asthma in ICS naïve subjects is related to MAN airway sensitivity and clinical improvements with ICS over 6 weeks were related to improved airway reactivity to MAN. Following ICS, control improved though was no longer related to MAN sensitivity. These data raise the possibility that airway sensitivity to MAN be used as an objective monitor of clinical control.

**Conflict of Interest** JD Brannan receives royalties for Aridol™.

## AIRWAY RESPONSE TO MANNITOL FOLLOWING REGULAR INHALED CORTICOSTEROIDS (ICS) IN ARMY AND POLICE RECRUITS

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**Introduction** Bronchial hyper-responsiveness (BHR) to mannitol has been shown to be useful for monitoring ICS responses in clinical trials, where adherence to ICS therapy is recommended. The New South Wales Police Force & the Australian Defence Forces recommend the use of mannitol for screening potential recruits (PR) with a past or current history of asthma who may get exercise-induced bronchoconstriction. We hypothesized that PRs are likely to be adherent to ICS therapy and documenting an absence of BHR would be common following ICS treatment in this population.

**Methods** Retrospective analysis of airway responses to mannitol (Aridol™) within a 12 month period from 2007–2012 in PRs before and following regular ICS. Airway sensitivity defined as the provoking dose of mannitol to cause a 10% and 15% fall in FEV<sub>1</sub> (PD<sub>10</sub>, PD<sub>15</sub>), airway reactivity (response-dose ratio, RDR) expressed as %fall/mg and spirometric indices (FEV<sub>1</sub>) were compared. Results expressed as mean ± SD.

**Results** Forty PRs (33 M:7 F), aged 22 ± 7 years had a normal FEV<sub>1</sub> (96 ± 13% pred) and mild BHR with a PD<sub>15</sub> to mannitol (geometric mean (95%CI) of 170 mg (128, 226). They returned 144 ± 80 days (range: 37–361) following regular ICS. Thirty-five PRs (88%) had no PD<sub>15</sub> following ICS and 26 (65%) had no PD<sub>10</sub>. RDR was significantly reduced from 0.123 ± 0.133 to 0.017 ± 0.018 %fall/mg (p < 0.001). FEV<sub>1</sub> increased to 99 ± 11% pred following ICS (p = 0.005).

**Conclusion** BHR to mannitol was significantly reduced or absent following ICS treatment in the majority of PRs. These data support clinical trials which suggest re-assessing BHR to mannitol during treatment with ICS may assist in monitoring outcomes of treatment.

**Conflict of Interest** JD Brannan receives royalties for Aridol™.

P020

WITHDRAWN

P021

### FRACTION EXHALED NO IN PATIENTS REFERRED TO PULMONARY FUNCTION LABORATORY (PFLAB) FOR MANNITOL CHALLENGE

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**Introduction** Bronchial hyperresponsiveness to mannitol (BHR+) is a predictor of clinical benefit with inhaled corticosteroids (ICS). FENO, a non-specific marker of inflammation, is also a predictor of benefit to ICS when FENO is >47 ppb using NIOX analysers. The relationship between these two outcomes is unknown in PFLab patients.

**Methods** A retrospective analysis of PFLab patients who expired at a flow rate of 50 mL/s into an FENO analyser (HypAir, Medisoft) before a mannitol challenge (n = 401). To account for the recognized high FENO readings using the HypAir a recommended 0.6 correction was used to equate with the cut-off values using NIOX.

**Results** BHR+ (19%) was twice as frequent compared with FENO > 47 ppb (8.7%). PD<sub>15</sub> values (Geomean 182 mg (95%CI: 141,235)) were weakly related to FENO ( $r_p = -0.2$ ,  $p < 0.05^*$ ). (\* $p < 0.01$ , # $p < 0.001$ ).

	n	FEV <sub>1</sub> (%)	FEF <sub>25-75</sub> (%)	FENO (ppb)	>47 ppb	<47 ppb	<25 ppb
BHR-	323	97 ± 14 <sup>^</sup>	94 ± 25 <sup>*</sup>	18 ± 12 <sup>#</sup>	12	311	261
BHR+	78	91 ± 17	93 ± 110	36 ± 29	23	55	36

In BHR+ subjects the mean level of FENO was double that observed in those BHR-. FENO values were higher in non-smokers compared with smokers in BHR+ subjects (40 ± 30 ppb vs 20 ± 13 ppb,  $p < 0.001$ ) but similar in the BHR- (17 ± 12 ppb vs 18 ± 12 ppb,  $p = 0.9$ ). BHR+ identified 66% of subjects with an FENO > 47 ppb whereas an FENO > 47 ppb identified only 30% of those with BHR+. In non smokers with BHR+ only 38% had a FENO > 47 ppb. Of those BHR+ 50% had normal FENO values < 25 ppb.

**Conclusion** FENO levels that suggest no benefit with ICS are common in PFLab subjects who demonstrate BHR+ to mannitol.

**Conflict of Interest** JD Brannan receives royalties for Aridol™.

P023

### GENDER DIFFERENCES IN PATIENTS EXHALED NO (ENO) REFERRED FOR BRONCHIAL PROVOCATION TEST (BPT)

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**Introduction** ENO, a non-specific marker of airway inflammation is used to identify subjects with asthma who may benefit from regular inhaled corticosteroids (ICS). BPTs are used extensively in the diagnosis of asthma by identifying bronchial hyper-responsiveness (BHR).

**Aim** To investigate the relationship between ENO and BPT in subjects at a tertiary care PFLAB.

**Methods** A retrospective analysis of subjects referred to PFLAB expired at a flow rate of 50 mL/s into an ENO analyser (HypAir, Medisoft) prior to performing either direct (methacholine) or indirect (mannitol / hypertonic saline) BPT. Correction to equate with published cut-off values using NIOX were performed using a 0.6 correction to account for the known high ENO readings with the HypAir.

**Results** 777 subjects were analyzed. Female subjects were found to have lower median ENO compared with males (22, IQR 16–34 vs 31 IQR 19–47  $p < 0.0001$ ). 26% of males had ENO > 47 ppb compared with 14.1% of females. BPT is positive in 24.7% of males and 21.1% of females ( $p = 0.02$ ). There is significant gender difference in ENO among BHR- group.

BHR- ( $p < 0.0001$ )	ENO < 25 ppb	ENO 25–47 ppb	ENO > 47 ppb
Male (%)	41.8	38.9	19.4
Female (%)	60.3	30.5	9.2

Subjects with ENO > 47 ppb showed no difference in the incidence of BHR+ rates regardless of type of BPT, ( $p = 0.9$ ) whereas those with ENO < 25 ppb showed higher incidence of BHR+ rates to methacholine compared to mannitol/saline BPTs ( $p = 0.01$ ). PD20 (direct BPT) correlate better with ENO values than PD15 (indirect BPT), ( $p = 0.03$  vs  $p = 0.5$ ).

**Conclusion** Higher levels of ENO were found in male subjects. ENO > 47 ppb are associated with higher incidence of BHR+ rates regardless of type of BPT. ENO values correlates better to PD20 than PD15.

**Conflict of Interest** JD Brannan receives royalties for Aridol™.

P022

### INFLUENZA INFECTION FACILITATES ALLERGIC SENSITIZATION

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**Aim** There is considerable evidence that early life respiratory viral infection is associated with the subsequent development of allergic asthma. We have previously shown that influenza infection disrupts epithelial barrier function *in vivo*, potentially providing a mechanism for aero-allergen sensitization. This study aimed to assess the effects of viral-induced epithelial barrier disruption on allergic sensitization.

**Methods** Adult female BALB/c mice were infected with 10<sup>4.5</sup> pfu of influenza A/Mem/71 or control solution. When inflammation and signs of clinical illness had completely resolved (day 21 after infection), mice were inoculated with 25 µg of house dust mite (HDM) protein daily for 10 days. 24 h after the last inoculation, blood was taken for assessment of total IgE and house dust mite specific IgG<sub>1</sub> via ELISA.

**Results** Mice previously infected with influenza A and exposed to HDM had significantly increased total IgE compared to uninfected controls (26.1 ± 8.7 ng/mL vs 16.4 ± 7.0 ng/mL respectively;  $p = 0.014$ ). There was no difference in levels of HDM specific IgG<sub>1</sub> ( $p = 0.586$ ).

**Conclusions** Influenza induced epithelial barrier disruption resulted in significantly increased IgE *in vivo*. These data support the notion that an abnormal airway epithelial barrier is a highly feasible explanation for the strong association between aero-allergen sensitization and asthma in population studies.

**Supported by** NHMRC.

**Conflict of Interest** No.

P024

### ALTERNATIVES TO INDUCED SPUTUM FOR IDENTIFYING PATIENTS WITH EOSINOPHILIC ASTHMA

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THE AMAZES STUDY

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**Introduction** Fractional exhaled nitric oxide (FeNO) is proposed as a surrogate marker for eosinophilic airway inflammation, but conflicting results are available for its use in corticosteroid treated asthma. The aim of this study was to examine the utility of FeNO and peripheral blood eosinophil counts (PBeos) to detect an eosinophilic inflammatory subtype (EA) in patients with poorly controlled asthma on inhaled corticosteroids.

**Methods** Participants with uncontrolled (n = 79, ACQ > 0.7) treated asthma underwent a clinical assessment, blood collection, FeNO measurement and sputum induction. Sputum was prepared using validated techniques. Cell viability and differential cell counts were recorded. EA was defined as sputum eosinophils ≥ 3%.

**Results** FeNO data were obtained in 70 patients (89%), adequate sputum cell differential in 60 (76%) and PBeos in all participants. Sputum eosinophils correlated with FeNO ( $r = 0.52$   $P < 0.001$ ) and PBeos ( $r = 0.54$ ,  $P < 0.001$ ). There was no association between sputum eosinophils, FeNO or PBeos with asthma control score (all  $P > 0.05$ ). Both FeNO and PBeos could predict the presence of EA (AUC 0.809 and 0.788 respectively). A cut-point for PBeos of 0.25 × 10<sup>9</sup>/mL predicted the presence of EA with sensitivity 81% and specificity 73%. The recommended FeNO cut-point of 44 ppb had 97% specificity (rule in EA) and the cut-point of 25 ppb had 70% sensitivity (rule out EA).

**Conclusions** FeNO and PBeos could detect EA. Incomplete data for sputum eosinophils and FeNO is a limitation of this analysis.

**Supported by** NHMRC project grant.

**Conflict of Interest** Nil.

P025

### NEUTROPHILIC ASTHMA IS CHARACTERIZED BY INCREASED GERD AND RHINOSINUSITIS WITH SLEEP DISTURBANCE

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**Introduction** Asthma is a heterogeneous inflammatory disease with eosinophilic, non-eosinophilic and neutrophilic subtypes recognized. Despite their clinical similarity, patients with non-eosinophilic asthma have different responses to treatment to those with eosinophilic asthma (EA) and little is known about the triggers of symptoms and inflammation. This study sought to characterize asthma control, exacerbation frequency and potential triggers of neutrophilic asthma.

**Methods** Adults with asthma (n = 65) were recruited from the Respiratory and Sleep Medicine Ambulatory Care Service at John Hunter Hospital, NSW. Questionnaires to assess asthma control, history of exacerbation, gastroesophageal reflux disease (GERD) and rhinosinusitis were completed. Sputum was induced, dispersed and a total and differential cell count was performed. Patients were categorized as EA (sputum eosinophils  $\geq$  3%, neutrophils < 61%), neutrophilic asthma (NA; sputum neutrophils  $\geq$  61% (eosinophils < 3%) or paucigranulocytic asthma (PGA; sputum eosinophils < 3% and neutrophils < 61%).

**Results** Participants with NA (n = 11, 23%) had a higher frequency of primary care visits for asthma exacerbations and a high rate (>70%) of chest infections in the past year. There was also an increased prevalence of rhinosinusitis (64%), increased symptoms of GERD compared to those with EA.

**Conclusions** The clinical pattern of NA is different from EA and PGA with evidence of abnormal upper airways responses. Specific and targeted treatment of these airway problems may assist in the control and management of neutrophilic asthma.

**Supported by** John Hunter Charitable Trust and HMRI project grants.

**Conflict of Interest** Nil.

P027

### SINGLE BUDESONIDE/FORMOTEROL INHALER AS MAINTENANCE AND RELIEVER THERAPY IS BENEFICIAL IN MAORI ASTHMA

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**Background** The 'SMART' regime (combination budesonide/formoterol inhaler for maintenance and relief) has a favourable risk-benefit profile compared with 'Standard' therapy (combination budesonide/formoterol inhaler for maintenance and salbutamol for relief) in a real world randomized controlled trial.

**Aim** To ascertain the health benefits of the SMART regime in Māori with asthma.

**Methods** 44/303 (15%) of patients randomized in the 24 week trial were Māori. Inhaler use was measured by electronic monitoring. Outcomes included: 1. Days of high use (HU) (>12 actuations/day of budesonide/formoterol in SMART or >16 actuations/day of salbutamol for Standard), 2. Days of underuse, 3. Severe exacerbations, 4. Asthma control. Difference in outcome for Māori vs non-Māori was assessed using an interaction term between ethnicity and treatment.

**Results** The SMART group had fewer days of HU (RR (95% CI) 0.57 (0.38–0.85), P = 0.006), days of HU without medical review (RR 0.49 (0.32–0.75), P = 0.001), and severe exacerbations (RR (95% CI) 0.54 (0.36–0.81), P = 0.003) when compared to Standard, with Māori benefiting to the same extent as non-Māori. Māori treated with SMART had improved Asthma Control Questionnaire scores compared to Māori treated with Standard (P = 0.001). Regardless of treatment regime, Māori demonstrated a greater health burden with more days of HU and HU without medical review, as well as more days of underuse.

**Conclusions** The SMART regime is effective in Māori with asthma. As Māori have a greater health burden, they are likely to have a greater absolute benefit using the SMART regime.

**Supported by** HRC NZ.

**Conflict of Interest** None.

P026

### PARTIAL OR POOR ASTHMA CONTROL IS RELATED TO ANXIETY AND DEPRESSION SCORES

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**Aim** To assess the relationship of anxiety and depression with asthma control.

**Methods** Cross-sectional study of research volunteers and respiratory outpatients with asthma, at the John Hunter Hospital Newcastle. Demographic details were collected and participants completed validated questionnaires including: the Juniper Asthma Control Questionnaire (ACQ) and the Hospital Anxiety and Depression Questionnaire (HADS). Spirometry and airway responsiveness to hypertonic saline were also measured.

**Results** Of 33 subjects (mean (SD) age 50 (14) years) over half were considered to have partial or poor asthma control, defined as an ACQ7 score of >0.75 (n = 20). Subjects with partial or poor control had lower %FEV1 and %FVC and were more likely to have airway hyper-responsiveness and had oral steroids in the past 2 years. Anxiety and depression scores were significantly higher in those with partial or poor control (median (IQR) anxiety: 3(1,7) vs 5(2,7) p = 0.042, depression: 1 (0,2) vs 4(2, 7) p = 0.003). In uncontrolled subjects 40% had anxiety and 15% had depression scores above the normal level (>7), and 2 subjects had abnormal levels of both anxiety and depression scores. Furthermore ACQ7 scores were positively related to both anxiety and depression scores (n = 31; r = 0.36, p = 0.047 and r = 0.48, p = 0.007).

**Conclusions** There was a high prevalence of partially or poorly controlled asthma in this cohort, with this group having higher scores of anxiety and depression.

**Nomination** Janet Elder International Travel Award.

**Conflict of Interest** No.

P028

### A HALF DOUBLING DOSE CHANGE IN BHR IN A POPULATION REPRESENTS AN IMPORTANT DIFFERENCE

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**Introduction** The prevalence of asthma has increased over recent decades and the reasons for this are poorly understood. A sensitive tool that can evaluate potential risk factors for asthma is bronchial hyperresponsiveness (BHR), a key physiological characteristic of asthma. However, the minimum important difference in BHR for a population is not defined.

**Methods** To assess the potential impact of a small absolute change in BHR across a population, we modelled the effect of different changes in BHR on the prevalence rates of moderate and severe BHR in an asthmatic population.

**Results** We calculate that a 0.5 doubling dose (dd) increase in BHR across a population would increase the prevalence of moderate and severe BHR by 30%. If accompanied by an equivalent increase in the population prevalence of moderate and severe asthma, this would be highly significant in public health terms.

**Conclusions** We propose that a 0.5 dd worsening in BHR is an important change when applied to a population.

DD worsening in BHR	Change in prevalence Rate ratio (95% CI)	Prevalence of moderately severe BHR, % (95% CI)	Prevalence of severe BHR, % (95% CI)
Baseline	—	41.2	6.6
-0.25	1.15 (1.12–1.17)	47.3 (46.3–48.1)	7.6 (7.4–7.7)
-0.5	1.31 (1.26–1.36)	54.2 (52.1–56.2)	8.7 (8.3–9.0)
-0.75	1.51 (1.42–1.59)	62.2 (58.6–65.6)	10.0 (9.4–10.5)
-1.0	1.73 (1.60–1.86)	71.4 (65.9–76.6)	11.4 (10.6–12.3)

**Supported by** Health Research Council, NZ.

**Conflict of Interest** No.

P029

**A MULTIDISCIPLINARY APPROACH TO MANAGEMENT OF MATERNAL ASTHMA (MAMMA®)—HOW CAN WE HELP?**

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**Aims** To determine whether a multidisciplinary approach involving asthma education and regular monitoring during pregnancy will decrease asthma exacerbations with the attendant maternal and perinatal hazards.

**Methods** We have commenced a randomized controlled trial comparing MAMMA®—involving asthma education and regular monitoring—to standard care. Intervention and control groups have their Asthma Control Questionnaire (ACQ) scores, use of oral corticosteroid and asthma-related hospital admissions at 3 and 6 months compared, along with adverse pregnancy and neonatal events at delivery. The use of FEV<sub>1</sub>/FEV<sub>6</sub> (forced expiratory volume in 6 s) will be also investigated during this trial to evaluate its utility as a marker of asthma control.

**Results** Pregnant women with asthma (n = 60) have been recruited from antenatal clinics in Melbourne. At baseline, FEV<sub>1</sub> mean (SD) was 2.53 L (0.094) and FEV<sub>1</sub>/FEV<sub>6</sub> median (interquartile range) was 0.81 (0.73–0.86). In addition, at baseline more than one-third of participants had poorly controlled asthma (ACQ > 1.5) and 10% reported having asthma-related hospital admissions and/or oral corticosteroid usage during their current pregnancy.

**Conclusions** If successful, this model of care could be widely implemented in clinical practice, justify more funding for support services for these women and warrant promotion of better awareness of the risks of poorly controlled asthma during pregnancy.

**Nomination** TSANZ Travel Award.

**Conflict of Interest** No.

P031

**USE OF RELIABLE ELECTRONIC MONITORS IS THE OPTIMAL METHOD TO ASSESS PATTERNS OF INHALED ASTHMA MEDICATION USE**

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**Background** Information on the performance of electronic monitors that measure inhaled asthma medication use allows researchers and clinicians to understand their utility and limitations. The SmartInhaler Tracker is an electronic monitor for metered-dose inhalers (MDIs) that records the date, time and number of actuations.

**Aim** To determine the performance of the monitors used in a 24-week randomized controlled trial of 303 asthma patients in a real-world setting.

**Methods** Pre-study use checks involved two actuations of the MDI, with a further two performed 2 h later. Within-study monitor checks, performed prior to dispensing at follow-up clinic visits, included a computerized check of monitor clock function, actuation accuracy and battery life. Within-study data checks involved computerized checks of monitor clock function prior to data upload.

**Results** 2678/2728 (98.2%) monitors passed pre-study use checks. 76/2642 (2.9%) monitors dispensed to participants failed within-study monitor checks. 51/2642 (1.9%) monitors malfunctioned prior to data upload, mostly as a result of fluid immersion. 93/2642 (3.5%) monitors were lost or thrown away by participants. Complete data were available from 2498/2642 (94.5%) of dispensed monitors and 2498/2549 (98.0%) of returned monitors.

**Conclusion** The Tracker is a reliable monitor for use in a real-world setting. Extensive monitor and data-checking protocols reduce data loss. Use of validated and reliable monitors is the optimal method to assess patterns of inhaled medication use.

**Supported by** HRC NZ.

**Conflict of Interest** None.

P030

**A NURSE-LED OMALIZUMAB CLINIC: THE PRINCESS ALEXANDRA HOSPITAL EXPERIENCE**

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**Background** Omalizumab, an anti-IgE monoclonal antibody, was approved for use in Australia in 2002, and has been available through the Pharmaceutical Benefits Scheme (PBS) since July 2011.

**Aim** To describe our experience in treating patients with severe allergic asthma via a nurse-led clinic.

**Results** Fourteen patients were evaluated for treatment with Omalizumab. We applied to the PBS for funding for 13 patients, and the remaining patient's treatment was funded by the local district hospital. The PBS rejected two applications. One application was rejected as the patient had no detectable allergic sensitization, despite having an elevated total IgE; the second was rejected as that patient had not taken Oral Corticosteroids (OCS) for a sufficient time. In total, we have treated 12 patients with Omalizumab, 11 through PBS funding. Two patients withdrew from treatment early—one who felt there was no benefit from the therapy, and the second withdrew due to needle phobia. Four patients were discontinued from therapy at the end of the initial six-month trial as they did not show respond. Five patients have continued as they have shown a good response to therapy by either an improvement in the Asthma Control Questionnaire (ACQ) of  $\geq 0.5$  from baseline, or a reduction in maintenance OCS dose by  $\geq 25\%$ . The remaining patient has recently commenced therapy, and is not expected to show a response at this time. Minor side-effects have included urticaria, itchy mouth and diarrhoea, but no anaphylaxis has occurred.

**Conclusion** The rate of patient response to Omalizumab at the Princess Alexandra Hospital is consistent with the current literature which shows a response rate of 50%.

**Conflict of Interest** MA Towers has previously received an honorarium from Novartis for presenting a talk about Omalizumab.

P032

**THE SYMPTOM OF POST NASAL DRIP AND COUGH IN RELATIONSHIP TO VISCOSITY OF INTRANASAL SOLUTIONS**

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Postnasal drip (PND) is a common symptom associated with upper respiratory tract disorders and symptoms of persistent cough and throat clearing. We postulated that altered viscosity of nasal secretions could result in the clinical symptom of PND and/or cough.

**Aim** To determine if the intranasal insertion of a hyperviscous solution would result in the sensation of postnasal drip and/or cough and whether the sensory perception was different between normal subjects and those with upper airway disease.

**Methods** 32 patients with rhinitis/rhinosinusitis and 33 nonrhinitic controls were studied. Baseline SNOT questionnaire and PND symptom score (PNDSS) sheet were completed. Solutions of 1% and subsequently 4% hydroxypropylmethylcellulose (HPMC) (viscosities 1.21 and 38.6 pascal/sec respectively) were inserted into the nasal cavity 1 cm distal to the inferior turbinate. After each procedure at 5 min a PND symptom score sheet was completed.

**Results** At baseline patients had significantly worse sino-nasal, globus/throat and mood symptom scores (p = 0.000). Baseline PND symptoms were significantly greater in patients compared with controls (p = 0.000). The control group recorded a significant increase in PNDSS after both the 1% (p = 0.001) and 4% (p = 0.000) solutions. In contrast the patients demonstrated no increase in PNDSS after either the 1% or 4% solution. The insertion of HPMC did not result in an increase in cough symptoms.

**Summary** In normal subjects the insertion of viscous solutions intra-nasally results in the sensation of PND. In patients with rhinitis and rhinosinusitis the sensation of PND is present at baseline and does not increase further with the insertion of hyperviscous solutions. Insertion of intra-nasal hyperviscous solutions does not result in the symptom of cough.

**Supported by** Nil.

**Conflict of Interest** Nil.



## CELL BIOLOGY/IMMUNOLOGY SIG: POSTER SESSION

P035

P033

## OXIDATIVE STRESS DECREASES FUNCTIONAL AIRWAY MANNOSE BINDING LECTIN IN COPD

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**Background** Mannose binding lectin (MBL) is a key mediator of innate immunity that has been shown to facilitate macrophage phagocytosis of both pathogens and apoptotic cells ('efferocytosis'). We have previously shown significantly reduced MBL in the airways of smokers and COPD patients and a correlation between airway MBL levels and efferocytosis; however, the reason for the reduced MBL remains unknown. MBL function is dependent on its capacity to form higher order oligomers. Since oxidative stress is considered to be a major driver of COPD pathogenesis, we hypothesized that oxidative conditions would disrupt the quaternary structure of MBL, thus reducing its capacity to form higher order oligomers and impairing its functional phagocytic capacity.

**Method** We applied blue native PAGE to investigate the oligomeric structure of plasma derived MBL (pdMBL) following oxidation with 2,2'-azobis(2-methylpropanamide) dihydrochloride (AAPH). We also investigated the functional capacity of non-oxidized/oxidized pdMBL by assessing alveolar macrophage efferocytosis and phagocytosis of non-typeable *Haemophilus influenzae* (NTHi).

**Results** Higher order oligomer formation was partially inhibited in oxidized MBL, associated with a reduced ability to phagocytose apoptotic cells and NTHi (by 60.4% and 38.0% respectively).

**Conclusions** Our findings suggest that oxidative stress-induced structural changes to MBL may be a potential cause for reduced levels of MBL and impaired phagocytic function in the airways in COPD.

**Supported by** NHMRC.

**Conflict of Interest** No.

**Nomination** TSANZ Travel Grant.

P036

## REGULATION OF E-PROSTANOID RECEPTOR EXPRESSION IN AIRWAY EPITHELIUM BY MICRO-RNA

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**Background** Airway disorders associated with persistent inflammation such as asthma show aberrant microRNA expression, which is modulated by pro- and anti-inflammatory mediators. Produced in the lung, Prostaglandin E2 (PGE2) is a major endogenous anti-inflammatory mediator and bronchodilator, acting via E-Prostanoid receptors (EP1–4). We hypothesized that airway inflammation-associated miRNAs target EP receptors in airway epithelial cells.

**Aim** To verify the target sites for miRNA on EP receptor transcripts.  
**Methods** Database searches identified potential 3'UTR target sites on EP receptors and EP3 isoforms and miRNAs linked to asthma and inflammation were chosen for analysis. 16HBE cells were stimulated with pro-inflammatory mediator IL-1 $\beta$ , anti-inflammatory mediator PGE2, a combination of both, or left unstimulated. RNA was extracted after 4 and 24 h, and miRNA and EP receptor mRNA expression levels were determined by qPCR.

**Results** Both PGE2 and IL-1 $\beta$  modulated the expression of miRNAs predicted to target EP receptors. miRNAs potentially targeting EP2 were increased by PGE2 and IL-1 $\beta$ , and mRNA levels were reduced. EP3 seemed to be regulated by all tested miRNAs with an inverse correlation between miRNA and EP3 receptor expression.

**Conclusions** Several miRNAs were identified that likely play a role in the rapid regulation of EP2 and EP3 in human airway epithelium. This provides us a better insight of the molecular mechanisms involved in PGE2 regulation and possible future management of severe airway inflammation.

**Conflict of Interest** No.

P034

## SERUM AMYLOID A DRAMATICALLY ALTERS MACROPHAGES IN VIVO

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Altered macrophages contribute to progression and acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD). Serum Amyloid A (SAA) is expressed at higher levels in COPD and influences the maturation of macrophages predominantly from M1 to M2 phenotype. M2 macrophages are critical for preventing bystander host tissue damage by clearing dead/dying immune cells, including apoptotic neutrophils after infection or tissue damage and promoting anti-inflammatory processes and wound healing. Despite the beneficial aspects of this subset, macrophages from COPD lungs function inefficiently. The aim of this study is to characterize SAA-induced macrophages *in vivo* using two SAA-induced mouse models of COPD; an acute model involving intranasal administration of 2  $\mu$ g of SAA and a chronic model involving 5 treatments of SAA once weekly. Macrophages were analyzed by flow cytometry for expression of F4/80, CD11c and CD11b. Three subsets of macrophages have been described, CD11c<sup>hi</sup>CD11b<sup>lo</sup> (tissue-specific), CD11c<sup>hi</sup>CD11b<sup>hi</sup> (intermediate) and CD11c<sup>lo</sup>CD11b<sup>lo</sup> (monocytic-like). SAA promotes the development of distinct macrophage populations that display a gene expression profile consistent with M1 and M2 subsets. The development of these intermediate and tissue-specific macrophages is dependent on the leukocyte growth factor, GM-CSF. Chronically, SAA causes the accumulation of tissue-specific macrophages that may have implications for the persistence of inflammation in the lung of COPD patients during acute exacerbation.

**Supported by** NHMRC.

**Conflict of Interest** No.

## CHARACTERIZATION OF THE SPHK/S1P PATHWAY IN HUMAN ALVEOLAR MACROPHAGES IN COPD AND LUNG CANCER

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**Background** We have shown that alveolar macrophages (AM) from subjects with COPD or lung cancer are defective in their ability to phagocytose apoptotic cells, associated with increased airway tissue damage; however, the exact mechanism for this defect is still unknown. Sphingosine 1 phosphate (S1P), the product of sphingosine kinases (SPHKs), is one of the most important sphingolipid molecules and its role in immune cell function has been shown in many studies. We hypothesized that the SPHK/S1P signalling system could play a role in the defective macrophage phagocytic function in COPD and lung cancer.

**Methods** We analyzed the expression profiles of SPHK/S1P signalling system genes (SPHK1 and 2, S1P receptors 1–5, S1P phosphatases (SGPP1 and 2) and S1P-lyase (SGPL1)) using Real-Time PCR in AM isolated from BAL from COPD or lung cancer patients and healthy controls. In order to investigate the potential effects of cigarette smoke on SPHK/S1P gene expression in macrophages we exposed a THP-1 cell line to cigarette smoke extract (CSE) *in vitro*.

**Results** We found significant increases in S1P1 mRNA in AM from both COPD and lung cancer patients ( $p = 0.033$  and  $p = 0.017$  respectively). SPHK2 and S1P3 mRNA were significantly increased in AM from COPD and lung cancer patients respectively (SPHK2, COPD:  $p = 0.046$  and S1P3, lung cancer,  $p = 0.029$ ). CSE significantly increased the expression of SPHK2 and S1P3, confirming the results in human AM and suggesting an effect of cigarette smoke on these mediators. S1P1 expression was unaffected by cigarette smoke, suggesting a COPD or lung cancer 'disease effect' rather than smoke effect *per se*.

**Conclusion** Our results suggest a potential link between the SPHK/S1P signalling system and defective AM phagocytic function in COPD and lung cancer.

**Funding** University of Tabuk, Saudi Arabia.

**Conflict of Interest** No.

**Nomination** TSANZ Travel Award.

P037

### DIFFERENCES BETWEEN DEPOSITED AND SOLUBLE FIBULIN-1 IN AIRWAY SMOOTH MUSCLE CELLS

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**Introduction** Fibulin-1 (FBLN-1) is a secreted glycoprotein that is associated with extracellular matrix (ECM) formation and rebuilding. Altered deposition of the ECM is a hallmark of many fibrotic diseases, such as COPD where the airway thickness is increased.

**Aim** To investigate the regulation of FBLN-1 in the presence of transforming growth factor beta 1 (TGF- $\beta_1$ ) (a pro-fibrotic stimulus) in human airway smooth muscle (ASM) cells from COPD and non COPD volunteers.

**Methods** ASM cells were plated at a density of  $1 \times 10^4$  cells/cm<sup>2</sup>, and stimulated with or without TGF- $\beta_1$  (10 ng/mL) for 72 h. Supernatant and cell free ECM were collected then the soluble and deposited FBLN-1 were measured by western blot and ELISA respectively. FBLN-1 mRNA fold change (during time course 4, 8, 24, 48, 72 h) was detected by real-time PCR.

**Results** TGF- $\beta_1$  decreased soluble FBLN-1 from human ASM cells isolated from both COPD and Non COPD volunteers (COPD n = 9, p  $\leq$  0.001, Non COPD n = 9, p  $\leq$  0.001), however, the deposition of FBLN-1 was increased (COPD n = 10, p  $\leq$  0.01, Non COPD n = 8, p  $\leq$  0.01). TGF- $\beta_1$  did not increase FBLN-1 gene expression. There was no difference between cells from people with or without COPD.

**Conclusions** The increased deposition of FBLN-1 in the ECM by TGF- $\beta_1$  is likely due to incorporation of soluble FBLN-1 rather than de novo synthesis.

**Supported by** National Health and Medical Research Council Project Grant, Chinese Joint PhD Student Scholarship.

**Conflict of Interest** No.

P039

### THE ROLE OF FIBULIN-1 PEPTIDES IN LUNG FIBROBLAST ASSOCIATED REMODELLING AND INFLAMMATION

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**Rationale** Fibulin-1 is an extracellular matrix (ECM) protein which mediates cellular process and tissue remodelling. In our previous research we have shown that the levels of fibulin-1 are elevated in serum and bronchoalveolar lavage fluid of asthmatic patients compared to healthy volunteers. Furthermore, *in-vitro* we found fibulin-1C, one of four fibulin-1 isoforms, promoted proliferation and wound repair in human airway smooth muscle cells.

**Aim** As it is not known which parts of the fibulin molecule are bioactive, we aimed to identify which regions of fibulin-1C promote remodelling and inflammation.

**Methods** Several fibulin-1C peptides were designed according to the principles described by Angelatti.<sup>1</sup> The peptides were either coated on the plates before lung fibroblasts were seeded or added onto the cells in soluble form. The effects of peptides on fibroblast attachment, proliferation, wound repair and pro-inflammatory cytokine release were measured.

**Results** Among the fibulin-1C peptides, peptides 1C1 (FBLN1C1), when coated on the plates, increased fibroblast attachment (35%, p < 0.05, n = 8) and proliferation (10%, p < 0.05, n = 4). In contrast, soluble FBLN1C1 decreased cell proliferation (17%, p < 0.05, n = 9), had no effect on wound repair but enhanced interleukin-6 release (25%, p < 0.05, n = 8) by lung fibroblasts.

**Conclusion** FBLN1C1 may be important in fibulin-1 induced remodelling and inflammation. Further investigation of this molecule and its receptor may help understand the role of fibulin-1 in the pathophysiology of chronic lung diseases.

**Supported by** NH & MRC.

**Conflict of Interest** No.

**Nomination** TSANZ Travel Grant to the 2012 ASM and Janet Elder International Travel Awards.

**Reference**

1 Angeletti R. Design of Useful Peptide Antigens. 1999 ABRF.

P040

### VARIATIONS IN EP RECEPTOR EXPRESSION IN HUMAN AIRWAY EPITHELIUM DURING AIRWAY INFLAMMATION

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**Background and Aim** Inflammation is a key characteristic of many airway conditions, including asthma and COPD. PGE2 is known to have an overall anti-inflammatory affect in the airway. The molecule exerts its action through 4 receptors, known as EP receptors. The effects of PGE2 can be highly varied, as stimulation of different receptors elicits different biological responses. The overall effect depends on the expression and activation levels of each EP receptor subtype. We aimed to investigate the regulation of EP receptors in human airway epithelial cells under physiological conditions and during inflammation.

**Methods** 16-HBE cells were stimulated with IL-1 $\beta$ , PGE2 (at a range of concentrations), or EP (1-4) receptor agonists either alone, or simultaneously. EP receptor mRNA and protein expression was then quantified using Real Time RT PCR and In Cell Western Assay respectively.

**Results** PGE2 modulates expression of EP receptors in airway epithelial cells in inflammation. IL-1 $\beta$  preferentially up-regulated EP2 and EP4 expression, while the affect of IL-1 $\beta$  was attenuated by PGE2. PGE2 alone stimulates expression of EP1 and EP3. mRNA levels were concentration dependant with EP1, 2 and 4 expression peaking after stimulation with 10 nM PGE2, and EP3 continuing to increase as PGE2 concentration rose. Protein expression however, tended to decrease as PGE2 concentration increased for all receptors. Furthermore, the stimulation of one EP receptor can modulate the expression of other subtypes, for example activation of EP1 receptor decreases EP2 mRNA expression.

**Conclusions** PGE2 influences expression of its receptors in a complex manner, which in turn affects the response to inflammation. As receptors subtypes have differing functions, changes in expression will result in varied responses. Knowledge of the regulation of EP receptors will increase our understanding of inflammatory response in the lung.

**Supported by** UWA, Asthma Foundation WA, ONO Pharmaceuticals.

**Nomination** TSANZ Travel Award.

**Conflict of Interest** No.

P038

### CCL20 PRODUCTION BY AIRWAY SMOOTH MUSCLE CELLS CONTRIBUTES TO MUCUS HYPERSECRETION AND INCREASE MUSCLE MASS IN ASTHMATIC AIRWAYS

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**Introduction** Asthma is associated with structural changes in the airway wall, including increase in airway smooth muscle (ASM) mass and mucus hypersecretion, termed airway remodelling. CCL20 previously has been identified as a factor released by epithelial cells which contributes to mucus hypersecretion by acting in an autocrine fashion binding to its unique receptor CCR6.

**Methods** To compare the profiles of gene expression from asthmatic (n = 3) and non-asthmatic (n = 3) human ASM cells, Affymetrix GeneChip Human Gene 1.0 ST Arrays were used. Gene candidates were confirmed by qPCR and proliferation assays were conducted by MTT.

**Results** CCL20 was found to be induced by IL1 $\beta$  by 67 fold (p < 0.001) in ASM cell and this induction was increased 4 fold (p < 0.001) by asthmatics. ELISA results identified that CCL20 protein is not expressed in non-stimulated cells while CCL20 is induced by 10 ng/mL IL1 $\beta$ , 10 ng/mL TNF $\alpha$ , 50 ug/mL POLY:IC, 10 ng/mL IL1 $\beta$  + 10 ng/mL TNF $\alpha$  (synergistic) and 10 ng/mL IL1 $\beta$  + 50 ug/mL POLY:IC (synergistic). CCR6 the receptor for CCL20 was shown to be expressed by RT-PCR and western blot in ASM cells with no difference between asthmatics and non asthmatics. CCL20 10 ng/mL increased the proliferation of immortalized human ASM cells by 1.27-fold (n = 3, p < 0.001).

**Conclusions** The production of CCL20 by the ASM cells in response to the inflammatory environment present in the asthmatic airways may contribute to mucus hypersecretion and may also act in an autocrine fashion increasing proliferation of ASM cells.

**Supported by** NHMRC and APA.

**Conflict of Interest** No.

P041

### PROPORTION OF T REGULATORY CELLS IN THE PERIPHERAL BLOOD OF SARCOIDOSIS PATIENTS

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**Introduction** The 'immune paradox' of sarcoidosis may be explained by the coexistence of Type 1 T helper cell (T<sub>H</sub>1)-dominated local inflammation and T regulatory (T<sub>reg</sub>)-induced peripheral anergy after presumed exposure to potential causative agents. This study aimed to investigate the proportion of T<sub>reg</sub> vs T<sub>effector</sub> cells in the peripheral blood of sarcoidosis patients compared to controls, with and without stimulation by potential pathogenic antigens.

**Methods** Using the OX-40 assay, peripheral blood mononuclear cells (PBMCs) were stimulated with CD3/CD28 Dynabeads, *Mycobacterium tuberculosis* ESAT-6/KatG peptides, and *Aspergillus fumigatus* crude proteins for 44 h. Following stimulation, PBMCs were stained with anti-human monoclonal antibodies and cell sorted into CD3<sup>+</sup>CD4<sup>+</sup>CD25<sup>+</sup>CD134<sup>+</sup>CD39<sup>+</sup> T<sub>reg</sub> and CD3<sup>+</sup>CD4<sup>+</sup>CD25<sup>+</sup>CD134<sup>+</sup>CD39<sup>-</sup> T<sub>effector</sub> cell populations by flow cytometry.

**Results** See table.

Conditions	Percentage of T <sub>reg</sub> cells (%)		p-value
	Controls (n = 18)	Patients (n = 12)	
Unstimulated	54.28 (24.23 (SD))	73.90 (23.57 (SD))	0.0365 (<0.05)
CD3/CD28 Dynabeads	29.73 (12.63 (SD))	57.01 (24.83 (SD))	0.0004 (<0.05)
ESAT-6/KatG	50.58 (20.63 (SD))	71.93 (24.21 (SD))	0.0150 (<0.05)
<i>Aspergillus fumigatus</i> crude proteins	56.85 (4.550–83.80)	77.30 (27.60–97.00)	0.0033 (<0.05)

**Conclusion** Peripheral anergy in sarcoidosis may be explained by a greater proportion of T<sub>reg</sub> to T<sub>effector</sub> cell population compared to normal subjects.

**Conflict of Interest** No.

P042

### IFN- $\gamma$ LEVELS IN EXHALED BREATH CONDENSATE AND PERIPHERAL BLOOD OF SARCOIDOSIS PATIENTS REFLECT AN IMMUNE PARADOX

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**Introduction** Sarcoid granulomatous inflammation in the lungs is dominated by Type 1 T helper (T<sub>H</sub>1) immunity, whereas immunological anergy exists in the periphery. Recently, IL-17 has been detected in sarcoid granulomas. This study aimed to investigate the sarcoid immune paradox in the exhaled breath condensate (EBC) and peripheral blood of sarcoidosis patients by measuring levels of IFN- $\gamma$  and IL-17.

**Methods** EBC and peripheral blood samples were collected from controls and sarcoidosis patients. EBC levels of IFN- $\gamma$  and IL-17 were measured with high sensitivity ELISAs, while peripheral blood levels were determined using standard ELISAs.

**Results** See table.

Samples	Levels of IFN- $\gamma$ (pg/mL)		p-value
	Controls (n = 17)	Patients (n = 15)	
EBC	0.2721 (0.1422–3.875)	5.215 (0.2169–13.49)	0.0005 (<0.05)
Peripheral blood	1.688 (0.0–22.43)	0.3107 (0.0–1.567)	0.0423 (<0.05)

IL-17 levels did not differ significantly between controls and patients.

**Conclusions** Increased IFN- $\gamma$  levels in EBC but decreased levels in peripheral blood of patients reflect the sarcoid immune paradox. IFN- $\gamma$  may serve as a potential inflammatory biomarker of sarcoidosis in EBC. In this study, IL-17 was not implicated in sarcoid immunopathogenesis.

**Conflict of Interest** No.

P043

### TRANSFORMING GROWTH FACTOR- $\beta$ INDUCES GLUCOCORTICOID RESISTANCE IN HUMAN BRONCHIAL EPITHELIAL CELLS

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**Introduction** Glucocorticoid (GC) resistance limits the successful treatment of chronic inflammatory diseases. The epithelium is a target for GC action. However, mechanisms of GC resistance are under-explored in this cell type. We have previously shown that TGF- $\beta$  impairs GC transactivation in A549 lung epithelial cells, partly through decreased nuclear translocation of GR $\alpha$ . We therefore aimed to further investigate the relevance of this finding in a different epithelial cell line, and to ascertain the molecular mechanisms through which TGF- $\beta$  impairs epithelial GC action.

**Methods** BEAS-2B bronchial epithelial cells were used in this study. GC Response Element (GRE) activity was assessed by transient transfection of a GRE-SEAP reporter. GC-responsive gene expression was measured by RT-PCR. The TGF- $\beta$  canonical signalling pathway was investigated using siRNA targeting SMAD4 and the known non-canonical signalling pathways were investigated using small molecule kinase inhibitors and transfection of a GR $\alpha$ -YFP construct was used to examine GR $\alpha$  nuclear translocation.

**Results** TGF- $\beta$  impaired dex-induced GRE activation by 85.1  $\pm$  0.1% (n = 3, p < 0.05) and impaired the expression of a variety of GC-inducible genes, including GILZ, ENAC $\alpha$  and SLPI. This impairment is not prevented by knocking down SMAD4 by siRNA, nor by inhibiting the known non-canonical signalling pathways, and was not a result of impaired GR $\alpha$  nuclear translocation.

**Conclusions** TGF- $\beta$  potently and effectively impairs GC action in BEAS-2B human bronchial epithelial cells. However, unlike the A549 cell line, this cannot be attributed to impaired GR $\alpha$  nuclear translocation. Glucocorticoid insensitivity cannot be prevented by inhibiting prototypical TGF- $\beta$  signalling pathways suggesting an untargeted screening approach may reveal novel targets to treat glucocorticoid resistance.

**Supported by** NHMRC.

**Conflict of Interest** No.

**Nomination** Janet Elder International Travel Award.

P044

### TISSUE PLASMINOGEN ACTIVATOR (TPA) POTENTLY INDUCES PLEURAL EFFUSION IN MICE VIA AN MCP-1 MEDIATED MECHANISM

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Pleural infection affects >1 million patients worldwide a year. Intrapleural delivery of fibrinolytics (eg tPA) are commonly used to break up adhesions to enhance drainage. Combination use with DNase dramatically improved patient outcome (NEJM 2011). Clinical studies show that intrapleural fibrinolytics consistently induce release of large volumes of pleural fluid, the mechanism of which is unknown. MCP-1 is known to induce pleural fluid formation in animal models of pleural cancers.

**Aim** To determine the mechanism by which tPA induces pleural fluid formation.

**Methods** CD1 mice were given i) intrapleural injections of different fibrinolytics  $\pm$  DNase; ii) different MCP-1 antagonists intraperitoneally.

**Results** *Fluid induction* Intrapleural tPA injection induced significant pleural fluid in mice over DNase or saline controls (123  $\pm$  44 v 6  $\pm$  6 vs 0  $\pm$  0  $\mu$ L respectively, p < 0.05) after 6 h. This effect was reproduced using streptokinase (SK) and urokinase (UK). Pleural fluid MCP-1 levels strongly correlated with the amount of fluid (r = 0.7302, p = 0.003) and were significantly higher than serum MCP-1 (p < 0.001).

*Role of MCP-1* 54 mice given intrapleural tPA were treated with anti-MCP1 antibody 30  $\mu$ g (or its isotype control) or an MCP-1 receptor (CCR2) antagonist (or vehicle control) given intraperitoneally 12 h prior to and at the time of tPA injection. A significant decrease in pleural fluid formation was seen both with anti-MCP-1 antibody (27  $\pm$  17  $\mu$ L vs controls 169  $\pm$  73  $\mu$ L; p < 0.05) or CCR2 antagonist (62  $\pm$  58 vs controls 165  $\pm$  89  $\mu$ L, p = 0.0049).

**Conclusion** tPA (and other fibrinolytics) are potent inducers of exudative pleural fluid release, in a mechanism mediated via MCP-1.

**Supported by** Westcare (Western Australia).

**Conflict of Interest** No.

P045

### HUMAN RHINOVIRUS INFECTION INITIATES AIRWAY EPITHELIAL TIGHT JUNCTION DISASSEMBLY RESULTING IN BARRIER FUNCTION DISRUPTION

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**Introduction** To directly correlate live human rhinovirus (HRV) infection with tight junction (TJ) disassembly, leading to barrier compromise.

**Methods** Polarized human epithelial colorectal adenocarcinoma cells (Caco-2) and human airway epithelial cell (NuLi-1) were infected with HRV-1B at various multiplicity of infection (MOI) over 72 h. Viral receptor and replication were assessed via qPCR. Cell viability and apoptosis was assessed via proliferation and apoptotic assays. TJ protein expression of occludin, claudin-1 and zonal occludin-1 (ZO-1) was evaluated using in-cell western assays. Barrier integrity was assessed via trans epithelial electrical resistance (TEER) measurements and permeability assays.

**Results** Viral receptor expression and replication increased following infection in both cell types while proliferation and apoptotic assays demonstrated a time and MOI-dependent effect on cell viability. Both cell types showed diminished expression of membrane TJ protein post infection which corresponded with a decrease in TEER values and an increase in permeability but a greater effect was observed in NuLi-1 cells.

**Conclusion** Loss of epithelial barrier function following infection at lower MOI was attributed to disassembly of TJ proteins, resulting in increased trafficking of small particles into the sub-epithelial space. This could contribute towards further inflammatory responses and increased susceptibility to subsequent infections.

**Supported by** Asthma Foundation, NHMRC, PMH Foundation.

**Nomination** TSANZ Travel Award.

**Conflict of Interest** None.

P046

### DOXYCYCLINE INHIBITS RHOA-GTPASE ACTIVITY IN MOUSE EMBRYONIC FIBROBLASTS

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**Introduction** Lymphangioliomyomatosis (LAM) is a rare lung disease in which mutational inactivation of the tuberous sclerosis complex (TSC) (predominantly TSC2) is associated with enhanced cellular proliferation and migration. We have previously reported that doxycycline inhibits the enhanced migratory capacity of TSC2-null mouse embryonic fibroblasts (MEF) whereas rapamycin (inhibitor of LAM cell proliferation) had no effect (1). The aim of this study was to investigate the mechanism through which doxycycline inhibits the enhanced migration of TSC2-null MEF.

**Methods** RhoA activity and phosphorylation of p70S6 Kinase (p-p70S6K) were measured using a RhoA activation assay and western blot in TSC2-positive and TSC2-null MEF treated with doxycycline, rapamycin or the Rho-associated protein kinase (ROCK) inhibitor Y-27632.

**Results** RhoA activity was 3.8-fold (basal) and 2.5-fold higher (stimulated with 10% FBS) in TSC2-null MEF than in TSC2-positive MEF (n = 4, p ≤ 0.05). In TSC2-null MEF doxycycline (1–30 µg/mL, n = 4, p ≤ 0.05) and Y-27632 (10 µM, n = 4, p ≤ 0.05) inhibited RhoA activity by 26.8–34.3% and 38.4% respectively, while rapamycin had no effect (200 nM, n = 4, p ≥ 0.05). In contrast, doxycycline had no effect on p-p70S6K (n = 5, p ≥ 0.05), whereas this was reduced by rapamycin (2–200 nM, n = 5, p ≤ 0.05).

**Conclusions** These data demonstrate that doxycycline but not rapamycin inhibits RhoA activity in TSC2-null MEF and provides further understanding of the mechanisms involved in the regulation of migration in cells deficient for TSC2.

**Supported by** LAM Australasia Research Alliance (LARA), CRC for Asthma and Airways, The New Zealand LAM Charitable Trust.

**Conflict of Interest** No.

**Reference**

HY Ng, BGG Oliver, JK Burgess, VP Krymskaya, JL Black, LM Moir. *Respirology* 2011; 16(Suppl.1): 37–86, TP-046.

P047

### NOX2β: A NOVEL SPLICE VARIANT OF NOX2 THAT PROMOTES ROS PRODUCTION IN MACROPHAGES

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**Aim** To determine whether Nox2, a reactive oxygen species (ROS) generating enzyme that contributes to oxidative lung tissue damage, undergoes alternative mRNA splicing.

**Methods** Western blotting, RT-PCR, DNA sequencing and L-012-enhanced chemiluminescence to measure ROS production, were performed on a variety of mouse tissues, primary and immortalized macrophages and human alveolar macrophages.

**Results** Immunoscreening for the presence of truncated Nox2 proteins identified a 30-kDa protein in lung and alveolar macrophages from wild-type mice. RT-PCR analysis of mRNA from mouse macrophages, and from human alveolar macrophages, identified a truncated Nox2 transcript which, upon sequence analysis, was found to be a product of the 'exon skipping' mode of alternative splicing, lacking exons 4–10 of the Nox2 gene. The predicted protein is comparable in size to that identified by immunoscreening and contains two transmembrane helices with binding sites for NADPH and the Nox organizer protein p47phox. Selective siRNA-mediated knockdown of the transcript reduced expression of the 30-kDa protein in macrophages, and suppressed ROS production.

**Conclusion** Nox2 undergoes alternative mRNA splicing to yield a 30-kDa protein – herein termed Nox2β – that regulates NADPH oxidase activity and the oxidative burst in mouse and human macrophages. Nox2β is likely to play a role in pathological processes, in particular lung diseases.

**Supported by** ARC, NHMRC.

**Conflict of Interest** No.

P048

### INNATE IMMUNE CELLS INFLUENCE STEM CELL ACTIVITY IN THE DEVELOPING AND ADULT LUNG

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It is well established that the stem cell microenvironment regulates the proliferation and differentiation of epithelial stem and progenitor cells. There is also increasing evidence that innate immune cells in particular play a significant role in regulating stem cell activity in specific organs including the liver, kidney and mammary glands. We hypothesize that immune cells also regulate epithelial stem cell activity in the lung. In this study we analyzed the role of macrophages in epithelial stem cell regulation in the lung.

**Methods and Results** Using a unique three-dimensional clonogenic assay we have previously shown that mesenchymal cells are a key component of the epithelial stem cell microenvironment in the adult mouse lung. Here we report for the first time that adult lung macrophages similarly share the ability to support the proliferation of adult lung epithelial stem cell/progenitor cells *in vitro*. We also show that in developing lungs, fetal macrophages are located near the distal tips of the developing lung epithelium, in close proximity to a previously described population of embryonic progenitor cells. Selective depletion of fetal macrophages from cultured mouse lung explants disrupted airway morphogenesis and resulted in reduced airway branching, while culture in the presence of a mouse macrophage colony-stimulating factor (CSF-1) resulted in increased epithelial cell proliferation.

**Conclusions** Our data reveals a role for lung macrophages in supporting epithelial stem and progenitor cell function in both the embryonic and adult lung. These findings have significant implications for the regeneration of the lung epithelium after injury, particularly in chronic inflammatory diseases of the lung, in which there are marked increases in immune cells the lung.

**Supported by** NHMRC.

**Conflict of Interest** No.

## COPD SIG: POSTER SESSION 1. COMMUNITY MANAGEMENT OF COPD

P049

### TELEPHONE HEALTH MENTORING IMPROVES SELF-MANAGEMENT CAPACITY IN COMMUNITY-RECRUITED COPD

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**Aim** Effective self-management and positive health behaviour changes can improve quality of life in chronic obstructive pulmonary disease (COPD) and prevent worsening severity. We compared telephone-delivered patient-centred support from community-nurse health mentors to regular non-specific phone contact and usual care.

**Methods** In a cluster-randomized study in moderate or severe COPD, outcomes assessed by questionnaires at 6- and 12-months were: chronic disease self-management capacity (partners in health PIH), quality of life (St George's Respiratory, Medical Outcomes Short Form SF36), psychological morbidity (Hospital Anxiety and Depression HADS-A/D).

**Results** In 192 participants (mean age 68 years, 52% male) mentoring was delivered with moderately good fidelity to training. In mixed model regression analyses, adjusted for age, gender, smoking status and airflow limitation, health mentoring increased self-management capacity over 12 months (PIH overall 0.30; 95% confidence interval (CI) 0.06, 0.58) and knowledge (PIH knowledge 0.50; 95% CI 0.00, 1.0) but not quality of life; although in both groups anxiety decreased (HADS-A -0.70; 95% CI -1.30, -0.08) and self-management coping improved (PIH coping 0.30; 95% CI 0.08, 0.52).

**Conclusions** Health mentoring improved self-management capacity although this did not translate into better quality of life compared to regular phone contact and usual care, which had positive effects where decline is expected.

**Supported by** NHMRC, BI/ALF COPD award, RHH Research Foundation.

**Conflict of Interest** No.

P050

### WEIGHT LOSS AND EXACERBATION MANAGEMENT: PATIENT PRIORITIES IN HOME-BASED PULMONARY REHABILITATION

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**Aim** To describe the health goals set by participants in a home-based pulmonary rehabilitation program.

**Methods** Participants with COPD undertook an 8-week pulmonary rehabilitation program at home. Patient-centred education and self management training took place weekly by telephone. Consistent with the principals of motivational interviewing, participants identified their most important health concerns each week. Structured telephone modules were used to build motivation for change, then move towards commitment and action. Health goals were documented each week.

**Results** Thirty-three participants of mean age 70 (SD10) years, FEV<sub>1</sub> 54(17)%predicted and BMI 30(8) kg.m<sup>-2</sup> took part. Participants attended 206 out of a possible 231 telephone sessions (89% attendance). A total of 198 health goals were documented in 182 sessions, with goals identified in 88% of sessions. The health goals most frequently identified related to weight loss (18% of goals), management of chest infections (16%), smoking cessation (10%) and maintenance of exercise following pulmonary rehabilitation (10%). Other frequently identified goals related to management of mood (5%), medications (5%), dyspnoea (5%), cough (5%), and having an influenza vaccination (5%).

**Conclusions** Participants in a home-based pulmonary rehabilitation program frequently identify health goals related to weight loss and management of acute exacerbations. To facilitate goal attainment in these important areas, consideration should be given to provision of appropriate community based supports for people with COPD undergoing pulmonary rehabilitation at home.

**Supported by** Australian Lung Foundation.

**Nomination** Nil.

**Conflict of Interest** No.

P051

### TELEREHABILITATION AT HOME IS SAFE AND FEASIBLE FOR PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**Aim** To evaluate the safety and feasibility of a low cost, real time model of telerehabilitation for people with chronic obstructive pulmonary disease (COPD).

**Method** Eight participants of mean age 66 (SD 8) years and FEV<sub>1</sub> 66(8) %predicted were recruited. Telerehabilitation equipment in the participant's home included a step-through exercise bike; tablet computer with webcam; freely available and low bandwidth videoconferencing software; and a pulse oximeter positioned such that the display was visible via videoconferencing. Participants undertook supervised aerobic training twice weekly for 8 weeks, with two participants and a clinician attending each class via videoconferencing from separate locations. Primary outcomes were adverse events, sessions attended and system usability. Secondary outcomes were 6-min walk distance (6MWD) and Chronic Respiratory Questionnaire (CRQ).

**Results** No major adverse events occurred. Minor adverse events were desaturation <88% (1 session) and heart rate > 150 bpm (6 sessions). Participants attended 76% of possible sessions. System usability ratings were excellent when sessions were delivered using the university network (94%) but lower when using the hospital network (59%), with 67% of technical issues related to network connectivity. Five participants completed the program, with clinically significant improvements in 6MWD (mean 25 (40) m and dyspnoea (4 (4) units).

**Conclusions** A low-cost, home-based model of telerehabilitation is safe and feasible for people with COPD. Ensuring adequate network capability is key to effective delivery of telerehabilitation.

**Supported by** Windermere Foundation, Telstra, La Trobe University.

**Nomination** Nil.

**Conflict of Interest** Nil.

P052

### SEASONAL VARIATION AND LIVING ALONE ARE RELATED TO NON-COMPLETION IN A PULMONARY REHABILITATION PROGRAM

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**Aim** To examine differences in characteristics between pulmonary rehabilitation program completers and non-completers; and to improve the understanding of the factors that affect program completion.

**Methods** Participants with COPD who attended a standardized eight week pulmonary rehabilitation program between 2010 and 2012 were recruited. Participants who attended <12/16 sessions were classified as a non-completer. Non-completers were asked to participate in a survey about their pulmonary rehabilitation experience. Baseline measures used to assess for differences between completers and non-completers included lung function, comorbidities, 6-min walk distance, quadriceps strength, quality of life, self-efficacy, the BODE index, smoking history and social support.

**Results** Twenty-six participants (23.4%) of the 111 eligible participants, mean (± SD) age was 67.4 ± 9.2 years and FEV<sub>1</sub> 54.6 ± 22.3%, were classified as non-completers. The only independent predictors associated with pulmonary rehabilitation program non-completion were participants living alone (Exp B: 2.925, 95% CI: 1.039–8.229, *p* = 0.042) and programs commencing in winter (Exp B: 0.255, 95% CI: 0.090–0.727, *p* = 0.011). The common reasons reported for non-completion included illness and transport difficulties.

**Conclusions** Despite the program's subtropical location, only programs commencing in winter and participants who lived alone were associated with program non-completion.

**Supported by** TPCH Foundation, QLD Health HP Research Scheme.

**Nomination** Physiotherapy award.

**Conflict of Interest** No.

P053

**A NURSE PRACTITIONER LED CASE MANAGED PROGRAM FOR COPD PATIENTS IN THE COMMUNITY WILL REDUCE HOSPITAL ADMISSIONS**

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**Aim** To determine if a case management program for high risk patients with COPD will reduce emergency department presentations and hospital admissions.

**Methods** This service utilizes the advanced and extended respiratory nursing skills of nurse practitioners in order to case manage complex respiratory clients through collaboration with the general practitioner and specialists. It utilizes best practice guidelines in order to achieve optimal patient outcomes, with a focus on hospital avoidance strategies. Patients who have three or more admissions for a COPD exacerbation in the last 12 months and 4 or more significant risk factors that may be reversible are offered case management. Data are collected for each client retrospectively and prospectively for 12 months on the number of COPD and 'all cause' emergency presentations and admissions.

**Results** For the 64 case managed clients over the last 2 years there has been a 47% reduction in the number of COPD admissions, 44% reduction in occupied bed days for COPD admissions and a 46% reduction in ED presentations for COPD. This reduction is significant in a group of patients with severe and progressive disease.

**Conclusions** Case management by respiratory nurse practitioners can decrease emergency presentations and admissions in patients with severe and complex disease.

**Supported by** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

P055

**VALIDATION OF NON-WEAR TIME DURING ACTIVITY MONITORING IN PEOPLE WITH COPD**

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**Aim** To explore different criteria for estimating non wear time in accelerometry data.

**Background** Profiling daily activity in people with chronic disease is of increasing interest. Determination of activity monitor wear time is essential when estimating time spent in sleep, sedentary and active behaviours. As ambulatory monitoring devices become more accessible to both researchers and clinicians so has the need to define thresholds for non-wear. It is unknown whether procedures and criteria commonly applied to accelerometry data in children and adults in the general population appropriately estimate non wear time in people with COPD where prolonged periods low level physical activity are common.

**Methods** 60 participants, with and without a diagnosis of COPD (COPD n = 30 Age 74.4 ± 7.5 years, FEV<sub>1</sub> 52% ± 19%, non-COPD Age 70.3 ± 10.2 years, FEV<sub>1</sub> 102% ± 25%), wore SenseWear Pro3 armbands and Actigraph GT3X<sup>+</sup> accelerometers over six consecutive full days, reporting non wear time using a diary. Diary and SenseWear non-wear times were compared to accelerometry estimates using conventional (30 and 60 min) and extended (90 and 120 min) inactivity count cut off points.

**Results** After excluding incomplete data sets, 53 participants were included in the analysis. SenseWear compliance was 96% during waking hour's Preliminary analysis indicates GTX3+ estimated non-wear is higher in people with COPD despite similar diary and SenseWear reports.

**Conclusion** The procedures and criteria commonly used with accelerometry data in children and general adult populations are likely to overestimate non wear time in people with COPD.

**Conflict of Interest** No.

P056

**RESPIRATORY CLINIC REFERRAL PATTERNS TO AN OUTPATIENT PULMONARY REHABILITATION PROGRAM**

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**Aim** To identify barriers to referral to pulmonary rehabilitation (PR) from specialist respiratory outpatient (ROP) clinics.

**Methods** Medical staff were invited to complete a brief checklist for each patient seen in a ROP clinic over a 3 month period at a tertiary hospital in Melbourne. Sleep clinics were excluded. Questions consisted of whether or not the patient was referred to PR; if referral was declined, and why.

**Results** Responses were received for 471 (87%) of 539 appointments. Patients had a mean (SD) age of 60 (16) years and 242 (51%) had a diagnosis of COPD. Other common diagnoses were sleep disorders 140 (29%), asthma 31 (6%), ILD 14 (3%) and chronic cough 8 (2%). Of patients with COPD, referral to PR was made for 31 (13%), a further 25 (5%) declined. One non-COPD patient with dyspnoea and obesity was referred. A total of 211 patients with COPD were not referred to PR for the following reasons reported by their doctor:

	No benefit/not applicable	No symptoms	Already enrolled or exercising	Other medical limitation	Second opinion	Unable	Not interested	Clinical trial	No reason
Patient declined	12	3	1	—	—	3	3	—	3
Doctor	78	24	39	13	4	4	1	2	21
Total	90	27	40	13	4	7	3	2	24

**Conclusion** 29% of patients with COPD attending a ROP clinic were referred to PR or were already enrolled. The main reasons for non-referral was lack of perceived benefit by patients, or PR deemed not applicable by doctors. Previously reported patient-related barriers to attendance such as access or transport were not significant factors in referral. Patients with chronic respiratory disease other than COPD were not referred to PR.

**Support** Nil.

**Conflict of Interest** Nil.

P054

**COMPONENTS FOR DEVELOPMENT OF A NURSING APPROACH MODEL SUITABLE FOR EARLY-STAGE PATIENTS WITH COPD**

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**Aim** To review previous studies on chronic disease management (CDM) and nursing intervention models and thereby investigate components that are important for developing intervention models in order to develop a nursing intervention model suitable for early-stage patients with COPD.

**Methods** Using the keywords 'chronic disease management', 'nursing', and 'life skill', we searched for previous studies published on the electronic database 'CINAHL with Full Text', and critiqued a total of 228 studies that were found.

**Results** 1. CDM consisted mainly of case management programs for patients with chronic disease such as diabetes and heart failure. 2. The effects of CDM were disease prevention, decreased number of admissions, and enhanced QOL. 3. The contents of CDM were aimed at improving the self-management skills of patients, and incorporation of the components of psychosocial and emotional management skills in addition to skills related to medical treatment was important. 4. Issues for nurses involved in CDM were evidence-based nursing practice, enhancement of patient education techniques that promote behavioural modification in patients.

**Conclusion** In the development of a nursing intervention model suitable for early-stage patients with COPD, it is important to investigate models based on the components elucidated herein regarding the contents of existing patient education programs for COPD.

**Supported by** Grants-in-Aid for Scientific Research <KAKENHI>.

**Nomination** No.

**Conflict of Interest** No.

P057

### WHAT COPD CARERS WANT – RESULTS OF A THEMATIC ANALYSIS

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**Introduction** Many COPD patients are highly dependent on primary carers (often partners) who are central to providing daily tasks and support. However, little is known about the needs of carers that often provide this assumed enabling role. The aim of the present study was to identify the perceived needs of the primary carers of COPD patients.

**Method** Twenty-one patient-carer dyads recruited from databases at the Repatriation General Hospital in South Australia. Carers (mean age 71.1, SD 9.8' 66.7% female) of COPD patients (mean age 75.2, SD 7.6, 66.7% male) attended a semi-structured, 60–90 min focus group meeting facilitated by a psychologist.

**Results** Data were processed using inductive thematic analysis. Emergent latent themes were identified. The 'impacts' on the carer were identified as physical, emotional, social and financial. 'Handicaps' noted were social and work/study related. Identified 'barriers' to providing care included physical and emotional problems of either carers or patients, lack of knowledge/education, lack of inclusion in discharge or treatment plans, difficulty coping with role reversal for both patients and carers, lack of respite and patient perception of the caring role as a natural extension of the existing familial or spousal role. 'Enablers' to providing care included respite support, counselling, peer debriefing opportunities, education and involvement in treatment.

**Discussion** The significant impact and handicaps associated with the carer role remain under-supported. Findings suggest the potential value of carer recognition, support, upskilling and involvement in COPD treatment planning.

**Supported by** Daw Park Research Foundation.

P059

### PULMONARY REHABILITATION REDUCES HOSPITAL ADMISSIONS – AN OBSERVATIONAL STUDY

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**Aim** To review the referral rate and patient uptake rate of Pulmonary Rehabilitation (PR) at the Royal Brisbane & Women's Hospital (RBWH); and to compare the patients' hospital admissions and costs in the year before and after completion of PR.

**Methods** A 5-year (2006–2011) review of PR was conducted. The rate of referral to PR of those admitted to the RBWH with exacerbation of their chronic respiratory disease was evaluated; and uptake to PR of those referred was determined. The number and cost of hospital admissions in the year prior to attending PR was compared to the year after attending PR of those who completed PR.

**Results** In the 5-year period studied, 1053 patients were admitted to RBWH with exacerbation of their chronic respiratory diseases; 173 of these patients were referred to PR (referral rate 16.4%). A total of 486 patients (including those referred from other sources) were screened by the PR team, 182 patients participated in the PR program and 147 completed the program (uptake rate of 37.4% and completion rate 80%). Following completion of PR, a review of these 147 patients showed that there was a 52% reduction in the number of patients requiring hospital admissions (58 to 28;  $p < 0.01$ ) and a 71% reduction in the total number of admissions to RBWH (140 to 41;  $p < 0.01$ ). The reduction in hospital admissions in the 12 months following induction into PR equates to hospital cost saving of \$427,000.

**Conclusion** Pulmonary Rehabilitation reduces hospitalization costs at the Royal Brisbane & Women's Hospital.

**Conflict of Interest** No.

P058

### COMMUNITY-BASED MAINTENANCE (PHASE 3) PULMONARY REHABILITATION – UPTAKE, ATTRITION AND HOSPITALIZATION

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Weekly physiotherapist-supervised exercise training helps to maintain the benefits of an initial (Phase 2) pulmonary rehabilitation program (PRP).

**Aim** To examine uptake, attrition and hospitalization trends in patients referred to a community-based maintenance PRP (Phase 3).

**Methods** Data were collected on all patients referred to Phase 3 PRPs over a 6-year period. Reasons for lack of uptake and program attrition were recorded. Hospitalization data (self-report verified from hospital database) were collected for the 12 months prior to referral, and for 12 and 24 months following referral for individuals who continued to attend.

**Results** 584 individuals (266 M/318 F) with chronic lung disease (COPD 474 [81%]), aged 71 ± 8 years were referred. 81 (14%) never attended. 182 (36%) were still attending at 12 months and 127 (25%) at 24 months. The main reason for lack of uptake and attrition was illness (21%). In those still attending at 2 years, there was a reduction in admissions (adm) and total bed days for respiratory-related illness (Table).

	12 months pre-adm (bed days)	12 months post-adm (bed days)	24 months post-adm (bed days)
Attended 12 months (n = 182)	62 (346)	37* (176*)	—
Attended 24 months (n = 127)	38 (210)	13* (46*)	20 (84*)

\* $p < 0.05$  compared to data at 12 months pre-PRP.

**Conclusion** Attendance at a Phase 3 community-based PRP appears to be associated with reduced hospitalization for respiratory-related illness.

**Conflict of Interest** No.

P060

### HEALTH OUTCOMES FOR PATIENTS AND CARERS AFTER TRAINING FOR CARERS OF PEOPLE USING HOME OXYGEN THERAPY (HOT): AN RCT

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**Aim** To analyze health outcomes for patients and carers from training carers to support severely disabled people with HOT for chronic lung diseases.

**Methods** Patients residing at home with a primary caregiver who were receiving HOT through public hospitals in Adelaide were invited to enter an RCT of a carer training intervention conducted over 2008–2010. Carer Health related Quality of Life (QOL) and aspects of carer burden, and patient QOL for all 197 enrolled patient-carer dyads were evaluated at baseline then 3, 6 and 12 months after the intervention.

**Results** Across arms, carers had similar QOL (SF36) to age-matched Australian populations but slightly elevated carer burden, while patients' QOL was severely impaired (SF36 and Chronic Respiratory Questionnaire, CRQ). Between arms, the intervention was associated with significant improvements in carer SF36-Role Physical ( $p = 0.0092$ ) as well as patient CRQ-mastery ( $p < 0.0001$ ) and CRQ-fatigue ( $p = 0.0167$ ). There was, however, unanticipated imbalance in patient mortality over 1 year—patients whose carers received training had significantly worse 1-year mortality rates than those in the control group (31% vs 11%,  $p = 0.001$ ).

**Conclusion** Training carers to provide more informed help to HOT patients improved patients' QOL but had little effect on carer QOL or burden, and was associated with unexpected excess of patient mortality.

**Supported by** NHMRC Grant #426737.

**Conflicts of Interest** No.

P061

**IMPLEMENTING A HOME OXYGEN CLINIC: THE IPSWICH HOSPITAL EXPERIENCE**A DE KLERK-BRAASCH, A FRANKLIN  
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**Aim** To improve the assessment, treatment and follow-up of patients requiring home oxygen, a Home Oxygen Therapy Clinic (HOT) was started in February 2010 at Ipswich Hospital.

**Methods** The HOT clinic complies with the TSANZ position statement on the prescription of adult domiciliary oxygen therapy. Management consists of a focused medical interview and clinical assessment. Demographic data, diagnosis, smoking status, pulmonary function test and oximetry data are recorded. Arterial blood gas sampling and 6-min walk tests on and off oxygen are performed if clinically indicated. Patients are followed up within 3 months of starting oxygen and twelve monthly thereafter.

**Results** From February 2010 to August 2012 the clinic assessed 171 patients. Of the patients assessed, 66% were referred during a recent hospital admission. 125 (73%) had a principal diagnosis of COPD, 12 (7%) interstitial lung disease, 9 (5%) pulmonary hypertension, 19 (11%) cardiac conditions, 3 (2%) a palliative and 3 (2%) another diagnosis. Seventeen (10%) patients were current smokers. Eighty (47%) of the patients assessed had other medical issues requiring further assessment. The mean FEV1 for patients with COPD was 37.1% and 62% for those with cardiac conditions. A significant number of patients were not prescribed O2 or their prescriptions ceased: 53 (31%) did not qualify for oxygen at the initial visit. Of the 47 (27%) patients assessed 4 months later, 24 (51%) qualified for home oxygen. At the 12 months assessment 37 of the 44 (84%) continued with O2 treatment.

**Conclusions** A dedicated Home Oxygen Therapy Clinic resulted in cost-effective appropriate prescription, management and follow-up of patients requiring oxygen according to the current guidelines.

**Conflict of Interest** No.

P063

**FACTORS AFFECTING THE DIETARY INTAKE OF PEOPLE ON HOME OXYGEN THERAPY (HOT) DUE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE**L MATTHEWS<sup>1</sup>, G CROSS<sup>2</sup>, P FRITH<sup>3</sup>  
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**Aim** To identify factors that affect dietary intake in a small sample of outpatients with chronic obstructive pulmonary disease (COPD) receiving HOT in a qualitative pilot study.

**Methods** Detailed semi-structured face-to-face interviews were conducted with four people with stable COPD using HOT. Interviews were audio-recorded, transcribed and analyzed to identify factors affecting the dietary intake of participants. Analysis was supported by the software program QSR NVivo10 (QSR International Pty Ltd Australia). Additional nutritional data were collected using a self-completed Food and Symptom Diary (FSD); Mini-Nutritional Assessment (MNA) tool; Body Mass Index (BMI); and the COPD Assessment Test (CAT).

**Results** The main factors that influenced dietary intake in this group were a limited ability to access and prepare food, and COPD-related symptoms of dyspnoea and satiety. Dietary intake was significantly higher if a residential spouse or carer was present. HOT was not perceived to influence food intake. The MNA identified two participants at risk of malnutrition, and all participants failed to meet the Recommended Dietary Intakes (RDI) for numerous micronutrients.

**Conclusions** This qualitative pilot study identifies some food and dietary related challenges faced by outpatients with COPD receiving HOT. Their dietary intake is influenced by many of the same factors already known to affect people with COPD not receiving HOT. Further research is warranted to clarify what influence HOT has on these nutritional issues.

**Conflicts of Interest** No.

**COPD SIG: POSTER SESSION 2. ADVANCES IN CARE**

P064

**AMBULATORY OXYGEN FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A COCHRANE META-ANALYSIS**F AMEER<sup>1,2</sup>, KV CARSON<sup>2,3</sup>, ZA USMANI<sup>2,3</sup>, BJ SMITH<sup>2,3</sup>  
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**Aim** To determine the longer term efficacy of ambulatory oxygen therapy only for patients with chronic obstructive pulmonary disease (COPD) who do not meet the criteria for long term oxygen treatment, with respect to improvements in mortality, exercise capacity, quality of life and hospital utilization amongst other outcomes.

**Methods** The Cochrane Airways Group's specialized register, electronic databases and the bibliographies of identified studies were searched. Included studies were randomized controlled trials or cross-over studies comparing long term (>2 weeks) ambulatory oxygen therapy to a control group (placebo air cylinders, usual medical care or no intervention) in COPD patients. Ambulatory oxygen was provided through portable oxygen cylinders or with liquid oxygen canisters.

**Results** From 163 citations four studies met all of the eligibility criteria for inclusion within the review, with a total of 330 participants. There was no evidence of effect for survival or exercise capacity in the reported studies. Two studies produced a statistically and clinically significant benefit in favour of the oxygen group for dyspnoea post exercise (Mean Difference (MD) -0.58; 95%CI -1.15 to -0.02; p = 0.04) and all four studies investigated quality of life, producing a statistically and clinically significant benefit in favour of the intervention group for the dyspnoea (MD 0.28; 95%CI 0.04 to 0.53; p = 0.02) and fatigue (MD 0.16; 95%CI 0.01 to 0.32; p = 0.04) domains.

**Conclusion** Despite ongoing use in clinical practice, this review does not allow firm recommendations to be made for the clinical utility or effectiveness of ambulatory oxygen therapy for COPD patients. Well designed randomized controlled trials are required to understand the role of ambulatory oxygen in COPD management.

**Support** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

P062

**CLINICAL REVIEW OF HOME OXYGEN THERAPY IN A QUEENSLAND SUBURBAN HOSPITAL: PRESCRIPTION AND ADHERENCE TO NATIONAL GUIDELINES**AHT LAU, J STROUD, K TRAN  
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**Aim** To assess the usage of home oxygen therapy in a Queensland suburban hospital, indications, difference in medical sub-specialties, accuracy of prescription and adherence to national guidelines.

**Design** Retrospective observational study.

**Methods** Logan Hospital patients who were receiving government-funded home oxygen therapy in 2011. Data were extracted on demographics and initial home oxygen prescription.

**Results** 105 patients were using home oxygen therapy. 101 patients (95%) met national guideline for initiation of home oxygen therapy. All patients had 4 months reassessment follow-up. COPD was the most common indication (74%). 62% of patient were approved for chronic hypoxemia (best evidence), 36% of patient were approved for exertional hypoxemia or nocturnal hypoxemia (less evidence). Respiratory medicine prescribed more home oxygen therapy (69%) compared to other medical sub-specialty. Almost half of the prescription were done during inpatient admissions and based on ward observation (48%). Home oxygen was more commonly prescribed by junior medical officer and often contains inaccurate information, in 42% of prescription.

**Conclusions** Prescription of home oxygen was in keeping with national guidelines. Junior medical staff did most of home oxygen prescription and errors in application were common.

**Grant Support** No.

**Nomination** No.

**Conflict of Interest** No.



P065

### AECOPD: DIFFERENCES IN CARE BETWEEN RESPIRATORY AND NON-RESPIRATORY SPECIALISTS

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**Introduction and Aim** Both respiratory specialists (RS) and non-respiratory specialists (NRS) manage patients with acute exacerbations of chronic obstructive pulmonary disease. The aim of this study was to review the patterns of care and clinical outcomes for COPD patients treated by RS and NRS in the Gold Coast Health Service District.

**Methods** A retrospective review was undertaken of consecutive COPD patients admitted over a three-month period. Electronic medical records, medical case notes, pathology and radiology data for the admission were reviewed. Fisher's exact test was used to compare categorical variables.

**Results** There were 201 COPD exacerbations in 170 patients (50.2% male, mean age 74). RS managed 117 (58.3%) exacerbations while NRS managed 84 (41.7%) exacerbations. RS performed spirometry (38.5% vs 9.5%,  $p < 0.001$ ) and arterial blood gas analysis (60.7% vs 27.4%,  $p = 0.001$ ) more frequently compared with NRS. RS discharged patients more frequently with salbutamol (88% vs 75%,  $p = 0.023$ ), tiotropium (78.6% vs 50%,  $p = 0.001$ ), combination long-acting bronchodilator and inhaled corticosteroids (82.9% vs 69%,  $p = 0.027$ ), oral prednisolone (80.3% vs 67.9%,  $p = 0.046$ ) and oral antibiotics (68.4% vs 48.8%,  $p = 0.006$ ). Median length of stay was increased in the patients managed by RS compared with NRS (5 days vs 3 days,  $p = 0.001$ ). There were no differences with regards to 12-month re-admission (45% vs 35%,  $p = 0.664$ ) or mortality rates (7% vs 9%,  $p = 0.292$ ).

**Conclusion** There are differences in the care provided by RS and NRS to COPD patients but not in clinical outcomes. Further study is required to identify the reasons responsible for the differences in care.

**Conflict of Interest** No.

P067

### PREVALENCE OF AIRFLOW OBSTRUCTION IN A REMOTE AND ABORIGINAL AUSTRALIAN POPULATION: THE KIMBERLEY BURDEN OF LUNG DISEASE (BOLD) STUDY

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**Aim** To measure the prevalence of airflow obstruction in a representative sample of Aboriginal and non-Indigenous Australians aged 40 years and older living in remote northern Australian communities.

**Methods** A representative sample was identified in five remote and very remote communities in the Kimberley region of northern Australia. Standardized questionnaires relating to risk factors, symptoms and diagnoses were administered and quality-controlled spirometry conducted. FEV1, FVC and their ratio were measured before and after bronchodilator.

**Results** Complete data were available for 704 participants. In the Kimberley region, the prevalence of COPD, defined as post-bronchodilator FEV1/FVC ratio  $< 0.7$  and FEV1  $< 80\%$  predicted, in the Aboriginal population (7.6% (4.3 to 10.8)) was similar to that seen in the non-Indigenous population (8.2%, (5.7 to 10.7)),  $p = 0.89$  for difference). The odds of having FVC below the lower limit of normal (NHANES III) were higher in Aboriginal than non-Aboriginal participants (OR 27.2,  $p < 0.0001$ ).

**Conclusions** This is the first accurate assessment of airflow obstruction in a representative sample of the Aboriginal Australian population. Low vital capacity may be associated with reduced respiratory reserve in the setting of intercurrent infection, and account for the increased overall impact of COPD on Indigenous people.

**Supported by** NHMRC, Robert Pierce Grant in Aid – TSANZ.

**Conflict of Interest** No.

P066

### CLINICAL FEATURES ASSOCIATED WITH HOSPITAL ADMISSION IN COPD PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT

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**Introduction** Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality in Australia. Hospitalization for the treatment of acute exacerbations of COPD is not only associated with adverse clinical outcomes but also is also responsible for high health care costs. However, little is known about the factors that are associated with hospitalization in COPD patients presenting to the emergency department (ED).

**Aim** The aim of this study was to review the clinical data of COPD patients presenting to the ED and compare them between patients who were admitted to hospital against those patients who were discharged.

**Methods** A retrospective review was undertaken of consecutive patients with a diagnosis of COPD presenting to the Gold Coast Hospital ED over a six-month period. Electronic medical records, pathology and radiology data were reviewed. Fisher's exact test was used to compare categorical variables.

**Results** There were 176 exacerbations in 123 patients (52% male, mean age 72), of which 84% required hospitalization. Patient characteristics associated with hospitalization were increased age ( $p = 0.002$ ), ex-smoker ( $p = 0.03$ ), home oxygen use ( $p = 0.001$ ) and more than 1 COPD related hospitalization in the previous 12 months ( $p = 0.012$ ). Patients who had presented despite prior treatment by their GP ( $p = 0.008$ ), required oxygen in ED ( $p < 0.001$ ) and with increased WCC ( $p = 0.013$ ), neutrophils ( $p = 0.007$ ) and CRP ( $p = 0.018$ ) were also more likely to be hospitalized.

**Conclusion** The majority of COPD patients presenting to our ED were hospitalized. Further study is required to determine whether better ED management will translate to reductions in hospitalization for COPD patients in the Gold Coast Health Service District.

**Conflict of Interest** No.

P068

### NSW PULMONARY REHABILITATION SERVICES – A 10-YEAR HEALTH CHECK

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**Background** Pulmonary Rehabilitation (PR) reduces hospitalization and has been shown to be cost effective (COPDX Plan). PR services were widely established across NSW during the Priority Health Care Program (2000–2003). The ACI Respiratory Network reviewed mandatory NSW reporting of patients referred to, commenced and completed PR data which demonstrate decreased activity from 2008 to 2011.

**Method** An online survey which identified key aspects of program structure, resources and workforce in 2011 which was completed by 98% of active PR sites ( $n = 84$ ).

**Key PR Results** *Resources:* 27% PR services are coordinated by a clinician with 4 or less designated hours per week. *Experience:* 22% of staff had 1 year or less experience in PR. *Referral source:* 3% sites identified practice nurses as a major referral group. *Activity:* 64% programs had less than 50 patients commence in 2011. *Service issues:* 62% sites reported inability to fill vacant positions as a major issue. *Workforce needs:* 57% sites reported access to PR education and training as a major issue.

**Conclusion** A statewide health check of existing services has identified key areas to target with the aim to enhance PR services capacity and quality.

**Support** Nil.

**Conflict of Interest** Nil.

P069

### COMPARISON OF TWO QUALITY OF LIFE ASSESSMENT TOOLS IN PATIENTS WITH COPD REFERRED FOR PULMONARY REHABILITATION

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**Background** The COPD (chronic obstructive pulmonary disease) Assessment Test (CAT) is a new tool used to measure health status in patients with COPD, which has been validated in the USA, Europe and China. The CAT demonstrated strong correlation with the SGRQ-C (shorter form of the St George Respiratory Questionnaire (SGRQ)).

**Aim** To compare the CAT with SGRQ in an Australian context in patients with COPD assessed for and/or completing pulmonary rehabilitation (PR).

**Methods** Retrospective chart review of patients assessed for PR in Western Sydney, with further analysis of a subgroup who completed the CAT post PR.

**Results** Assessment data were available for 286 patients: 51% male; age 69.7 ± 9.1 years (mean ± SD); FEV<sub>1</sub> 40 ± 17% predicted; Medical Research Council (MRC) Dyspnoea scale 4 ± 1 arbitrary units (au); 6-min walk distance (6MWD) 367.9 ± 96.5 m; CAT 20.5 ± 7.0 units; SGRQ Total 57 ± 15%. There was a strong correlation between the CAT and SGRQ ( $r = 0.6$ ,  $p < 0.05$ ) and moderate correlation between the CAT and MRC Dyspnoea scale ( $r = 0.3$ ,  $p < 0.05$ ). Post PR, data were available for 74 patients. For the group, mean improvement in 6MWD was 61.0 ± 71.5 m ( $p < 0.05$ ). The CAT score decreased by 1.3 ± 5.9 units ( $p = 0.06$ ) and SGRQ Total by 6 ± 13% ( $p < 0.005$ ). However there was no correlation between the change in CAT and change in SGRQ or change in 6MWD.

**Conclusion** The CAT provides a good assessment of baseline health status in COPD, but does not appear to be as sensitive to improvements in health status with PR.

**Conflict of Interest** No.

P071

### CLINICAL PRACTICE AUDIT: WARD-BASED NON-INVASIVE VENTILATION (NIV) AT GOLD COAST HOSPITAL (GCH)

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**Aim** NIV has been an integral part of the acute management of patient with respiratory failure for many years, especially in COPD. The aim of this study is to review the current practice of non-invasive ventilation (NIV) in the respiratory ward at Gold Coast Hospital (GCH). We assessed the indications for NIV, efficacy, complication, blood gas assessments and contingency plans if NIV failed.

**Methods** Prospective data were collected for all patients on NIV in the respiratory ward at GCH from January to October 2012. Informed consent was obtained. Patient's data, demographics, co-morbidities, arterial blood gases, complications and outcomes were recorded.

**Results** 33 patients were commenced on NIV over the 10 months period, with Emergency (58%) being the primary site of initiating NIV. NIV was initiated for hypercapnic respiratory failure in 84% 64% had COPD. Blood gases improved while on NIV.

**Table 2** Arterial blood gas

	Baseline, n = 24 (73%)	After NIV, n = 27 (82%)	Before discharge, n = 20 (61%)
pH	7.25 (SD ± 0.07)	7.33 (SD ± 0.1)	7.34 (SD ± 0.09)
pO <sub>2</sub>	83 mm Hg (SD ± 71)	92 mm Hg (SD ± 49)	90 mm Hg (SD ± 70)
pCO <sub>2</sub>	79 mm Hg (SD ± 21)	65 mm Hg (SD ± 21)	63 mm Hg (SD ± 15)

70% of the patients improved on NIV and were successful discharged. Average duration on NIV was 3.4 days. 6 patients (18%) died despite treatment.

**Conclusions** NIV was an effective therapy on the ward. However, a significant proportion (16%) of patients was started on NIV with non-hypercapnic respiratory failure.

**Supported by** Nil.

**Nomination** No.

**Conflict of Interest** No.

P070

### MODELS OF CARE FOR ACUTE NON-INVASIVE VENTILATION IN COPD-COMPARISON OF THREE TERTIARY CENTRES (ACT3 STUDY)

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**Aim** Non-invasive ventilation (NIV) improves clinical outcomes in patients with acute hypercapnic COPD, although the optimal site of care (general ward v HDU v ICU) is not known.

**Methods** Prospective observational non-inferiority study comparing the effectiveness of NIV treatment of acute hypercapnic COPD located on a general ward (1:4 nurse to bed ratio), a high dependency unit (HDU) (1:2 ratio) and an ICU (1:1 ratio) in three separate public teaching hospitals in Melbourne. Analysis of variance was used.

**Results** (mean ± SD). Over a 14-month period, the ward-based service treated significantly more patients ( $n = 38$ ) than the HDU ( $n = 28$ ) and ICU ( $n = 15$ ) corrected for hospital size ( $p < 0.001$ ). There was no difference in baseline age (70 ± 10 years), FEV<sub>1</sub> (0.84 ± 0.35 L), initial pH (7.29 ± 0.08) or PaCO<sub>2</sub> (72 ± 22 mm Hg) of patients treated at the three centres. There was no difference with NIV treatment in the increase in pH (0.12 ± 0.07) and the fall in PaCO<sub>2</sub> (12 ± 18 mm Hg) between the three centres ( $p = 0.2$ , 0.6 respectively). Patients in the ward centre (compared with HDU and ICU respectively) received significantly more NIV during the first 24 h (12.3 ± 4.8 vs 7.9 ± 4.1 vs 8.4 ± 5.3 h  $p < 0.05$ ) whilst more ICU patients were intubated (0 vs 0 vs 20%,  $p < 0.05$ ) and had a longer hospital LOS (9 ± 11 vs 7 ± 7 vs 13 ± 28 days,  $p < 0.002$ ).

**Conclusion** The three NIV centres treated patients with COPD of similar disease severity and achieve equivalent physiological improvements. An economic analysis is currently underway to access which model of care is most cost-effective.

**Conflict of Interest** No.

**Nomination** TSANZ travel grant.

P072

### POSITIVE EXPIRATORY PRESSURE DOES NOT IMPROVE VENTILATION INHOMOGENEITY IN INDIVIDUALS WITH COPD AND CHRONIC SPUTUM EXPECTORATION

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**Background** Positive expiratory pressure (PEP) has been used to promote airway clearance in individuals with COPD, however little is known about its mechanism of action. This study tested the hypothesis that PEP improves ventilation inhomogeneity via changes in lung volumes.

**Methods** Twelve participants with stable COPD (mean FEV<sub>1</sub> 45% pred.) and chronic sputum expectoration performed PEP mask therapy (10–20 cm H<sub>2</sub>O) or controlled huffing and coughing in random order on separate days. Measures of acinar and conductive airways ventilation ( $S_{acin}$ ,  $S_{cond}$ ), lung volumes, spirometry and sputum weight were recorded before, immediately following and 90 min following treatment. Ease of expectoration (visual analogue scale [VAS]) and oxyhaemoglobin saturation ( $SpO_2$ ) were assessed immediately following treatment.

**Results** No significant difference existed between the two test conditions for any test parameter at any time point. Immediately following the PEP and control conditions, mean  $S_{acin}$  was 0.463 L<sup>-1</sup> vs 0.443 L<sup>-1</sup>, respectively, and  $S_{cond}$  0.042 L<sup>-1</sup> vs 0.040 L<sup>-1</sup>. Mean sputum weights were 7.06 g vs 6.15 g, respectively and VAS scores 4.8 cm vs 4.1 cm.

**Conclusion** Any therapeutic benefits of PEP mask therapy in individuals with COPD are unlikely to be mediated by improvements in ventilation inhomogeneity or changes in lung volumes.

**Supported by** La Trobe University, Faculty of Health Sciences support grant.

**Nomination** Physiotherapy prize.

**Conflict of Interest** No.

P073

### ASSOCIATION BETWEEN EXERCISE SESSION ATTENDANCE AND IMPROVEMENTS IN EXERCISE OUTCOMES IN PEOPLE WITH COPD

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**Introduction** Current pulmonary rehabilitation guidelines do not require attendance data to be reported. Non-attendance may impact upon training load and consequent improvements in exercise outcomes. We have evaluated the association between reported exercise session attendance and improvements in functional exercise capacity.

**Methods** A systematic review identified studies published in English, which reported exercise attendance rates for people with COPD participating in exercise or pulmonary rehabilitation programs of at least 2 weeks. Associations between attendance and improvements in exercise outcomes were explored descriptively (Pearson  $r$ ,  $p < 0.05$ ).

**Results** 234 out of 752 citations met the inclusion criteria. Of these, 86 (37%) reported attendance at training sessions. Twenty studies reported sufficient data to calculate both exercise session attendance and mean changes in functional exercise tests before and after intervention. Little to no relationship between improvements in functional exercise capacity and training volume was found ( $r = -0.24$ ;  $p = 0.18$ ).

**Conclusion** The absence of the expected association between training volume and improvements in functional exercise outcomes is likely to be a function of the low number of studies reporting attendance, variable reporting of attendance metrics and lack of intention to treat analyses. Consistent and explicit reporting of exercise session attendance in future studies would permit further analyses of dose-response characteristics of COPD exercise training.

**Conflict of Interest** No.

P075

### EXERCISE TRAINING MAY CHANGE PHYSICAL ACTIVITY DURING DAILY LIFE IN PATIENTS WITH COPD

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**Aim** To explore changes in physical activity (PA) following completion of a pulmonary rehabilitation program (PRP) in people with chronic obstructive pulmonary disease (COPD).

**Methods** 18 patients (7 males) with stable COPD (mean  $\pm$  SD) aged 72 (6) years with an FEV<sub>1</sub> of 53 (16) % predicted attended twice weekly supervised exercise training and education over 10 weeks. Before and after the PRP, measures were made of exercise capacity (6-min walk distance [6MWD]) and health-related quality of life (Chronic Respiratory Disease Questionnaire [CRDQ]). In addition, before and after the PRP, PA during daily life was measured during waking hours of 5 days, using the Sensewear Armband.

#### Results

	Pre-exercise	Post-exercise	P-value
6MWD (m)	351 (97)	360 (89)	0.30
CRDQ – dyspnoea domain	4.7 (1.3)	5.5 (1.2)	<0.01
CRDQ – fatigue domain	3.9 (1.3)	4.8 (1.2)	<0.01
Steps per day	2816 (1641)	3458 (2060)	<0.05
Time spent in PA (min)	21 (20)	25 (31)	0.56

**Conclusions** Pulmonary rehabilitation reduced dyspnoea and fatigue and appeared to increase the number of steps taken each day.

**Supported by** Canadian Respiratory Health Professionals.

**Nomination** Physiotherapy and COPD prize.

**Conflict of Interest** No.

P074

### MINIMAL DETECTABLE DIFFERENCE FOR THE ENDURANCE SHUTTLE WALK TEST FOLLOWING GROUND WALKING TRAINING IN PEOPLE WITH COPD

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**Aim** To determine the minimal detectable difference (MDD) for the endurance shuttle walk test (ESWT) following supervised ground walking training in people with COPD.

**Methods** Participants with COPD performed supervised ground walking training, for 30–45 min, 2–3 times/week for 8–10 weeks. The ESWT was performed before and after the training period. Participants were asked to rate their change following training using a 7-point global rating of change scale. An anchor-based method was applied using the global rating of change scale, with responses collapsed into categories that represented no, small, moderate and large change. A distribution-based method was also applied, namely a value equivalent to 0.5 of the standard deviation (SD) of the change.

**Results** 78 participants (44 males), aged 70  $\pm$  8 years (mean  $\pm$  SD) and FEV<sub>1</sub> 43  $\pm$  15% pred completed the training program. The correlation between the change in ESWT and global rating of change categories for time and distance was  $r = 0.25$ ;  $p > 0.05$ ; which was inadequate to use this approach. Using the distribution-based method, 0.5SD of the change for time was 156 sec while that for distance was 188 m.

**Conclusions** Using a distribution-based method, a change in ESWT performance of 156 sec or 188 m represents the MDD following a supervised ground walking training program.

**Supported by** NHMRC project grant: 570814.

**Nomination** Physiotherapy Prize, COPD Prize.

**Conflict of Interest** Nil.

P076

### EXERCISE FOR THE MAINTENANCE OF LUNG FUNCTION POST-PULMONARY REHABILITATION: A CASE STUDY

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**Aim** To determine if a circuit based exercise program is effective for improving exercise capacity, quality of life and maintaining lung function post-acute pulmonary rehabilitation in a community based setting.

**Methods** Participants were referred into the exercise program after completing an 8 week acute pulmonary rehabilitation program at a local hospital. Participants attended a 1-h exercise class up to twice weekly which involved resistance, aerobic, balance and flexibility exercises, delivered as a circuit class. Measurements of anthropometry (waist and hip girth), respiratory function (spirometry), exercise capacity (6-min walk test) and quality of life (St George's Respiratory Questionnaire), were assessed at baseline, 3, 6 and 9 months.

**Results** Six participants, 71 years (range 56–83), mean baseline FEV<sub>1</sub> 64.5  $\pm$  35.6% predicted completed the study. There was no significant decline in FEV<sub>1</sub>/FVC % ( $p > 0.05$ ), no change in waist or hip girth, BMI, weight or height. There was a clinically important difference in the symptoms score as identified through St George's Respiratory Questionnaire, however there was a significant decline in the activity score and no change in impact of their disease on quality of life (psychosocial dysfunction). The culmination of these three factors demonstrated no overall change in total score.

**Conclusions** Attending a weekly exercise class demonstrated that participants have maintained lung function, in the 9 months post pulmonary rehabilitation, however this did not impact on their exercise capacity or total quality of life.

**Conflict of Interest** No.

P077

**WHICH IS THE BETTER PREDICTOR OF EXERCISE CAPACITY IN COPD PATIENTS, RV/TLC OR FEV1?**

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**Introduction** Dyspnoea in COPD is complex and multi factorial. FEV1 is a measure of airflow limitation and RV/TLC is a measure of air trapping. 6-min walk test (6MWT) is one of the objective measurements of functional exercise capacity.

**Objective** The objective of the study is to compare the correlation between exercise capacity using 6MWT and FEV1 with exercise capacity and RV/TLC in COPD patients.

**Methods** This was a retrospective study. All COPD patients undergoing both 6MWT and spirometry and lung volumes in CGH from 1/1/2008 till 9/11/2011 were included.

**Results** 143 subjects were included in this study. Mean age (years) was 69.12 ( $\pm$  8.93). 138/143 (96.5%) were male. Mean FEV1 (L) was 1.33 ( $\pm$  0.57). There was statistically significant correlation between FEV1 and 6MWT distance (simple linear regression coefficient,  $r = 28.99$ ,  $p = 0.021$ , 95% confidence interval 4.42 to 53.57). After adjusting for cardiovascular disease, the correlation was still statistically significant ( $r = 29.00$ ,  $p = 0.021$ , 95% CI 4.36 to 53.63). There was statistically significant inverse correlation between RV/TLC and 6MWT distance ( $r = -1.12$ ,  $p = 0.034$ , 95% CI -2.15 to -0.09). After adjusting for cardiovascular disease, the inverse correlation was still statistically significant ( $r = -1.10$ ,  $p = 0.037$ , 95% CI -2.15 to -0.07). FEV1 was better correlated with 6MWT distance (functional exercise capacity) ( $p = 0.021$ ) than RV/TLC ( $p = 0.037$ ) in COPD patients.

**Conclusion** FEV1 is better correlated with 6MWT distance (functional exercise capacity) than in COPD patients in our study. Thus, we concluded from this study that FEV1 is a better predictor of exercise capacity than RV/TLC in COPD patients.

**Conflict of Interest** No.

P079

**THE IMPACT OF A CLINICAL PHARMACIST IN A THORACIC OUTPATIENT CLINIC**M CANNING<sup>1</sup>, P MASEL<sup>2</sup>, T TSE<sup>1</sup><sup>1</sup>Pharmacy Department, The Prince Charles Hospital, Queensland 4032, and <sup>2</sup>Thoracic Department, The Prince Charles Hospital, Queensland 4032

**Aim** To categorize the number and types of drug-related problems (DRP's) identified by a pharmacist in a thoracic outpatient clinic. To determine the common respiratory-related DRP's and their significance.

**Methods** A clinical pharmacist attended a weekly thoracic outpatient clinic for 17 weeks where medication history interview and pharmaceutical review were undertaken on available patients. DRP's identified were communicated to the treating respiratory physician or registrar and patient. DRP's were reviewed retrospectively and classified according to the Pharmaceutical Care Network Europe (PCNE) Classification V 6.2.

**Results** 97 DRP's were identified in 66 patients reviewed; an average of 1.47 DRP's per patient. 50 were non-respiratory related and 47 respiratory-related. The most common DRP was 'effect of drug treatment not optimal' ( $n = 35$ , 36%) followed by 'non-allergic adverse drug event' ( $n = 23$ , 23.7%) and 'untreated indication' ( $n = 23$ , 23.7%). The two most common respiratory-related DRP's were poor medication adherence (36%,  $n = 17$ ) and poor inhaler technique (19%,  $n = 9$ ). The most common pharmaceutical intervention performed was 'patient (medication) counselling' ( $n = 55$ , 83%). 37% ( $n = 36$ ) of DRP's were deemed to be high or extremely high risk by an independent pharmacist and 44% ( $n = 43$ ) high risk by a consultant thoracic physician.

**Conclusion** Pharmacists attendance at a thoracic outpatient clinic allows respiratory and non-respiratory DRP's to be identified and interventions proposed. Pharmacist attendance provides an opportunity for patient education on inhaler technique and to promote medication adherence. A significant number of DRP's were deemed to be high or extremely high risk.

**Conflict of Interest** No.

P078

**RELIABLE SPIROMETRY CAN BE PERFORMED DURING HOSPITAL ADMISSION IN ACUTE EXACERBATIONS OF COPD**B ZHANG<sup>1,3</sup>, C LANteri<sup>2,3</sup>, G NOLAN<sup>2,3</sup>, M BARNES<sup>1,2,3</sup>, CF MCDONALD<sup>1,2,3</sup><sup>1</sup>University of Melbourne, VIC 3010, <sup>2</sup>Department of Respiratory and Sleep Medicine, Austin Hospital, VIC 3084, and <sup>3</sup>Institute for Breathing and Sleep, VIC 3084

**Background** Spirometry in the appropriate clinical context is required to diagnose and optimally manage COPD. In a recent study, only 51% of Australian patients admitted with a clinical diagnosis of acute exacerbation of COPD (AECOPD) had spirometry in the previous 5 years.<sup>1</sup>

**Aim** To assess the feasibility and clinical benefits of performing spirometry during hospital admission for patients experiencing AECOPD.

**Methods** Participants admitted to hospital with a clinical diagnosis of AECOPD attempted bedside spirometry daily until discharge. Treating physicians completed a survey regarding the perceived benefits of having spirometry results available during admission.

**Results** 17 of 20 participants completed at least one acceptable spirometry test during admission, 15 within 3 days. No statistically or clinically significant changes in lung function were observed between admission and discharge. Survey results suggest doctors like to have spirometry results available but management is unchanged.

**Discussion** An inpatient admission may be an opportune time to confirm a COPD diagnosis and assess severity. We recommend that spirometry on day 4 of admission could be included in routine care of patients admitted to hospital with AECOPD.

**Conclusions** It is possible for sick patients to perform accurate and reliable spirometry during AECOPD, and doctors indicated a desire to have such results available during admission.

**Supported by** GSK (purchase of a portable spirometer).

**Nomination** N/A.

**Conflict of Interest** No.

**Reference**

1 Pretto JJ *et al.* *Internal Medicine Journal* 2012; **42**: 380–87.

**COPD SIG: POSTER SESSION 3. DISEASE MECHANISMS AND THERAPIES**

P080

**THE ROLE OF BENZODIAZEPINES IN BREATHLESSNESS: A SINGLE-SITE, OPEN-LABEL, PILOT OF OPIOID SPARING ABILITY**P ALLCROFT<sup>1</sup>, D CURROW<sup>2</sup>, V MARGITINOVIC<sup>1</sup>, A GREENE<sup>1</sup>, M AGAR<sup>2</sup>, K CLARK<sup>3</sup>, A ABERNETHY<sup>4</sup><sup>1</sup>Southern Adelaide Palliative Services, Repatriation General Hospital, SA 5041, <sup>2</sup>Discipline, Palliative and Supportive Services, Flinders University, SA 5042, <sup>3</sup>Palliative Care, Calvary Mater Newcastle, NSW 2310, and <sup>4</sup>Division of Medical Oncology, Duke University Medical Centre, NC 27705, USA

**Aim** Patients with severe respiratory disease often suffer from overwhelming dyspnoea despite maximal therapy. Morphine improves the symptom of dyspnoea. Anxiety co-exists in patients with severe respiratory disease. Benzodiazepines are used with anxiety, yet evidence to base this on is lacking. This pilot study explored the feasibility, safety and efficacy of adding Clonazepam to slow release Morphine to improve the sensation of breathlessness.

**Methods** Patients with COPD on maximal treatment were given Morphine 10 mg daily, Clonazepam 0.5 mg Nocte over a 4-day days. Patients with a significant response (>15% improvement in dyspnoea scores) were offered an extension period of 10 days.

**Results** Baseline data were recorded in 11 patients (9 males), all with severe COPD. The median age was 78 years. Baseline morning and evening dyspnoea scores were 69 mm (31–86) on a 100 mm VAS and 64 (9–75). Five patients had >15% improvement in dyspnoea scores, three progressing to an extension phase. During the initial 4-day period the morning and evening dyspnoea scores improved by a median of 9 mm and 6.5 mm respectively. The end-tidal CO<sub>2</sub> remained stable and no withdrawals from the study. No severe adverse events were noted by patients.

**Conclusions** The addition of Clonazepam to Morphine improves the level of dyspnoea in patients with COPD, is safe, and the undertaking of a larger trial is feasible.

**Supported by** Grant from Daw Park Foundation.

**Conflict of Interest** None.

P081

### QVA149 SIGNIFICANTLY IMPROVES LUNG FUNCTION AND SYMPTOMS COMPARED TO TWICE-DAILY FLUTICASONE/SALMETEROL IN COPD PATIENTS: THE ILLUMINATE STUDY

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**Background** QVA149 is a novel dual bronchodilator combination of the LABA indacaterol and the LAMA NVA237 (glycopyrronium), in development for the treatment of COPD. QVA149 once daily (OD) vs salmeterol/fluticasone (SFC) twice daily (BID) was evaluated in moderate-to-severe COPD patients with no history of exacerbations in the previous year.

**Methods** In a double-blind, double-dummy, parallel-group study, 523 patients (QVA = 258, SFC = 264) were randomized to receive QVA149 110/50 µg OD (via the Breezhaler device<sup>®</sup>) or SFC 500/50 µg BID (via the Accuhaler device<sup>®</sup>) for 26 weeks.

**Results** Mean age was 63 years; mean post-bronchodilator FEV1 60% predicted. Mean FEV1 AUC0–12 h at day 1 and weeks 12 and 26 (primary endpoint) was significantly higher with QVA149 vs SFC ( $p < 0.001$  for all comparisons). Serial spirometry showed significantly higher and clinically meaningful improvements in FEV1 with QVA149 vs SFC at all time points from 5 min to 12 h at day 1 and weeks 12 and 26 ( $p < 0.001$ ). QVA149 significantly improved the Transition Dyspnoea Index score vs SFC (treatment mean: 2.16 vs 1.41, respectively;  $p = 0.003$ ), reduced rescue medication use (−0.39 puffs/day;  $p = 0.019$ ) and improved other lung function measures over 26 weeks. The safety profile of QVA149 was similar to that of SFC.

**Conclusion** QVA149 OD provided significant and clinically meaningful improvements in lung function vs SFC BID over 26 weeks, with significant symptomatic benefits.

**Support** Novartis Pharmaceuticals.

**Conflict of Interest** C Frenzel is an employee of Novartis Pharmaceuticals.

P083

### SYSTEMIC CORTICOSTEROIDS ARE STILL INAPPROPRIATELY PRESCRIBED IN HOSPITAL PATIENTS WITH COPD EXACERBATION

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**Aim** To investigate the use of systemic corticosteroids in hospital patients with acute exacerbation of COPD regarding the appropriate initial dose and length of treatment, and to compare that to the knowledge of the junior medical staff.

**Method** Data of patients with COPD exacerbation were collected retrospectively over 12 months. The initial dose, form and total length of systemic corticosteroid were analyzed. The cost of treatment was estimated. A questionnaire was performed by junior medical staff (JMOs) on systemic corticosteroid in COPD.

**Results** There were 627 presentations of COPD exacerbation. Intravenous (IV) Hydrocortisone and oral Prednisolone were used initially in 16.2% and 83.8% respectively. Of the patients given oral Prednisolone, 83.9% received an initial dose between 30 and 50 mg/day. 18.9% of patients received corticosteroids for more than 14 days. The mean cost per patient given IV Hydrocortisone was significantly more than for patients given oral Prednisolone (AUD\$88.78 vs 2.96). 109 JMOs participated in the questionnaire. 79.7% would prescribe the initial dose of 30–50 mg/day and 90.8% would prescribe corticosteroids for no more than 14 days. Only 30.3% and 66.1% knew the costs of Hydrocortisone and Prednisolone respectively.

**Conclusions** There is still a small portion of patients for whom systemic corticosteroids are over-prescribed. There is a significant extra cost to the healthcare system, and the awareness among the JMOs needs to be improved.

**Conflict of Interest** No.

P082

### INHALED CORTICOSTEROID IS EFFECTIVE ON ONLY SOME ASPECTS OF BRONCHIAL VASCULAR REMODELLING IN COPD

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**Introduction** We have previously reported that in smokers with COPD, compared with non-smoking controls, the bronchial mucosa in larger airways is hyper-vascular in the reticular basement membrane (Rbm) and epithelium, but hypo-vascular in the lamina propria (LP). Rbm vessels stained for vascular endothelial growth factor (VEGF) and transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) were increased. Rbm hyper-vascularity may be related to epithelial-mesenchymal transition (EMT), a likely pre-cancerous condition.

**Methods** This study derived from a double-blinded randomized controlled trial in 34 subjects to compare the effect of inhaled corticosteroid (ICS, fluticasone propionate, 0.5 mg twice daily for 6 months) vs placebo on vascular remodelling in mild to moderate COPD (median age 61 years old, 17 current smokers). Bronchial biopsies, before and after treatment, were stained with anti-factor VIII antibody, VEGF and TGF- $\beta$ 1.

**Results** There were no significant baseline differences between the two groups. Rbm vessels or vessels stained for VEGF or TGF- $\beta$ 1 in the Rbm did not respond in either group. However, there was a strong trend for increase in the number of LP vessels per mm<sup>2</sup> with ICS, but not with placebo [median (range) 289 (158–585) before vs 386 (213–444) after ICS,  $p = 0.08$  and 277 (200–641) before vs 295 (173–377) after placebo,  $p = 0.5$ ]. This ICS effect was significant in current smoking COPD [median (range) 219 (158–437) before vs 356 (213–413) after ICS,  $p = 0.05$ ].

**Conclusions** Thus, ICS treatment had no anti-angiogenic activity in the Rbm, but restored LP vessels to normal in current smokers with COPD.

**Supported by** NHMRC project grant 490023.

**Conflict of Interest** None.

P084

### EPITHELIAL-MESENCHYMAL TRANSITION IN A CULTURED BRONCHIAL EPITHELIAL CELL LINE: A POTENTIAL MODEL OF COPD

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**Introduction** We have recently shown evidence that small airway epithelium in COPD patients undergoes epithelial to mesenchymal transition (EMT) which may contribute to airway remodelling. For further investigation of this phenomenon, it would be useful to move from a static examination of human biopsy material to an *in vitro* cell culture system where real-time changes can be observed. Here we assessed the potential of cultured bronchial epithelial cells to undergo EMT under controlled conditions.

**Methods** BEAS-2B cells were stimulated with either Transforming Growth Factor Beta (TGF $\beta$ ) or Tumour Necrosis Factor Alpha (TNF $\alpha$ ) for a period of 24 or 72 h. Expression of EMT markers E-cadherin (epithelial) and Vimentin, S100A4 and N-Cadherin (mesenchymal) were assessed by RT-PCR and immunocytochemistry.

**Results** Increased expression of *SMAD6* mRNA in TGF $\beta$  treated cells and *IkB $\alpha$*  mRNA in TNF $\alpha$  treated cells demonstrated that the TGF $\beta$  and NF $\kappa$ B signalling pathways respectively were indeed activated by the addition of cytokines. Increased expression of Vimentin was observed in cells treated with both TGF $\beta$  and TNF $\alpha$  as well as changes in intracellular localization. TNF $\alpha$  treatment increased expression of S100A4 and decreased E-cadherin. N-cadherin expression was increased in TGF $\beta$  treated cells.

**Conclusions** Preliminary results suggest that this stable bronchial epithelial cell line can be stimulated by inflammatory cytokines to produce some of the classic hallmarks of EMT.

**Supported by** NHMRC.

**Conflict of Interest** No.

P085

**COPD PERIPHERAL BLOOD NEUTROPHILS HAVE ENHANCED RELEASE OF IL-1 $\beta$  WHEN STIMULATED**

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**Aim** Neutrophilic activation is associated with severe airflow limitation and systemic inflammation in COPD. Activation of the inflammasome is important in regulating inflammatory responses of neutrophils. We sought to determine if following an inflammatory stimuli, there is enhanced inflammasome activation in human peripheral blood neutrophils from COPD patients.

**Methods** We recruited 20 COPD patients and 6 healthy controls, clinical data were recorded, serum and neutrophils were obtained from peripheral blood by Percoll-gradient centrifugation, and cells were then treated with 5% CSE, 100 ng/mL LPS, 1  $\mu$ M fMLP and media. At time points, IL-1 $\beta$  was measured in cultured supernatant by ELISA, NLRP 3 and Caspase 1 was detected by real time PCR.

**Results** In unstimulated neutrophils at baseline, NLRP3 mRNA was higher in healthy subjects compared to those COPD (Fold change, COPD 0.6105 (0.05) vs Healthy Controls 1.1 (0.18),  $p = 0.019$ ). Neutrophils were then stimulated with LPS. Both groups demonstrated a significant increase in release of IL-1 $\beta$ . IL-1 $\beta$  levels were significant higher in COPD patients compared to healthy control (Mean (SEM) pg/mL, COPD 16.23 (3.219) vs Healthy Controls 4.056 (1.573),  $p = 0.0225$ ). However there were no differences in mRNA induction of NLRP3 (Fold Change, COPD 1.876 (0.2205) vs Healthy controls 2.768 (0.474),  $p = 0.08$ ) and Caspase1 (Fold Change, COPD 3.316 (0.3) vs Healthy Controls 4.962 (1.48),  $p = 0.23$ ) mRNA detection between COPD and healthy group.

**Conclusions** COPD neutrophils have lower baseline NLRP3 RNA expression, but they release heightened levels of IL- $\beta$  when stimulated with LPS. This suggests COPD neutrophils are more responsive to inflammatory stimuli than neutrophils from healthy controls.

**Supported by** University of Newcastle.

**Acknowledgement** Chinese Scholarship Council; Centre for Asthma and Respiratory Disease, University of Newcastle.

P087

**REDOX-ACTIVE TRANSITION METAL ACTIVITY IN EXHALED BREATH OF COPD PATIENTS AND THE INFLUENCE OF CONDENSER MATERIAL IN ITS MEASUREMENT**

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**Aim** 1) Compare the transition metal activity in the exhaled breath condensate (EBC) of COPD patients and healthy controls by ascorbate oxidation assay. 2) Assess the influence of two different EBC condenser materials on this activity.

**Methods** Using custom-made glass and Teflon<sup>®</sup> collection devices of the same design, EBC samples were collected from stable COPD patients and healthy controls. Participants breathed tidally into the appropriate devices for 10 min each. The rate of ascorbic acid oxidation was measured spectrophotometrically as a marker of transition metal activity in EBC.

**Results** (see table)

Comparison	Group characteristics, sample size (n)	Mean percentage decrease in absorbance in 5 min (% (SD))	Mean decrease in absorbance (pm per minute) (SD)
COPD patients vs healthy controls	Glass EBC apparatus, n = 31	19.93 (23.18) vs 20.39 (28.44), $p = 0.963$	43.12 (47.98) vs 51.97 (71.00), $p = 0.711$
	Teflon <sup>®</sup> EBC apparatus, n = 28	9.65 (7.35) vs 12.00 (6.75), $p = 0.386$	23.55 (21.62) vs 29.09 (22.27), $p = 0.497$
Glass vs Teflon <sup>®</sup> EBC apparatus	All subjects (COPD patients and healthy controls), n = 23	23.91 (29.27) vs 12.10 (7.09), $p = 0.0669$	54.36 (67.16) vs 30.91 (23.01), $p = 0.108$
	COPD patients, n = 10	21.77 (25.07) vs 11.79 (7.70), $p = 0.235$	47.99 (51.45) vs 29.60 (23.02), $p = 0.263$
	Healthy controls, n = 13	25.56 (33.05) vs 12.34 (6.89), $p = 0.179$	59.27 (78.89) vs 31.92 (23.89), $p = 0.244$

**Conclusion** Although the degradation of ascorbic acid was numerically less in COPD patients, it did not reach statistical significance. Teflon<sup>®</sup> appeared to be associated with a non-significant trend to a lesser decline in oxidation than glass. Thus, we have been unable to demonstrate increased oxidation in COPD EBC, but caution is warranted when comparing EBC transitional metal activity when it is collected from different condensers.

**Conflict of Interest** None.

P086

**AGE-RELATED CHANGES IN DNA METHYLATION IN THE LUNG**

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There is increasing evidence for age-related changes in DNA methylation; however, this has not been systematically tested in the lung. We aimed to identify age-dependent methylation profiles in lung tissue.

**Methods** Methylation profiling of lung tissue DNA from 83 patients (training set) was performed using the Illumina HumanMethylation27 BeadChip. Fourteen top-ranked CpGs differentially methylated with age were technically replicated using Sequenom EpiTYPER, and significant associations were biologically validated in an independent cohort of 146 patients (test set, matched lung tissue and blood).

**Results** Methylation profiling of lung DNA identified 3,915 CpG sites (3,172 genes) differentially methylated with age ( $P < 0.05$ ). Technical replication was performed on the top ranked CpGs (based on significance and degree of methylation) across 10 genes; 33 CpG loci (out of 150) were significantly ( $P < 0.05$ ) differentially methylated across all analyses. In the biological validation, 14 CpG loci (4 genes) displayed hypermethylation with increasing age after adjusting for clinical covariates: sex, cumulative smoking exposure and pulmonary function (FEV<sub>1</sub>). CpGs in *TFAP2E* displayed consistent associations with age in lung DNA in the training and test sets. CpGs in *TFAP2A*, *TSGA14* and *KLF14* also displayed some associations with age. We identified age-related methylation patterns in lung tissue that were absent in blood DNA.

**Conclusions** This is one of the first studies to provide evidence of age-related DNA methylation alterations in the lung. These appear to be tissue-specific and independent of specific clinical factors. A more detailed appreciation of how age shapes the lung methylome may contribute to better understanding of how lung diseases develop with ageing.

**Supported by** AFQU/UB SBMS Honours Bursary, TPCH Foundation, NHMRC CDF (IY), OHMR.

**Nomination** Nil.

**Conflict of Interest** No.

P088

### CLINICAL UTILITY OF VENOUS BLOOD GASES IN THE MANAGEMENT OF ACUTE EXACERBATIONS OF COPD

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**Background** Controversy exists over the clinical utility of venous blood gases (VBG) in the management of acute exacerbations of COPD (AECOPD).

**Aims** (1) To study the clinical outcomes of AECOPD patients with acute respiratory acidosis on initial and subsequent VBG (2) Identify a venous pH cut-off that correlates with worse clinical outcomes (3) To compare those receiving NIV based on VBG to a previously studied cohort managed with arterial blood gases (ABG).

**Methods** Prospective observational study of all AECOPD patients with acute respiratory acidosis on initial VBG (venous pH  $\leq 7.35$ , PvCO<sub>2</sub>  $\geq 50$ ) at two tertiary referral centres. Serial VBG, clinical outcomes including hospital length of stay (LOS), NIV usage, ICU admission, intubation rate and mortality rate were collected. The NIV VBG subgroup was compared with a previously studied NIV ABG group at the same centre. The t-test was used to compare differences between groups.

**Results** Over 4 months, VBG was used in 87% (n = 102) of all patients (n = 122) to diagnose acute respiratory acidosis and 67% (n = 82) had predominantly serial VBG during admission. The [mean (SD)] venous pH was 7.3 (0.06) and PvCO<sub>2</sub> 64 (11) mm Hg. The mean LOS was 6.5 (5.5) days, 23% received NIV, 7.3% were admitted to ICU, 2.4% were intubated and 12% died. A venous pH cut-off  $\leq 7.25$  was associated with a higher mortality rate (p = 0.02) and a trend towards intubation (p = 0.06) despite greater NIV usage (57% vs 11%). Compared to the NIV ABG cohort, the NIV VBG cohort had reduced hospital LOS (p < 0.01) and intubation rates but increased mortality (p < 0.05).

**Conclusions** VBG is commonly used for AECOPD in our health service. Patients with venous pH  $\leq 7.25$  are more likely to receive NIV and have worse clinical outcomes. Compared to ABG, VBG usage with NIV is associated with increased mortality.

**Conflict of Interest** No.

P090

### IS OBESITY IN COPD PROTECTIVE FOR OSTEOPOROSIS?

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Osteoporosis is a well-known comorbidity of COPD; the increased risk in COPD is related to systemic inflammation, reduced physical activity, low lean muscle mass, corticosteroid use, smoking and age. Obesity in COPD is also increasingly common. We hypothesized that in COPD, obesity is protective against osteoporosis.

**Aim** To determine the association between COPD, body weight and osteoporosis.

**Methods** Participants with COPD underwent an assessment to measure body composition and bone mineral density (BMD) by DEXA scan, systemic inflammation (CRP) and spirometry. They were stratified into 2 groups; obese (BMI  $\geq 30$  kg/m) and non-obese (BMI < 30 kg/m).

**Results** Of the 41 participants, 21 (51%) were female with a mean (SD) age of 71 (8.7), BMI of 28 (0.7) and FEV<sub>1</sub>, % predicted of 51.2 (19). There were 24 (58%) who were obese. The total BMD of the obese group was significantly higher than the non-obese group (1.1 (0.14) vs 0.88 (0.22); p = 0.0003). Similarly the total body BMD T score was significantly better in the obese group (-0.008 vs -2.186; p < 0.0001). Fewer obese participants were in the osteopenic or osteoporotic range compared with the non-obese group (9 (37.5%) vs 15 (88.3); p = 0.001). Using linear regression analysis, appendicular skeletal muscle mass (ASMM), log CRP and BMI were all positively associated with BMD T Score. In a multiple regression model (r<sup>2</sup> = 0.5692; p = 0.001) adjusted for age, gender and BMI, ASMM was the only positive predictor of BMD T score.

**Conclusion** Obesity is protective of poor bone health in COPD; this may be another key to the understanding of the obesity paradox in COPD. Assessing bone health in COPD patients with normal BMI is important.

**Supported by** John Hunter Hospital Charitable Trust, HMRI.

**Conflict of Interest** Nil.

**Nomination** JRS Early Career Development Award.

P089

### DIFFERENTIAL AIRWAY GENE EXPRESSION IN COPD

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Gene and environment interactions leading to airway inflammation and remodelling are important in the pathogenesis of chronic obstructive pulmonary disease (COPD).

**Aim** To examine alterations in gene expression, gene ontologies and pathways of sputum samples from subjects with COPD compared to healthy controls.

**Methods** Induced sputum was collected from subjects with COPD (n = 43), and healthy controls (n = 14). Sputum RNA was extracted, amplified and gene expression profiles were generated using Illumina's HumanHT-12 v4 Expression BeadChips (>47,000 probes). Data were analyzed using GeneSpring GX12.1.

**Results** There were 7217 genes differentially expressed (adjusted p < 0.05) in the sputum of COPD patients compared to healthy controls. This included 1017 genes that had a fold change of greater than 2, with 264 genes down-regulated and 753 genes upregulated in COPD. There was significant down-regulation of genes related to antigen processing and presentation (including major histocompatibility complex class II antigens *HLA-DMA*, *HLA-DMB*, *HLA-DRB3*, *HLA-DQB2*, *HLA-DRB4*, and *HLA-DQA1*), lipoprotein transport and oxidation-reduction processes. There were significant alterations to cellular pathways including the T cell receptor (TCR, p = 0.017), transforming growth factor- $\beta$  receptor (TGFB $\beta$ , p = 0.009), and B cell receptor (BCR, p = 0.026) pathways.

**Conclusions** COPD is characterized by vast changes in the gene expression profile of induced sputum samples. Follow up studies should investigate impairment of antigen presentation including the level of MHC Class II molecules expressed on antigen presenting cells in COPD.

**Supported by** The Australian Lung Foundation.

**Conflict of Interest** Nil.

P091

### SUITABILITY OF RESPIRATORY-IMPAIRED PATIENTS FOR TESTING ON THE LION INTOXYLIZER 8000 BREATH ANALYSIS SYSTEM

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It is a legal requirement for drivers to present a breath analysis sample when requested by NSW Police. The evidential device used (Lion Intoxilyzer) requires at least a 1-L sample at a flow rate of 8 L/min (taking 7.5 s to achieve). From time to time it is argued in court that a person could not provide a sample because of lung disease. The aim of this study is to determine whether there is a threshold below which a valid sample can be provided with this equipment.

**Methods** Clinic patients with confirmed moderate or severe chronic obstructive lung disease (COPD) or interstitial lung disease (ILD) were recruited. Spirometry was performed to document current status. Subjects were asked to perform routine breath analysis following the NSW Police Standard Operational Procedure. Three efforts are allowed. No subject had used this equipment previously. Reasons for failure to produce evidence were recorded. Simple statistical analysis identified the percentage of subjects failing to supply evidence.

**Results** 22 COPD patients [mean (SD) age 65 (13) and FEV<sub>1</sub> 48(12)% predicted] and 9 ILD patients [age 65 (21); FVC 72 (21)% of predicted] were tested. 21 COPD subjects (95%) were able to provide evidence, with 14 successful on the first attempt. Seven ILD subjects (78%) were able to provide evidence, with 4 passing on the first attempt. The single COPD subject who failed had FEV<sub>1</sub> 23% predicted and FVC of 1.16 L. One ILD patient with scleroderma with facial involvement could not achieve a mouth seal and one with FVC of 1.45 L could not provide sufficient sample volume.

**Conclusion** Unless there is very severe COPD or very low FVC an adequate evidential exhaled gas sample should be obtained using the Lion Intoxilyzer 8000 breath analysis system.

**Supported by** NSW Police Breath Analysis Unit.

**Conflict of Interest** No.

P092

**DETECTION OF EXCESSIVE DYNAMIC AIRWAY COLLAPSE IN COPD USING DYNAMIC 320-SLICE CT**P LEONG<sup>1</sup>, K LOW<sup>1</sup>, M CROSSETT<sup>2</sup>, E KUO<sup>1</sup>, C DALEY<sup>1</sup>, K HAMZA<sup>3</sup>, K LAU<sup>2,3</sup>, P BARDIN<sup>1,3</sup><sup>1</sup>Monash Lung and Sleep, Monash Medical Centre, VIC 3168, <sup>2</sup>Department of Diagnostic Imaging, Monash Medical Centre, VIC 3168, and <sup>3</sup>Monash University, VIC 3800

**Introduction** Excessive dynamic airway collapse (EDAC) is an expiratory condition in which the posterior membrane of the trachea moves forward with a greater than 50% reduction in cross-sectional area. The ensuing airflow limitation can exacerbate breathlessness. This may be pertinent in COPD where the trachea often elongates and becomes 'floppy'. Diagnosis is by fibre-optic bronchoscopy but this method is subjective, requires sedation and is difficult to conduct during acute breathlessness. We have developed novel methods using dynamic CT to obtain real-time images of upper airway function in COPD.<sup>1</sup>

**Methods** Healthy individuals (n = 15) were recruited and evaluated using 320-slice CT of the larynx and trachea. Patients (n = 9) with stable COPD and unselected patients admitted with acute exacerbations of COPD (AECOPD; n = 7) were imaged in the same manner. Tracheal area was measured on axial views and analyzed as ratio of minimum expiratory tracheal area to maximal inspiratory area over a breathing cycle.

**Results** Detailed real-time images were obtained by CT at low radiation doses (2–4 mSv). In healthy persons there was minor tracheal narrowing identified and the normal limit was confirmed as narrowing less than 50%. However, in both stable COPD (n = 5) and in AECOPD (n = 5) upper airway collapse occurred with expiratory narrowing >50% (EDAC).

**Conclusion** Dynamic upper airway CT allows diagnosis and quantification of EDAC. Further studies in stable and AE COPD are warranted.

**Support** No external support.

**Conflicts of Interest** No.

**Reference**

1 Joosten *et al.* *Thorax* 2012; **67**: 95–6.

P094

**EXPERIENCE OF ENDOBRONCHIAL VALVE MANAGEMENT OF CHRONIC AIRFLOW LIMITATION**M BAYFIELD<sup>1</sup>, RL RUSHWORTH<sup>2</sup>, M DUNCANSON<sup>2</sup>, MA MALIK<sup>2</sup>, J NADEL<sup>2</sup><sup>1</sup>Cardiothoracic Surgery, Royal Prince Alfred Hospital, NSW 2050, and <sup>2</sup>University of Notre Dame, School of Medicine Sydney, NSW 2010

**Aim** The aim of this study is to assess functional outcomes and in-patient morbidity of endobronchial valve (EBV) management in CAL patients.

**Methods** An analysis of one of the world's largest case series in this field was completed. Hospital records of 69 patients that underwent bronchoscopic implantation of endobronchial valves were analyzed. A total of 112 procedures were recorded, among which 98 were EBV implantations and 14 were EBV removals. Data for FVC, FEV<sub>1</sub>, 6-min walk distance (6MWD) and St. George Questionnaire (SGQ) was evaluated for changes before and after the procedure. FVC and FEV<sub>1</sub> data for 69 procedures was retrieved, 6MWD data for 43 procedures was retrieved and SGQ data for 33 procedures was retrieved. Patients' hospital stay time of 90 procedures was also noted. All post-operative complications were documented.

**Results** Improvement in FVC and FVC% predicted was 0.13 L (5.5%) (p = 0.05) and 3.53% (5.8%) (p = 0.04) respectively. Improvement in FEV<sub>1</sub> and FEV<sub>1</sub>% predicted was 0.05 L (5.8%) (p = 0.02) and 1.96% (5.9%) (p = 0.02) respectively. Increase in 6MWD was 18.72 m (5.1%) (p = 0.05) and change in SGQ was -8.57 (p = 0.01). The average hospital stay per procedure was 2.0 days, (8.9% = <1 day, 54.4% = 1 day, 17.8% = 2 days, 7.8% = 3–5 days, 7.8% = > 5 days). The most common postoperative complications were RTI's (16 patients), expectoration of valves (6 patients) and pneumothorax (6 patients).

**Discussion** Management of emphysema with EBV implantation shows improvement in pulmonary function, exercise tolerance and quality of life. Bronchoscopic implantation is less invasive than Lung Volume Reduction Surgery and lowers patient morbidity by reducing hospital stay and decreasing postoperative complications.

**Conflict of Interest** No.

P093

**CIGARETTE-SMOKING IS ASSOCIATED WITH REDUCED COLLAPSIBILITY AND VOLUME FRACTION OF AIRWAY SMOOTH MUSCLE IN HUMAN BRONCHIAL SEGMENTS**RL JONES<sup>1,2</sup>, AL JAMES<sup>1,2</sup>, HW MITCHELL<sup>3</sup>, A CAIRNCROSS<sup>3</sup>, JG ELLIOT<sup>1</sup>, PK MCFAWN<sup>3</sup>, PB NOBLE<sup>3,4</sup><sup>1</sup>Department of Pulmonary Physiology and Sleep Medicine, Sir Charles Gairdner Hospital, WA 6009, <sup>2</sup>School of Medicine and Pharmacology, <sup>3</sup>School of Anatomy, Physiology and Human Biology, and <sup>4</sup>Centre for Neonatal Research and Education, University of Western Australia, WA 6009

**Background** Different mechanisms of airway disease are likely in chronic obstructive pulmonary disease (COPD – smoking-related inflammation and remodelling) and asthma (inflammation and hypertrophy and hyperplasia of airway smooth muscle – ASM). Patients with COPD show less induced broncho-dilation AND less induced maximal airway narrowing compared with those with asthma.

**Aim** To examine the relationship between smoking cigarettes and the mechanical properties and structure of the ASM layer in human airways.

**Methods** Bronchial segments were obtained from subjects (n = 15, 66 ± 5 years) undergoing lobectomy for pulmonary neoplasms. Broncho-constriction (% volume) to acetylcholine and pressure to collapse were measured in an organ bath system. The area and volume fractions (V<sub>v</sub>) of muscle and matrix in the ASM layer were subsequently assessed in the fixed segments.

**Results** Pack-years of smoking were inversely related to broncho-constriction (r = -0.52, p < 0.05), pressure required to collapse airways (r = -0.73, p < 0.01) and V<sub>v</sub>muscle within the ASM layer (r = -0.52, p < 0.05). Smoking was not significantly related to thickness of the ASM layer, V<sub>v</sub>matrix or the size or number of ASM cells.

**Conclusions** The composition of the ASM layer, rather than changes in ASM cells, is altered by smoking and this restricts movement. This may contribute to the functional differences between COPD and asthma.

**Supported by** NHMRC Project Grant #513842.

**Nomination** Ann Woolcock Young Investigator.

**Conflict of Interest** No.

**CYSTIC FIBROSIS SIG: POSTER SESSION**

P095

**YKL-40 MEASURED IN BAL FLUID BUT NOT IN SERUM OR URINE IS A BIOMARKER OF LUNG DAMAGE IN CHILDREN WITH CF**

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**Introduction** Minimally invasive, reliable biomarkers of cystic fibrosis (CF) lung disease are essential for the early detection disease and monitoring of disease and treatments. YKL-40 is a glycoprotein associated with the pathogenic processes related to inflammation and tissue remodelling. It has been proposed as a biomarker of lung disease in asthma and in adults with CF.

**Aim** To determine whether YKL-40 measured in the bronchoalveolar lavage fluid (BALf), serum or urine of children with CF is reflective of lung damage.

**Methods** Fifty five samples of BALf, serum and urine from the AREST CF biobank were analyzed for levels of YKL-40. YKL-40 was measured using a commercially available ALPHALisa assay.

**Results** Samples from 36 children with CF aged between 0.28 and 10.16 years were analyzed. Detectable levels of YKL-40 were found in BALf and serum, but not in urine. Levels of YKL-40 in serum did not correlate with clinical markers of CF lung disease. Levels of YKL-40 measured in BALf were associated with inflammation (Neutrophil elastase [r<sup>2</sup> = 0.46, p < 0.001], macrophages [r<sup>2</sup> = 0.34, p < 0.001], neutrophils [r<sup>2</sup> = 0.74, p < 0.001], IL-8 [r<sup>2</sup> = 0.45, p < 0.001]) and infection in the lung (r<sup>2</sup> = 0.17, p = 0.002), particularly with *P. aeruginosa* (r<sup>2</sup> = 0.20, p = 0.007).

**Conclusion** YKL-40 measured in BALf, but not in urine or serum, is associated with clinical markers of lung damage. As YKL-40 measured in urine and serum is not detectable or not associated with lung damage, the search to find a minimally invasive, reliable biomarker of CF lung disease in children continues.

**Supported by** Cystic Fibrosis Foundation Therapeutics (AREST CF).

**Nomination** None

**Conflict of Interest** No.



P096

### USING XBOX KINECT™ IS HIGH-INTENSITY EXERCISE FOR YOUNG ADULTS WITH CYSTIC FIBROSIS

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**Aim** Exercise training is an integral component in the management of cystic fibrosis (CF). Interactive gaming consoles are a new trend in exercise. The aim of this study was to determine the exercise intensity of virtual training on the Xbox Kinect™.

**Methods** Participants with CF completed two assessment sessions separated by ≤10 days. The first session involved a cardiopulmonary exercise test (CPET) to measure maximum performance on an electronically braked cycle ergometer. The second session involved 20 min of exercise on the Xbox Kinect™ using the Your Shape™ Fitness Evolved program.

**Results** Ten participants (median [interquartile range] FEV<sub>1</sub> 58 [46] %, aged 29 [6] years, 6 males) completed the study. The intensity of exercise elicited during the Xbox Kinect™, expressed as a percentage of the peak heart rate achieved on the CPET, was 86% (95% confidence interval, 81 to 92%). This was equivalent to 6.1 [1.8] metabolic equivalents (METs).

**Conclusions** Exercise using the Your Shape™ Fitness Evolved program for Xbox Kinect™ was high intensity exercise for young adults with CF and may be a suitable alternative to conventional aerobic exercise modalities.

**Supported by** Heart & Lung Transplant Foundation of WA Inc.

**Nomination** Physiotherapy and cystic fibrosis prize.

**Conflict of Interest** No.

P098

### PERTURBATION OF SPUTUM MICROBIOTA BY INTRAVENOUS ANTIBIOTICS IN CYSTIC FIBROSIS IS SHORT-LIVED

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**Aim** To determine the effect intravenous (IV) antibiotics administered to adult patients with cystic fibrosis (CF) experiencing a pulmonary exacerbation (PE) on sputum bacterial community composition.

**Methods** Sputa were collected directly into RNA later® on day 0, and again on days 3–4 and 8–10 during IV antibiotic treatment for a PE. DNA was extracted from the sputum samples and the gene encoding bacterial 16S rRNA amplified by reverse transcription polymerase chain reaction followed by tag-encoded FLX amplicon pyrosequencing.

**Results** 19 adult CF patients (mean age 28 years, mean FEV<sub>1</sub> 40%) provided sputum samples over at least two time points. When compared to day 0–1, there was a significant reduction in the relative abundance of *Pseudomonas* ( $P < 0.05$ ) by days 3–4, with an accompanying increase in overall bacterial community diversity ( $P = 0.078$ ). However, sputum samples collected on days 8–10 demonstrated similar levels of bacterial community diversity and relative abundance of *Pseudomonas* compared to day 0–1.

**Conclusion** Perturbation of microbial diversity and relative abundance of *Pseudomonas* in response to IV antibiotics is short-lived during treatment of a PE in CF, suggesting a rapid adaptation of *P. aeruginosa* and the CF airway microbiome to antibiotic pressure.

**Supported by** NHMRC.

**Nomination** Nil.

**Conflict of Interest** No.

P099

### AIRWAY IRON IN CYSTIC FIBROSIS IS ASSOCIATED WITH INCREASED INFLAMMATION, ENHANCED PSEUDOMONAS AERUGINOSA INFECTION AND REDUCED AIRWAY PH

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**Introduction** Iron and acid-base homeostasis may be abnormal within the Cystic Fibrosis (CF) airway.

**Aims** To determine the relationship between infection, airway inflammation, iron and pH in CF.

**Methods** Sputa were processed for quantitative *P. aeruginosa* load and expressed as colony forming units per milliliter (CFU/mL) of sputum. Anaerobic bacterial numbers were quantified in the same way following anaerobic culture on horse blood agar for 48 h. Sputum total cell counts were performed using a hemocytometer and iron concentrations were measured in cell free supernatants using a colorimetric method. Sputum pH was measured with an IFSET® meter.

**Results** Sputum iron in stable CF patients chronically infected with *P. aeruginosa* was negatively correlated with pH ( $R^2 = 0.31$ ,  $p = 0.007$ ) and positively correlated with *P. aeruginosa* CFU/mL ( $R^2 = 0.25$ ,  $p = 0.03$ ). In stable patients not infected with *P. aeruginosa*, sputum iron and TCC were strongly and positively correlated ( $R^2 = 0.58$ ,  $p = 0.002$ ). Sputum pH and TCC were negatively correlated ( $R^2 = 0.15$ ,  $p = 0.009$ ). There was no relationship between anaerobic bacterial load and sputum indices, irrespective of *P. aeruginosa* infection status.

**Conclusions** Increased iron within the CF airway may promote *P. aeruginosa* replication and appears to be associated with alterations in acid-base balance. Increased iron in patients not infected with *P. aeruginosa* is associated with inflammation, which may provide the milieu for later *P. aeruginosa* colonization.

**Supported by** NHMRC.

**Nomination** Nil.

**Conflict of Interest** No.

P097

### OBSERVATIONAL RETROSPECTIVE STUDY OF DIFFERENT TREATMENT REGIMES USED IN TREATING ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS IN THE PRINCE CHARLES HOSPITAL 2009–2011

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**Aim and Objectives** 1. To evaluate diagnostic processes, current treatment practices and regimes of Allergic Bronchopulmonary Aspergillosis (ABPA) in The Prince Charles Hospital (TPCH). 2. To assess epidemiology in this patient group. 3. To evaluate outcomes of treatment.

**Method** We analyzed data retrospectively of patients with a diagnosis of ABPA who had been treated between 2009 and 2011 in TPCH in Brisbane.

**Results** A total of 26 patients identified. 17 patients had cystic fibrosis (CF). Equal number of males and females (50%). Mean age 64 years for non CF patients, 30 years for CF patients. Out of 9 non-CF patients, seven had central bronchiectasis type ABPA; none with serologic ABPA. 80% of non CF patients' skin prick tests were positive. 77% had elevated IgE levels but only two had eosinophilia. All non-CF patients had at least two lines positive on aspergillus precipitin testing. Six out of nine non-CF patients were treated with steroids alone. Combined steroids and itraconazole were used in the CF group (1) and the non CF group (3).

**Conclusion** Treatment regimes and diagnostic criteria and follow-up used by respiratory clinicians are heterogeneous in the field of ABPA management. This emphasizes the importance of therapeutic guidelines for ABPA.

**Conflict of Interest** No.

P100

### PERIPHERAL AIRWAY FUNCTION AND SEVERITY OF (CYSTIC FIBROSIS) CF LUNG DISEASE—A CROSS-SECTIONAL STUDY FROM CHILDHOOD TO LATE MIDDLE AGE USING SF6 MULTIPLE BREATH WASHOUT

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**Background** Ventilation inhomogeneity (VI) measured by inert gas multiple breath washout (MBW) is a characteristic feature of CF. The lung clearance index (LCI) is a global VI index, and Scond and Sacin indicate VI in the conductive and the acinar airway zones.<sup>1</sup>

**Aim** To assess the relationships among spirometry (FEV<sub>1</sub>), and global and small airway specific indices in CF lung disease of varying severity.

**Subjects** 71 subjects with CF aged 7–55 years (median 17 years).

**Methods** SF<sub>6</sub> MBW in triplicate using a mass spectrometer and spirometry. MBW results were related to reported normative data (1) and spirometry results to modern reference data.<sup>2</sup>

**Results** FEV<sub>1</sub> was abnormal (SDS < -1.96) in 38%, LCI in 80%, Scond in 94% and Sacin in 56% of CF subjects. Scond was the most sensitive index but did not correlate with FEV<sub>1</sub> (r<sup>2</sup> = 0.00) or LCI (r<sup>2</sup> = 0.00). Sacin had lower sensitivity but correlated with LCI (r<sup>2</sup> = 0.75; p < 0.001) and FEV<sub>1</sub> (r<sup>2</sup> = 0.46; p < 0.001). LCI correlated with FEV<sub>1</sub> (r<sup>2</sup> = 0.63; p < 0.001).

**Conclusions** LCI is more useful than Scond or Sacin in monitoring CF lung disease and reflects spirometric overall disease severity better. Scond is, however, an early marker of lung involvement in CF.

**Support** Västra Götaland Region Research Council, Sweden.

**Conflict of Interest** None.

#### References

- 1 *Respiration* 2009; **78**: 339–55.
- 2 *Am J Respir Crit Care Med* 2008; **177**: 253–60.

P102

### PHYSICAL ACTIVITY DECLINES FOLLOWING RESPIRATORY EXACERBATION IN ADULTS WITH CYSTIC FIBROSIS

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**Aim** To investigate physical activity participation immediately upon discharge, and 1-month post discharge, in adults with Cystic Fibrosis (CF) requiring intravenous (IV) antibiotics for a respiratory exacerbation.

**Methods** Adults with CF, who had previously undertaken physical activity assessment using the Sensewear Pro3 activity monitor when stable, were recruited. Activity monitoring for 3–7 days occurred immediately after discharge, and again 1-month after discharge. Time spent in moderate intensity physical activity (≥4.8 METs and <7.2 METs) was compared between baseline, discharge and 1-month after discharge.

**Results** Twenty-three adults (9 males), mean (SD) age 34 (9) years with mean FEV<sub>1</sub> 52 (17) % predicted were assessed. Twelve participants received IV antibiotics in hospital, with 11 treated at home. Median time spent in moderate intensity activity was not significantly different at discharge (18 min; interquartile range (IQR): 8–44 min) compared to stable baseline (23 min; IQR: 7–47 min) (p = 0.7). From discharge to 1-month post discharge time spent in moderate intensity activity declined significantly (median 12 min; IQR: 4–28 min) (p = 0.02), equating to a 33% decline in physical activity time.

**Conclusion** Time spent in moderate intensity physical activity was not reduced immediately following IV antibiotics for a respiratory exacerbation in adults with CF compared with time when stable. However, there was a significant decline in time spent in moderate intensity physical activity at 1-month after discharge. Further investigation is warranted to ascertain reasons for the decline at 1-month post discharge in order to target appropriate intervention strategies.

**Support** NHMRC, Cystic Fibrosis Australia.

**Nomination** TSANZ travel award; Physiotherapy prize.

**Conflict of Interest** No.

P101

### RELATIONSHIP BETWEEN NITROGEN MULTIPLE BREATH WASHOUT (N<sub>2</sub> MBW) INDICES OF GLOBAL AND PERIPHERAL AIRWAY FUNCTION AND FEV1 IN CHILDREN WITH CYSTIC FIBROSIS (CF)

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**Background** Ventilation inhomogeneity (VI) measured by MBW is a characteristic feature of CF. The lung clearance index (LCI) is a global VI index, and Scond and Sacin indicate VI in the conductive and the acinar airway zones.<sup>1</sup>

**Aim** To see how FEV<sub>1</sub>, and different N<sub>2</sub> MBW indices are related in CF.

**Subjects** 26 CF subjects aged 7–18 years and 44 healthy controls aged 7–18 years.

**Methods** N<sub>2</sub> MBW in triplicate using the Exhalyzer D, EcoMedics AG, Duernnen Switzerland. MBW results were related to the control group findings and spirometry results to modern reference data.<sup>2</sup>

**Results** FEV<sub>1</sub> was abnormal in 19%, LCI in 88%, Scond in 100% and Sacin in 58% of CF subjects. Scond did not correlate with FEV<sub>1</sub> and only weakly with LCI (r<sup>2</sup> = 0.27; p = 0.006). Sacin correlated with both LCI (r<sup>2</sup> = 0.73; p < 0.001) and FEV<sub>1</sub> (r<sup>2</sup> = 0.56; p < 0.001). LCI and FEV<sub>1</sub> correlated closely (r<sup>2</sup> = 0.70, p < 0.001). LCI thus reflected spirometric overall disease severity (FEV<sub>1</sub>) better than Sacin or Scond and was also more sensitive than Sacin.

**Conclusions** These cross-sectional findings suggest that LCI is more useful than Scond or Sacin in monitoring CF lung disease. Scond may, however, be used as an early marker of lung involvement in CF.

**Support** Västra Götaland Region Research Council, Sweden.

**Conflict of Interest** Dr Per Gustafsson has given extensive intellectual support to EcoMedics AG, but free of charge.

#### References

- 1 *Respiration* 2009; **78**: 339–55.
- 2 *Am J Respir Crit Care Med* 2008; **177**: 253–60.

P103

### EXERCISE PRESCRIPTION FROM THE MODIFIED SHUTTLE TEST-25 IN ADULTS WITH CYSTIC FIBROSIS

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**Aim** Ascertain whether exercise prescription based on final running speed achieved on the Modified Shuttle Test-25 (MST-25) provides adequate training intensity for adults with cystic fibrosis (CF).

**Methods** Adults with CF and stable respiratory health undertook MST-25 with simultaneous portable metabolic monitoring using the Sensewear Pro3 Armband. Clinical and test parameters associated with peak exercise intensity (peak METs) achieved during the MST-25 were examined. Independent contribution of running speed to peak exercise intensity was determined. MET intensity achieved at 80% of final running speed was compared to peak METs achieved to test utility of MST-25 for exercise prescription.

**Results** Sixty-two participants (33 male), mean (SD) age 26 (8) years and mean FEV<sub>1</sub> 66 (20) were assessed. Peak exercise intensity (METs) correlated with MST-25 total distance (r = 0.73; p < 0.001) and final speed (r = 0.74; p < 0.001). Independent predictors of peak exercise intensity (METs) were final MST-25 speed (km/hr) (= 0.44; p = 0.001) and mean daily energy expenditure (= 0.29; p = 0.002). Exercise intensity (METs) achieved at 80% of final MST-25 running speed was mean (SD) 89 (8)% of peak MET value (range 59–100%).

**Conclusion** Final speed predicts peak exercise intensity on the MST-25. Prescribing exercise intensity based on final MST-25 speed achieves an adequate training intensity.

**Supported by** NHMRC and Cystic Fibrosis Australia.

**Nomination** TSANZ travel award; Physiotherapy prize.

**Conflict of Interest** No.

P104

P106

### CF MOUSE SURVIVAL IS IMPROVED BY AIRWAY LENTIVIRAL CFTR GENE TRANSFER

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**Background** Long-term (>12 months) partial CFTR correction can be achieved in timed-group studies in CF mice. Here, we used a repeated-measure study design to examine the effects of partial CFTR gene correction in individual CF mouse nasal airways.

**Methods** CF mice (*cftr*<sup>tm1unc</sup>) were tested under 3 experimental conditions. Controls were pre-treated with the airway surfactant lysophosphatidylcholine (LPC, 0.3%, 4 ul) prior to a lentiviral (LV -20 ul) vector with no gene included (LV-MT, n = 6); or pretreated with saline (PBS, 4ul) prior to the therapeutic gene (LV-CFTR, n = 6). The primary treatment group received LPC prior to LV-CFTR (n = 12). Viral titre was 0.6–2.5 × 10<sup>10</sup> tu/mL. CFTR function was assessed by nasal potential difference (PD) at 1 week, 1 and 3 months, and then at three monthly intervals. Differences in mouse survival (Kaplan-Meier) were determined by the Mantel–Cox log rank test.

**Results** Significant and persistent functional CFTR gene transfer (p < 0.05, RM ANOVA) was present for up to 12 months ( $\Delta$ PD<sub>Cl</sub>, range 12–54% towards normal) in CF mice treated once with LPC/LV-CFTR, compared to controls. This treated group showed significantly extended median survival (20 months), compared to either control group PBS/LV-CFTR (14 mo) or LPC/LV-MT (9 months).

**Discussion** Lentiviral CFTR gene transfer targeted to only CF mouse nasal airway significantly improved the CF mouse lifetimes. Nasally-dosed vector could reach lung airways (and gut) via dose 'spillover', and potentially improve CFTR function with direct or indirect benefits. Further studies are essential to determine the reasons for the substantial improvement in animal survival following such limited airway gene transfer.

**Support** NHMRC and Cure4CF Foundation.

**Conflict of Interest** None.

### MOLECULAR SURVEILLANCE AND PREVALENCE OF ACQUIRED CARBAPENEM RESISTANCE IN PSEUDOMONAS AERUGINOSA (PA) AMONGST AUSTRALIAN CYSTIC FIBROSIS (CF) PATIENTS

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**Introduction** Emergence of carbapenem (CPM) resistant *Pa* due to metallo-beta-lactamase (MBL) associated with class I integrons (*int1*) poses a health risk to persons with CF. Currently, there are no guidelines for MBL screening and the prevalence of MBL-producing *Pa* among Australian CF patients is unknown.

**Aims** We sought to: i) compare five MBL phenotypic screening tests, and ii) determine MBL/*int1* prevalence among *Pa* isolates collected from Australian CF patients.

**Methods** *Pa* isolates collected from 5 Australian adult CF centres were included. 50 randomly selected CPM resistant and 50 matched CPM susceptible isolates were analyzed using the MBL Etest, Double Disc Diffusion test (DDDT), Combined Disc test (CDT), Modified Hodge test (MHT), and antibiogram evaluation. In addition, 509 CPM resistant isolates were screened for *int1* and MBL genes by real-time PCR.

**Results** Etest, MHT and stringent antibiogram criteria correctly identified MBL in 2 (Non-CF) *Pa* reference strains but variable specificity (20%; 86%; 88%, respectively) was observed when applied to CF *Pa* isolates. Stringent antibiogram has the best positive predictive value (25%). Molecular screening of the 509 isolates (173 patients) revealed that 22 isolates (4.3%) harboured the *int1* gene. Interestingly, the AUST-02 strain was associated with higher prevalence of *int1* (OR: 2.8; p = 0.04). No MBL-producing isolates were identified.

**Conclusions** In isolates collected in 2007, no MBL *Pa* isolates were identified. The use of stringent antibiogram criteria and PCR confirmation could be adopted for future MBL surveillance.

**Supported by** TPCH Foundation, Children's Health Foundation Queensland, NHMRC Postgraduate Scholarship.

**Conflict of Interest** No.

P105

P107

### OBSERVATIONAL STUDY OF THE CLINICAL EFFECTS OF IVACAFTOR IN PATIENTS WITH SEVERE CYSTIC FIBROSIS (CF) LUNG DISEASE

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**Introduction** Ivacaftor is an oral cystic fibrosis transmembrane regulator (CFTR) potentiator with proven clinical benefit in CF patients with at least one G551D allele. A Named Patient Program (NPP) commenced in 2012 allowing compassionate access for CF patients with this mutation and who are lung-transplant (LTx) listed or with FEV<sub>1</sub> ≤40%.

**Aim** To study the early clinical outcomes of Ivacaftor (150 mg bd) in patients with severe CF lung disease and approved for the NPP.

**Methods** Clinical measurements of respiratory function, sweat chloride, body mass index, 6-min walk distance, C-reactive protein (CRP), quality of life and sino-nasal symptoms were performed at baseline and at 2, 4, 8 and 12 weeks.

**Results** 3 patients (2 female), mean (SD) age 29 (4.5) years were enrolled (2 based on LTx criteria and 1 based on FEV<sub>1</sub> ≤40% criteria). A mean reduction of -49 mmol/L in sweat chloride levels was observed at 2 weeks and sustained at 3 months. At 2 weeks, a mean increase of 6% in FEV<sub>1</sub> occurred, and an improvement in 6-min walk distance of 29 metres. All patients achieved an improvement of the minimum clinically important difference in the respiratory domain of the Cystic Fibrosis Questionnaire Revised (CFQ-R) of 4 units at 8 weeks and reported less sino-nasal symptoms.

**Conclusions** Early clinical improvements in lung function, sweat chloride measurements and quality of life is observed in patients with severe lung disease receiving Ivacaftor.

**Supported by** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

### SPECTRUM OF MUTATIONS IN THE CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) GENE IN A QUEENSLAND ADULT CYSTIC FIBROSIS POPULATION

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**Introduction** New therapies targeting specific gene mutations in cystic fibrosis (CF) have increased the need to characterize individual patient *CFTR* mutations. Standard testing currently screens the 9 most common *CFTR* mutations, but more than 1800 *CFTR* mutations exist.

**Aims and Methods** To fully characterize *CFTR* gene mutations in a Queensland adult CF population. 289 adults with CF who attended TPCH ACFC in 2011/2012 were included in this study and whole genome sequencing was performed if two *CFTR* mutations were not previously identified using standard testing.

**Results** The spectrum of sequence changes comprised 54 different *CFTR* mutations. Four allelic mutations were present in more than 1% of the CF population; F508del (86.5% of patients with 45% homozygotes), G551D (9.3% of patients; one homozygote), G542X (3.5% of patients) and R117H (2.1% of patients). Of the 50 other mutations, 14 were present in more than one patient (including four sibling pairs), and 36 patients possessed unique mutations. Gene sequencing is still to be completed in 28 of the patients with one allelic mutation remaining uncharacterized. Eleven patients had rare *CFTR* mutations described in less than 100 patients worldwide (frequency < 0.1%). Comparison with *CFTR2* and *ACFDR* databases are underway and will be discussed.

**Conclusion** A wide spectrum and relatively high proportion of rare and unique mutations in a Queensland CF population may reflect founder effects of settlement from many different European countries.

**Supported by** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

P108

### CULTURING SUCCESS OF CF AIRWAY EPITHELIAL CELLS (AEC) IS ASSOCIATED WITH DISEASE SPECIFIC FACTORS

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**Introduction** Researching mechanisms of structural disease in CF is assisted by bronchial brushing techniques providing AECs for culturing, however this disease cohort present unique culturing challenges.

**Method** Children with CF undergoing clinically directed annual surveillance visit were brushed in the main bronchus and cell samples were cultured.

**Results** A total of 280 brushings were used for cell culture (mean age 3.31 years). 103 (36.8%) specimens did not expand beyond P0, 114 (40.7%) expanded to passage one (P1), 63 (22.5%) to passage two (P2). P2 cultures had significantly higher initial cell count than P0 only ( $2.37 \times 10^6$  cells vs  $1.64 \times 10^6$ ,  $p = 0.0005$ ). Proportion of severe CFTR mutation phenotype was higher amongst P0 only cultures ( $\chi^2$  (1,  $n = 230$ ) = 7.25,  $p = 0.007$ ). Airway infections were more common in concurrent bronchoalveolar lavage (BAL) of children whose brushing specimen co-cultured contaminating flora ( $\chi^2$  (1,  $n = 280$ ) = 12.06,  $p = 0.0005$ ). Mean IL-8, but not neutrophil elastase, concentration in BAL was significantly higher for the P0 only group (4.07 ng/mL vs 2.19 ng/mL,  $p = 0.006$ ).

**Conclusion** Passage rates of CF AEC cultures contrasted significantly with excellent passage rates (>90%) reported previously for other airway diseases. Culture success was significantly associated both with traditional (cell yield, contamination) and non-traditional factors (CFTR phenotype, inflammation).

**Supported by** NHMRC, UWA, CFWA.

**Conflict of Interest** No.

**Nomination** Travel Award.

P109

### IN VITRO AIRWAY EPITHELIAL CELL MODELS DIFFER IN THEIR FUNCTIONAL RESPONSE TO NEUTROPHIL ELASTASE EXPOSURE

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**Introduction** Although long associated with airway destruction, the exact interactions of neutrophil elastase (NE) on airway epithelial cell (AEC) migration and repair remain unclear.

**Methods** Three AEC models were compared; SV40 immortalized (16HBE and CFBE), hTERT immortalized (10KT and CuFi-1) and primary cell cultures. During 48-h incubation with NE, cell models were assessed for viability and proliferative capacity using MTS formazan assay, LDH assay and time-lapse imaging (Essen IncuCyte™). Cytokine (IL-8, IL-6) and matrix metalloproteinase production were assessed by ELISA and gelatin zymography respectively.

**Results** Cell viability following incubation with 100 nM of NE varied between AEC models. No loss of viability was observed for the SV40 immortalized cells 16HBE140- and CFBE. Viability over 48 h was decreased for both 10KT and CuFi-1 ( $28.3\% \pm 9.9$  and  $36.1\% \pm 4.7$ ) and for primary derived healthy and CF AECs ( $8.4\% \pm 4.8$  and  $40.1\% \pm 18.9$ ). Proliferation of hTERT immortalized AECs was inhibited (14.2% and 9% of control) but not 16HBE140- and CFBE (both 100% of control).

**Conclusion** Different responses between AEC models suggests careful selection of the appropriate airway epithelium model is required for assessing NE. Primary derived cells remain the gold standard model however, hTERT immortalized cells are appropriate substitutes.

**Supported by** NHMRC, UWA, CFWA.

**Conflict of Interest** No.

## INTERVENTIONAL PULMONOLOGY & BRONCHOLOGY SIG POSTER SESSION

P110

### COMPARISON OF LOWER AIRWAY INFECTIONS IN CHILDREN WITH CYSTIC FIBROSIS BETWEEN AREST CF STUDY CENTRES

E HART<sup>1,2,3</sup>, S RANGANATHAN<sup>1,2,4</sup>, ON BEHALF OF THE AUSTRALIAN RESPIRATORY EARLY SURVEILLANCE TEAM FOR CYSTIC FIBROSIS (AREST CF)

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**Aim** To identify and compare the microorganisms present in the lower airways of children with cystic fibrosis (CF) participating in the AREST CF early disease surveillance program at Perth and Melbourne treatment centres.

**Methods** Study participants received a comprehensive assessment of lung health annually, which included bronchoscopy and bronchoalveolar lavage (BAL). BAL fluids ( $n = 997$ ) obtained between January 2006 and September 2012 were analyzed using conventional diagnostic techniques to identify any microorganisms present.

**Results** At annual review, on average 28.3% of Perth, and 54.7% of Melbourne study participants returned culture-positive BAL specimens. *S. aureus* (18.3% cases/year Melbourne; 6.5% cases/year Perth), *H. influenzae* (13.6% Melbourne; 4.8% Perth), *P. aeruginosa* (8.6% Melbourne; 7.8% Perth) and *A. fumigatus* (8.9% Melbourne; 4.1% Perth) were among the most common organisms detected, and the reported annual incidence was higher in Melbourne than in Perth. Infections with *E. coli*, *M. catarrhalis* and RSV were consistently more common among Melbourne study participants, and the detection of *Haemophilus* species increased in this group in recent years. A notable reduction of *S. aureus* infections among Perth, but not Melbourne, study participants was also observed.

**Conclusions** Respiratory pathogens were commonly isolated from the lower airways of children with CF, and there was a notable difference in infection rates between Perth and Melbourne treatment centres.

**Supported by** Australian Cystic Fibrosis Research Trust.

**Conflict of Interest** No.

P111

### AUDIT OF PLEURAL SERVICE AT BOX HILL HOSPITAL 2011-2012

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**Aim** To review and audit pleural disease management by respiratory department at Box Hill hospital in 2 years.

**Methods** Prospective data collection including patients' demographics and outcomes.

**Results** There were 146 referrals to respiratory team. Thoracic ultrasound showed 39 (27%) did not have effusion and 107 patients had pleural procedure. The number of cases referred to the unit increased dramatically from 1 case per month in February 2011 to 13 in July 2012. The average age of patients was 70.4 years (17-94). Five procedures performed for management of pneumothorax. Thirteen cases had parapneumonic effusion of which 5 had intrapleural enzyme treatment with 100% success rate. Three cases were diagnosed with pleural TB. Six cases had lung cancer. Eight patients with recurrent pleural effusion had talc pleurodesis via chest drain with 62.5% success rate. One patient was diagnosed with oesophageal rupture and one had pleural effusion due to peritoneal dialysis. The procedure was well tolerated with no major complications. Vasovagal episodes in 3 patients, pain in 1 patient, small pneumothorax in one patient, air leak related to procedure in 4 patients and only one patient needed second tube inserted. Follow-up of patients showed a mortality of 32% (40% in exudative effusions and 20% in transudative effusions).

**Conclusions** Bedside ultrasound-guided pleural procedure is safe and well tolerated. Pleural disease should be regarded as a subspecialty and pleural services providing high-quality and prompt intervention will improve patient care and reduce complications.

**Conflict of Interest** No.

P112

### THE IMPACT OF PORTABLE ULTRASOUND IN THE MANAGEMENT OF PLEURAL EFFUSION BY RESPIRATORY REGISTRARS

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Thoracocentesis with real-time thoracic ultrasound (US) guidance is recommended as best practice for management of pleural effusions. Physician-delivered portable thoracic US for pleural procedures has been shown to be both safe and effective.

**Aim** To assess the impact of implementing respiratory registrar-delivered portable thoracic US on the time to drainage from admission and length of stay (LOS) for patients who presented to the emergency department (ED) at Austin Hospital for management of a new undiagnosed pleural effusion.

**Methods** 32 cases were prospectively recruited during ED presentation with new undiagnosed pleural effusions requiring admission. US with real-time needle drainage was conducted or supervised by respiratory registrars accredited by the Australasian Society for Ultrasound in Medicine (using a Sonosite M-Turbo). Information collected was compared to a historical data set of 32 consecutive cases from a similar time period in 2011 in which thoracocentesis was performed either under real-time US guidance or separately in ward following 'X' marking in the US department.

#### Results

	Time from triage (mean ± standard deviation) (hours)			
	US marking	Drainage	Result	Discharge
Pre	60 ± 45	71 ± 50	140 ± 67	192 ± 30
Post	38 ± 30	38 ± 30	131 ± 48	247 ± 208

Compared to historical data set, the new US guided pleural drainage program shortened the time to US marking ( $p = 0.028$ ) and drainage ( $p = 0.0032$ ). There were no significant changes for duration to result or LOS. The need for surgical procedure significantly increased LOS ( $p = 0.0006$ ).

**Conclusions** The new US program improved delivery of patient care without shortening LOS.

**Conflict of Interest** No.

P114

### PHYSICIAN-PERFORMED ULTRASOUND CAN RELIABLY SCREEN FOR A VULNERABLE INTERCOSTAL ARTERY PRIOR TO CHEST DRAINAGE PROCEDURES

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**Introduction** Laceration of the intercostal artery (the vessel) during pleural procedures is a rare but serious complication. This study evaluates the utility of thoracic ultrasound (US) to screen for a vulnerable vessel compared with the gold-standard Computed Tomography (CT).

**Methods** Before undergoing contrast-enhanced CT chest, thoracic US was performed on 50 patients with a high-end and portable machine, and an attempt made to visualize the vessel at three positions across the back to the axilla. These positions were labelled with radio-opaque fiducial markers. On both US and CT images, the location of the vessel at each position, relative to the overlying rib, was calculated and compared.

**Results** The vessel was seen in 113 of 132 positions it was visible on CT. The sensitivity, specificity and negative predictive value of portable US to image the vessel, when it was vulnerable within the intercostal space on CT, was 0.97(0.88–0.99), 0.97(0.89–0.99) and 0.89(0.65–0.98) respectively. The performance of a high-end machine was not significantly better. The median time required for a pulmonologist to locate the vessel was 42 s and 18 s for the portable and high-end US respectively.

**Conclusions** US can be used to screen for a vulnerable vessel prior to pleural procedures, in a time amenable to use in clinical practice. Further, it is achievable by a pulmonologist using a portable US machine. If thoracocentesis or chest tube insertion is being performed on a patient at increased risk of bleeding, we would recommend screening for a vulnerable vessel with US prior to beginning the procedure.

**Supported by** University of Queensland.

**Conflict of Interest** No.

**Nominations** Janet Elder Travel Award.

P113

### AUDIT OF INTERCOSTAL CATHETER MANAGEMENT OF PLEURAL EFFUSION AND SPONTANEOUS PNEUMOTHORAX

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**Background** Intercostal catheters (ICC), used for management of pleural diseases, are generally considered safe but reports of mortality have been reported. Recent guidelines have identified strategies to improve the safety of ICC insertion and management. There is currently no information about ICC management at Gold Coast Hospital (GCH).

**Aim** To review the indications, outcomes and complications of intercostal catheter (ICC) management of pleural effusions and non-traumatic pneumothoraces at GCH.

**Methods** Retrospective audit of all ICCs inserted at GCH over a 12 month period. Data were collected on indication, ICC size and complications.

**Results** A total of 113 ICC insertions were documented in 89 patients. Indications were categorised as malignant effusions (32%), pleural infections (15%), other benign effusions (13%), primary spontaneous pneumothoraces (15%), secondary spontaneous pneumothoraces (18%) and iatrogenic pneumothoraces (7%). Small-bore ICCs (14 Fr or smaller) were used for 51 of 68 (75%) pleural effusion indications and 32 of 45 (71%) pneumothorax indications. There was no significant adverse effect affected by the size of the ICC used. Use of large-bore ICCs was associated with a higher rate of minor complications than small-bore ICCs (33% vs 14%), however there were no major complications that led to significant morbidity or mortality. Image guidance was used for ICC insertion in 57% of effusions and 9% of pneumothoraces.

**Conclusions** ICCs are relatively safe and effective interventions for pleural effusions and pneumothoraces. There is scope for improvement particularly in using bedside image guidance prior to ICC insertions.

**Supported by** Nil.

**Nomination** No.

**Conflict of Interest** No.

P115

### UTILIZATION AND SAFETY OF BEDSIDE THORACIC ULTRASONOGRAPHY IN THE GOLD COAST HOSPITAL

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**Aim** Recently our department has acquired the training and equipment to perform bedside thoracic ultrasonography. The aim of this study was to evaluate the utilization and diagnostic accuracy of this new service in our institution.

**Methods** Prospective data were collected about the activity level and diagnostic accuracy of bedside thoracic ultrasound performed from the period of June to September 2012. The procedures were performed by one of three physicians. Diagnostic accuracy was assessed based on the presence of pleural pathology on another radiology modality. The success and complication rates of pleural procedures and radiology referral rate were recorded.

**Results** 72 ultrasound scans performed over 4 month period. The number of ultrasound scans increased over the time, as a result of availability of the service. Bedside thoracic ultrasonography performed by the physicians correctly identified the presence/absence of pleural fluid in 44/47 (93%) and pneumothoraces in 25/25 (100%). Based on the findings, interventional procedures were performed in 17 patients. No complications were noted in these patients. 2/47 (4%) of patients were referred to the Radiology Department for further investigations.

**Conclusions** Bedside thoracic ultrasonography is being performed accurately in our institution. The diagnostic accuracy and referral to radiology are consistent with other studies. Further study is required to identify if bedside thoracic ultrasonography has increased the safety of performing pleural procedures compared with conventional methods (clinical assessment and radiology marking).

**Supported by** Nil.

**Nomination** No.

**Conflict of Interest** No.

P116

**BRONCHOSCOPY YIELD IN FEBRILE NEUTROPENIC PATIENTS WITH HAEMATOLOGICAL MALIGNANCY**

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**Introduction** Patients with haematological malignancy who are febrile, neutropenic and develop pulmonary infiltrates have high morbidity and mortality. Fibre-optic bronchoscopy (FOB) is used in the diagnostic work up for these patients. FOB yield is variable and there are limited data on its benefit in this patient population.

**Aim** To determine the yield of FOB in patients with haematological malignancy presenting with fever, neutropenia and pulmonary infiltrates. To evaluate how FOB results impacted on therapy and outcome in these patients.

**Methods** A retrospective review was conducted on patients with haematological malignancy presenting with febrile neutropenia and pulmonary infiltrate that underwent FOB at our institute between January 2011 and January 2012. Demographic, clinical, radiological and microbiological data and treatment were recorded. Treatment modification based on bronchoscopy results, procedure related complications and short-term outcome were evaluated.

**Results** Of the 349 bronchoscopies performed, 23 patients had haematological malignancy. 9 patients met the inclusion criteria; 10 bronchoscopies with bronchoalveolar lavage or bronchial washings were performed. 4 of the 10 bronchoscopies yielded positive microbiological results (*Parainfluenzae 3* + scant fungal hyphae, *Candida albicans*, 2 with *Candida glabrata*). 2 of the 4 positive results were considered probable causative agents (*Parainfluenzae 3* and *C. glabrata*) and the other 2 were considered questionable. Antimicrobial treatment was modified in 2 patients with positive results (*Parainfluenzae 3* and *C. albicans*) and in 1 patient with a negative result. There were no major complications of the procedure. 4 deaths occurred and were considered to be unrelated to the procedure. 2 of the 23 patients (0.09%) died within 30 days of the procedure.

**Conclusions** FOB altered treatment in 30% of these patients. It did not have a major impact on patient outcome and did not cause significant morbidity or mortality.

**Conflict of Interest** No.

P118

**LUNG CANCER PATHWAY AT THE ROYAL ADELAIDE HOSPITAL: IMPACT OF TREATMENT INTENT AND PATIENT LOCATION**

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**Introduction** A previous 2010 audit at the Royal Adelaide Hospital (RAH) found delays in treatment initiation when compared to targets set in the United Kingdom (UK) National Cancer Plan. The aim of this study was to review our performance in 2011 and to explore the impact of curative or palliative treatment intent and rural or urban based location, in order to guide future improvement.

**Methods** Using a pathology database, we retrospectively reviewed case notes of patients referred to the RAH in 2011 with new histologically confirmed lung cancer. We identified treatment intent, patient location and key dates in diagnosis and treatment by radiation oncology, medical oncology, cardiothoracic surgery or palliative care before calculating median intervals between these points.

**Results** 132 patients (63 rural (of these, 40% inpatient) and 69 urban (29% inpatients)) were analyzed. 60 patients had the date of first referral currently available. The median time intervals were as follows: all-source referral to first appointment: 5 days; first appointment to histological diagnosis: 7 days. There was no significant difference between rural and urban patients in these categories. Median time from diagnosis to first treatment overall were as follows: 26.5 days (rural: 25 days, urban 30 days); palliative patients: 17 days (inpatients: 15 days, outpatients: 28 days); curative surgical patients: 31 days (rural: 25 days, urban: 40 days); curative non-surgical treatment: 28.5 days (rural: 23 days, urban: 24 days).

**Conclusions** For 2011, the RAH achieved UK targets for lung cancer diagnosis and treatment overall, however in subgroup analysis, targets were not met for urban curative surgical cases. Rural location improved waiting times. Multidisciplinary streamlined pathways for lung cancer management are required to further reduce delays and to improve time to curative treatment.

**Conflict of Interest** No.

**LUNG CANCER SIG: POSTER SESSION**

P117

**EGFR MUTATIONS OCCUR COMMONLY IN NON-SQUAMOUS NSCLC IN SYDNEY**E STONE<sup>1</sup>, T SAGHAIE<sup>2</sup>, A ABBOTT<sup>2</sup>, H AINGE ALLEN<sup>1</sup>, L MORGAN<sup>2</sup><sup>1</sup>St Vincent's Hospital Lung Cancer MDT, Darlinghurst, NSW, and <sup>2</sup>Nepean Lung Cancer Group, NSW

EGFR mutations occur in 10–15% of non-squamous NSCLC in European populations.

**Methods** Two Sydney lung cancer MDTs combined to assess local frequency of EGFR mutation in non-squamous NSCLC. The SVH dataset was collected prospectively from August 2011 to July 2012 from sequential cases presented at the institutional MDT with sample analysis at the Peter MacCallum Institute Melbourne, Victoria. The Nepean Hospital dataset was collected retrospectively from an audit of all cases sent for EGFR mutation testing between October 2010 and November 2012 with sample analysis by Healthscope, Vic.

**Results** 59 tumour samples were analyzed for EGFR mutation. Samples were obtained by surgical resection (n = 23), FNA (n = 10), core biopsy (n = 13), EBUS-TBNA (n = 8), endobronchial biopsy (n = 4) and pleural aspirate (n = 1). EGFR mutations were detected in 13/59 (22%) samples. 10/13 had classical activating mutations: 8/13 had exon 19 deletions, 2/13 had exon 21 L858R substitutions, 2/13 had non-activating/resistance mutations (1 each exon 20 insertion or deletion) and 1/13 had both an exon 20 insertion and an exon 21 substitution. 7 patients were Asian, 7 were Pacific Islander, 1 was Indian and the remainder Caucasian. There was confirmation of smoking history in 49 cases: 8 confirmed smokers, 22 ex-smokers and 19 non-smokers. Of the 13 cases with EGFR mutation, 9 were non-smokers, 3 were Asian, 11 were female.

**Conclusion** EGFR mutation occurs with a frequency of 22% in a Sydney lung cancer population selected only for non-squamous NSCLC. The phenotype of our patients with EGFR positive NSCLC extends beyond the previously described female Asian non-smoker.

**Support** Data collected at the SVH was supported by an unrestricted grant from Roche.

**Conflict of Interest** Nil.

P118

**CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH METASTATIC CEREBRAL DISEASE DUE TO NSCLC MANAGED AT THE PRINCESS ALEXANDRA HOSPITAL OVER A 5-YEAR PERIOD (2007–2011)**

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Patients with lung cancer often present with cerebral metastases. While this is often thought to be associated with a dismal prognosis, this may not be the case in all individuals. We therefore assessed the clinical features, treatment and survival of patients with non small cell lung cancer (NSCLC) presenting with cerebral metastases.

**Method** A retrospective cohort analysis of all patients with cerebral metastases due to NSCLC from 2007 to 2011 was performed using a centralized Thoracic Malignancy database.

**Results** 114 cases were identified (adenocarcinoma 54%, squamous 15%, NSCLC not otherwise specified 31%). Thirty-five percent had solitary and 65% of patients had multiple cerebral metastases. Thirty-seven percent of patients had surgery, 80% had whole brain radiotherapy. In the subset of patients with adenocarcinoma, there were 9 patients who survived for more than 30 months after surgery. This is compared to only 1 patient in the squamous group and 0 patients in the NSCLC NOS group. Common symptoms after radiotherapy or surgery were anorexia, nausea, fatigue and headache.

**Conclusions** Even though many patients did poorly, a subset of patients with adenocarcinoma had surprisingly good survival following successful resection of the cerebral metastasis.

**Key Words** lung cancer, cerebral metastases, surgery, radiotherapy, survival.

**Support** No financial support was received for this study.

**Conflict of Interest** There were no conflicts of interest in this study.

P120

### AN EVALUATION OF THE MULTI-DISCIPLINARY APPROACH IN THE MANAGEMENT OF LUNG CANCER: A SINGLE-CENTRE EXPERIENCE

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**Aim** To compare patients with newly diagnosed lung cancer managed through the St Vincent's Hospital Network multi-disciplinary team (SVHN MDT) with a contemporaneous control group of patients registered in the SVHN not managed through the MDT.

**Methods** A retrospective analysis was conducted for patients diagnosed between 2006 and 2010. Data for MDT patients was drawn from the MDT database which is a prospective, electronic database. Data for non-MDT patients was obtained through the Clinical Cancer Registry (ClinCR). Data points examined include: 1) Number of patients presented at MDT, 2) Number of cases with documented full TNM staging 3) Distribution of stage at diagnosis 4) Specifics of treatment 5) Proportion of patients with referral to psychosocial services and palliative care services, 6) Management of Stage IIIA disease, 7) Clinical trial enrolment.

**Results** Over the 5-year period, there were 844 cases of patients with lung cancer registered in the St Vincent's Network. There was a progressive increase in the proportion of patients that were presented at MDT meetings, from 26% in 2006 to 45% in 2010. Full TNM staging was documented more frequently in the MDT group (88% vs 79%). Greater numbers of patients in the MDT group were referred for psychosocial and palliative care referrals (78% vs 71% and 63% vs 60% respectively). A higher proportion of patients in the MDT group underwent a curative surgical procedure (57% vs 42%). Four clinical trials were run during this time, and 2 out of 59 patients that were screened were accrued.

**Conclusion** Patients managed through the MDT had more complete documentation of staging and greater number of referrals to psychosocial and palliative care services. For early stage disease, MDT patients had a higher curative surgical rate.

**Supported by** Nil.**Nomination** Nil.**Conflict of Interest** No.

P121

### DEREGULATED GP130/STAT3-DRIVEN INFLAMMATION IN LUNG CANCER DEVELOPMENT

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A causal correlation between lung cancer and cigarette smoking has been well established, however only 10–15% of smokers develop lung cancer, suggesting the presence of other ill-defined factors which predispose certain individuals to lung cancer. Lung inflammation is the hallmark of all lung cancer patients, however the inflammatory signalling mechanisms associated with the molecular pathogenesis of lung carcinogenesis are poorly understood. In this regard, the interleukin (IL)-6 cytokine family, which signals through the shared gp130 signal-transducing receptor subunit, has been implicated in inflammation and lung cancer. The engagement of gp130 triggers the activation of several downstream signalling pathways, in particular the latent transcription factor signal transducer and activator of transcription (Stat)-3 which plays a vital role in regulating pro-inflammatory and oncogenic cellular processes. Notably, an increased activation of Stat3 is linked with lung cancer. However, the mechanisms leading to, and the downstream consequences of, increased Stat3 activity in human lung diseases are ill defined. Therefore, we utilized several human cancer cell lines to investigate the molecular consequences of cooperation between gp130 signalling and lung cancer risk factors *in vitro*. Our data showed, for the first time, that IL-6 and potent cigarette smoke carcinogen, NNK, can modulate endogenous gp130/Stat3 signalling in human lung cancer cell lines at both the mRNA and protein level within an acute period, regardless of their constitutively active Stat3 level. These results will therefore provide a significant and original contribution to our fundamental understanding of the mechanisms involved in lung cancer development.

**Supported by** NHMRC.**Conflict of Interest** No.

P122

### SUCCESSFUL TREATMENT OF BRONCHORRHEA IN AN EGFR MUTATION NEGATIVE ADENOCARCINOMA WITH ERLOTINIB

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Bronchorrhoea is a rare presentation of lung adenocarcinoma. We report the case of a 65M diagnosed with adenocarcinoma, presenting with unresolving left lower lobe consolidation and progressive respiratory failure secondary to bronchorrhea. The bronchorrhea was unresponsive to high dose steroids, azithromycin, ipratropium and glycopyrrolate. Within 24 h of commencing Erlotinib 150 mg daily, bronchorrhea and ventilation parameters significantly improved, with successful extubation after 72 h. Subsequent EGFR mutation analysis was negative. Bronchorrhea is associated with high morbidity. Pooling of secretions and intrapulmonary shunt cause respiratory failure. Given the limited success of previous interventions including steroids, macrolides, inhaled indomethacin, methylxanthines and octreotide, a trial of tyrosine kinase inhibitors, which have been successful in previous case reports,<sup>1,2</sup> may be considered.

**Supported by** Nil.**Nomination** No.**Conflict of Interest** No.**References**

- 1 Thotathil Z. Erlotinib effective against refractory bronchorrhea form advanced NSCLC. *J Thoracic Oncol* 2007; **2**: 881–2.
- 2 Severe bronchorrhea in a patient with bronchioalveolar carcinoma. *Chest* 2012; **141**.

## OELD/POPULATION HEALTH SIG: POSTER SESSION

P123

### LUNG FUNCTION DECLINE IN ASBESTOS-EXPOSED INDIVIDUALS WITH RADIOLOGICAL ABNORMALITIES

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**Aim** Asbestos exposure causes abnormalities of the lung parenchyma (asbestosis) and pleura (diffuse thickening (DT) and pleural plaques (PP)). Lung function impairments are well established for asbestosis and DT but not for PP. This study investigated longitudinal changes in lung function in asbestos exposed individuals with asbestosis, DT and PP.

**Methods** Subjects had participated in the Asbestos Review Program (ARP), an annual clinical review that had been running since 1991. The ARP included a plain chest X-ray and lung function (spirometry). Data from participants who had at least 2 lung function measures were included in the current analyses. Longitudinal lung function changes were analyzed using a general linear mixed effects model, which included age, height, sex, presence or absence of abnormalities, smoking history, respiratory disease and cumulative asbestos exposure.

**Results** At any one time people with asbestosis and DT had significantly reduced FVC and FEV1, but not FEV1/FVC. Annual decline for these spirometric variables was not significantly greater than other asbestos exposed individuals. PP was not associated with reduced FVC or FEV1 but had a faster annual decline in FEV1 and FEV1/FVC compared with other asbestos exposed individuals. Cumulative exposure was associated with reduced FVC and FEV1 independent of abnormalities.

**Conclusions** The presence of PP does not impair lung function further than impairments caused by exposure alone, although it is associated with a faster decline in FEV1.

**Supported by** SCGH Research Advisory Committee.**Conflict of Interest** No.

P124

### RESPIRATORY SYMPTOMS AND QUALITY OF LIFE IN ASBESTOS-RELATED DIFFUSE PLEURAL THICKENING AND PLEURAL PLAQUES

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**Aims** To determine the impact of pleural plaques (PPs) and diffuse pleural thickening (DPT) on quality of life and respiratory symptoms.

**Methods** Individuals with PPs or DPT (classified according to the ATS statement on non-malignant asbestos-related disorders) and healthy controls completed the St George's Respiratory Questionnaire (SGRQ), SF-36 Health Survey, visual analog scale (VAS), full lung function, 6-min walk test (MWT) and chest CT scan.

**Results** 55 subjects were recruited (21 PPs; 18 DPT; 16 healthy controls). Results are shown in Table 1.

**Table 1**

Median (range), \*p < 0.05 PPs vs controls, \*p < 0.05 DPT vs controls

	Controls	Plaques	DPT
Age (mean (SD))	60 (10.6)	68 (9.6) <sup>#</sup>	69 (7.8) <sup>*</sup>
SGRQ symptom score	4.9 (25.2)	18.3 (76.8) <sup>#</sup>	22.7 (73.1) <sup>*</sup>
SGRQ total score	2.4 (27.5)	5.4 (39.2) <sup>#</sup>	16.5 (66.4) <sup>*</sup>
SF-36 General Health	82 (38)	77 (75)	58.5 (77) <sup>*</sup>
SF-36 Physical Component Score	55.7 (17.1)	50.4 (27.5) <sup>#</sup>	47.4 (37.7) <sup>*</sup>
6 MWT distance (mean (SD))	557 (64.6)	503 (115.6)	473 (93.5) <sup>*</sup>

In the DPT group, SGRQ symptom score correlated inversely with FEV<sub>1</sub>% (r = -0.57, p < 0.05) and SF-36 Physical Component Score correlated with FEV<sub>1</sub>% (r = -0.66, p < 0.01) and FVC% (r = -0.62 p < 0.01).

**Conclusions** Subjects with DPT and PPs have worse quality of life compared with healthy individuals.

**Supported by** Slater & Gordon Asbestos Research Fund; Lesley Pockley Clinical Research Trust.

**Conflicts of Interest** None.

P125

### QUANTITATIVE ASSESSMENT OF EMPHYSEMA USING AUTOMATED SOFTWARE IN SUBJECTS WITH ASBESTOS-RELATED PLEURAL DISEASE

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**Aim** To evaluate use of the Philips Lung Emphysema Software (LES) for automated quantification of emphysema in subjects with asbestos-related pleural disorders.

**Methods** High resolution CT scans were obtained using a standardized protocol, and emphysema quantified by LES. Correlations with lung function, respiratory symptoms, quality of life (QoL) and 6-min walk test were made.

**Results** 41 subjects were studied (23 with pleural plaques (PPs), 18 with diffuse pleural thickening (DPT). No differences were found in total lung volume (cm<sup>3</sup>), total emphysema volume (cm<sup>3</sup>) and emphysema ratio (%) between the two groups when assessed by the LES. Total LES lung volumetric measurement closely correlated with total lung capacity (DPT group r = 0.8, p < 0.01; PPs group r = 0.7, p < 0.01) measured by plethysmography. Inverse correlations were found between emphysema ratio (%) and FEV<sub>1</sub>/FVC ratio (r = -0.7, p < 0.01) and FEV<sub>1</sub> (r = -0.4, p < 0.01) when both groups were analyzed together; also in the PPs group (FEV<sub>1</sub>/FVC ratio r = -0.8, p < 0.01) and (FEV<sub>1</sub> r = -0.6, p < 0.01). Emphysema ratio (%) correlated negatively with 6-min walk distance in DPT group (r = 0.5, p < 0.05), but not in PPs. No correlation between emphysema ratio (%) and QoL scores was observed in either group.

**Conclusion** Emphysema was successfully measured in this group with asbestos related-pleural disorders using the Lung Emphysema Software. The Lung Emphysema Software correlated significantly with lung function in this study.

**Supported by** Slater & Gordon Asbestos Research Fund; Lesley Pockley Clinical Research Trust.

**Conflicts of Interest** None.

P126

### HYPERSENSITIVITY PNEUMONITIS SECONDARY TO CRICKET EXPOSURE

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**Introduction** Hypersensitivity pneumonitis (HP) is characterized by an inappropriate immune response and accumulation of activated T lymphocytes in the lungs. We present a case of HP secondary to long-term cricket (*Achetus domesticus*) exposure.

**Case Report** A 63-year-old male cricket breeder presented with a 6-week history of marked breathlessness and associated wheeze, chest tightness and fever on a background of 2 years chronic cough. Inspiratory crepitations were present and spirometry revealed a restrictive pattern. High resolution CT demonstrated extensive ground glass opacification throughout both lung fields with some sparing at the bases. BAL showed 30% lymphocytes. Transbronchial lung biopsy revealed inflammation and a granuloma suggestive of HP. Avian precipitin serology was negative. An Ouchterlony double diffusion test identified precipitating antibodies to cricket head, legs, wings and internal organ components. Western blot analysis using the patient's serum to probe PAGE analysis of the cricket body parts showed specific bands at 150, 120, 75 and 60 kDa. Preliminary mass spectrometry of the prominent 40 kDa band revealed arginine kinase, a known IgE-associated allergen in other insect species. Use of a mask and reduction in exposure to crickets led to improvement in his clinical symptoms, spirometry and CT abnormalities.

**Discussion** Allergic sensitization to cricket antigens has been previously reported in relation to asthma and immediate hypersensitivity, but this may be the first to be reported case of HP due to chronic cricket exposure.

**Conflict of Interest** None.

<sup>+</sup>Shared first authorship.

P127

### TALCOSIS SECONDARY TO BABY POWDER INHALATION

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**Case Report** Ms. L is a 49-year-old Samoan female with a past history of congenital cardiac defect repair, morbid obesity, and childhood tuberculosis. She is the mother of six children aged between 7 and 17 years and is an ex-smoker. She was referred for assessment after a routine preoperative chest x-ray revealed prominent coarse, reticulo-nodular densities throughout both lungs. Computed tomography (CT) chest confirmed bilateral extensive centrilobular nodules and also showed mass-like consolidation of the posterior segment of the right upper lobe. Her only respiratory symptom was mild breathlessness. Examination was normal apart from midline sternotomy scar. Vasculitic screen and bronchoscopy were normal. Pulmonary function testing revealed normal spirometry and a mildly reduced gas transfer factor. A CT guided biopsy of the right upper lobe mass demonstrated sheets of histiocytes, giant cells and macrophages containing birefringent crystalline material. Under polarized light diffuse crystalline material was seen, suggestive of silica or talc. Mycobacterial and fungal stains and cultures were negative. Routine questioning of occupational and environmental exposures was unrewarding. It was only when asked about her children that Ms. L revealed a history of deliberate deep inhalation of large quantities of baby powder for the duration of her pregnancies and beyond as she derived pleasure from the smell.

**Discussion** Talc is a mineral composed of hydrated magnesium silicate and is widely used in industries and cosmetics. It causes a rare form of silicate induced lung disease. Radiographic findings in talcosis include small centrilobular and subpleural nodules, heterogeneous conglomerate masses, and ground glass opacities. Polarized-light microscopy reveals birefringent needle-shaped particles in multi-nucleated giant cells and macrophages. Treatment is avoidance of further exposure and symptomatic support. This case reminds us of the rare talc-induced interstitial lung disease and reinforces the importance of thorough history taking.

**Conflict of Interest** No.



P128

### PARADOXICAL ASSOCIATION BETWEEN MATERNAL SMOKING AND PRE-BRONCHODILATOR FEV<sub>1</sub> IN NON-ASTHMATICS AGED SEVEN

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**Aim** To assess the relative and combined association of maternal and paternal smoking on childhood lung function when aged seven.

**Methods** Cross-sectional data were extracted from the population-based Tasmanian Longitudinal Health Study (TAHS) cohort first studied when aged seven in 1968 (n = 8,583) with questionnaire and pre-bronchodilator FEV<sub>1</sub>. Parental smoking was defined as neither, paternal, maternal or both parents smoking. FEV<sub>1</sub> percent predicted values were derived from the all-age reference ranges.<sup>1</sup> Linear regression, stratified by childhood asthma, was used to assess the association while adjusting for gender, recurrent childhood bronchitis, family history and social class as *a priori* confounders.

**Results** Of the 6,016 7-year-olds with complete data, current smoking was reported by 36% of mothers and 61% of fathers. Both parents smoked in 28% (n = 1,706). Among non-asthmatics, maternal smoking was associated with increased FEV<sub>1</sub> % predicted values [+2.0 (95%CI 0.7–3.4) p = 0.003], but not if combined with paternal smoking [–0.1 (–1.0 to +0.7)], p-value for interaction = 0.006]. Results were similar when restricted to those with a history of bronchitis, and there was no such association in asthmatics.

**Conclusion** Maternal smoking was linked to increased FEV<sub>1</sub> % predicted among non-asthmatics, but only when the father did not smoke. This may be in part due to residual confounding and the phenomenon of a 'healthy passive smoker', who has few symptoms such that their sole smoking mother has a tendency not to quit.

**Grant Support** NHMRC, Australian Postgraduate Award, ALF.

**Conflicts of Interest** None.

#### Reference

1 Stanojevic *et al.* *Am J Respir Crit Care Med* 2008; **177**: 253–60.

P130

### MORTALITY AND READMISSIONS IN PATIENTS WITH BRONCHIECTASIS—6-YEAR FOLLOW-UP

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**Aims** Bronchiectasis is a chronic respiratory disease that is associated with significant morbidity and mortality. There is a high prevalence of bronchiectasis in South Auckland and the prognosis for these patients is currently poorly understood. In New Zealand there is a paucity of data on the long term outcomes of bronchiectasis patients.

**Methods** All patients admitted to Middlemore Hospital in 2002 with an exacerbation of bronchiectasis were studied. Only patients with an HRCT diagnosis were included. Clinical notes, computerized records and data from the Ministry of Health were collected from 2001 to 2008. Demographics, co morbidities, and other factors associated with readmissions and long term mortality was examined.

**Results** One hundred patients with a mean age of 58 ± 18 were studied. Pacific and New Zealand Maori patients were overrepresented accounting for 73% of the cohort. The in-hospital mortality rate was 5% and the probabilities of all-cause death at one and 6 years were 16% and 44% respectively. There were a total of 904 acute admissions over a 7-year period, of which 687 (76%) were due to exacerbations. The readmission rate was high with 57% of patients having a further exacerbation within a year and 36% of patients having 2 or more exacerbations. Twenty seven patients were defined as frequent exacerbators requiring 2 or more admissions per year. These 27 patients accounted for 404 (58.8%) exacerbations of the total 687 in our cohort. The 6-year mortality rate in this group was 70.4%. Of all the patients who died, there was an increase in admission rate in their last year of life, with a median of 4.5 admissions and 84% having at least 2 or more admissions. Multivariate analysis shows the pneumonia severity index (PSI) and a previous exacerbation admission in the 12 months prior are identified to be the two independent predictors for 12-month mortality with area under ROC of 0.84.

**Conclusion** There is a high mortality rate in patients who have had an admission with an exacerbation of bronchiectasis in South Auckland. There is a high readmission rate with exacerbations of bronchiectasis. There is a subgroup of patients who had frequent exacerbations, and these patients had a higher mortality rate. The admission rate was highest in the last 12 months of life.

**Conflict of Interest** No.

P131

### ASTHMA BUT NOT ECZEMA IS ASSOCIATED WITH LARGE SKIN PRICK DIAMETER AND POLY SENSITIZATION TO TEMPERATE AND SUBTROPICAL GRASS POLLEN ALLERGENS

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**Background** Sensitization and exposure to grass pollen is an important trigger for symptoms in patients with allergic respiratory disease.

**Aim** To determine the relationship between atopic eczema and asthma diagnoses and gender and multi-sensitization to grass pollen by skin prick test and whether these associations differed between temperate and subtropical grasses.

**Methods** Patients resident in Canberra diagnosed with allergic rhinitis underwent skin prick testing using commercially available allergen extracts (subtropical grasses—Johnson and Bahia from the Panicoidae family, Bermuda and temperate grasses – rye grass and Kentucky blue from the Pooideae family). We used quantile regression for skin prick diameter and ordinal regression for skin test sensitization to examine associations with age, gender and doctor diagnosed atopic eczema and asthma.

**Results** Of n = 106, age 9–28 years, 58% were male, 37% had asthma and 22% had eczema. 73% were poly sensitized to temperate and 50% to subtropical grasses. For the subtropical grasses, only asthma was associated with a large ( $\geq 3$  mm) skin prick diameter (beta = 1.9, p = 0.03). Poly sensitization to temperate grasses was more common in males than females (OR = 3.1; 1.16–8.32) and in those with asthma (OR = 2.89; 0.94–8.93 p = 0.06) but not eczema (OR = 0.55; 0.17–1.83). Older patients were more likely to be poly sensitized (OR = 1.11; 1.02–1.24).

**Conclusion** Asthma (but not eczema) and being male were associated with large skin prick response and poly sensitization to grass pollen allergens which varied for temperate and subtropical grasses.

**Conflict of Interest** No.

P133

### TARGETING STEROID-RESISTANT PERIPHERAL BLOOD PRO-INFLAMMATORY CD28NULL T CELLS BY INHIBITING CD137 EXPRESSION: RELEVANCE TO TREATMENT OF BOS

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**Background** We have recently shown that bronchiolitis obliterans syndrome (BOS) is associated with reduced immunosuppression of T-cell pro-inflammatory cytokines, granzyme B and perforin particularly by steroid resistant peripheral blood CD28nullCD137+ T cells. We hypothesized that we could target these steroid resistant T cells by inhibiting co-stimulation through CD137.

**Method** Isolated PBMCs from transplant patients with stable lung function, patients with evidence of BOS and healthy controls were stimulated with anti-CD3 ± blocking anti-CD137 ± 10<sup>-6</sup> M methylprednisolone (± stimulatory anti-CD137 and isotyped matched control antibodies). Cytokine profiles, granzyme B and perforin expression on CD8+ and CD8-CD28null T-cell subsets were determined using flow cytometry.

**Results** There was a significant decrease in the percentage of CD8+ and CD8-CD28null T-cells producing IFN $\gamma$ , TNF $\alpha$ , granzyme B and perforin in all subjects in the presence of anti-CD137 blocking antibody compared with anti-CD3 alone (eg, 30% decrease in CD8+CD28nullTNF $\alpha$  cells). Stimulatory anti-CD137 was associated with an increase in pro-inflammatory/cytotoxic CD28null T cells (no change for control antibodies). Treatment with anti-CD137 blocking + prednisolone further reduced IFN $\gamma$ , TNF $\alpha$ , granzyme B/perforin in CD28null cells.

**Conclusions** Blocking CD137 expression in CD28null T cells is associated with downregulation of IFN $\gamma$ , TNF $\alpha$ , granzyme B and perforin. Targeting T-cell CD137 reduces pro-inflammatory/cytotoxic expression in steroid resistant CD28null T cells and may improve therapeutic strategies for patients with BOS where current treatments are ineffective.

**Supported by** NHMRC.

**Conflict of Interest** None.

**Nomination** Nil.

## OLIV SIG: POSTER SESSION

P132

### IS MUSCLE STRENGTH REDUCED IN LUNG AND HEART-LUNG TRANSPLANT RECIPIENTS? PRELIMINARY DATA

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Muscle dysfunction has been proposed as a limiting factor to exercise tolerance in lung transplant recipients.

**Aim** To explore differences in measures of biceps brachii and quadriceps force between lung transplant recipients and healthy controls.

**Methods** Data were collected in double lung or heart-lung transplantation recipients (6 months to 5 years post-procedure) and healthy controls. Height, weight and spirometry were measured. Force generating capacity of biceps brachii and quadriceps were assessed via maximal voluntary isometric contractions using a dynamometer (HUMAC Norm CMSi 2009).

**Results** Data (median [IQR]) are available for 8 transplant recipients (7 bilateral lung, 1 heart-lung, 3 males, age 42 [25] year, body mass index (BMI) 22 [6] kg/m<sup>2</sup>; FEV<sub>1</sub> 3.0 [0.1] L) and 8 matched controls (median [IQR] 4 males; age 41 [29] year; BMI 23 [1] kg/m<sup>2</sup>; FEV<sub>1</sub> 3.4 [0.9] L). Biceps torque was 35 [20] and 35 [29] Nm in the transplant and control group, respectively (p = 0.53). Quadriceps torque was 148 [83] and 183 [120] Nm in the transplant and control groups, respectively (p = 0.40).

**Conclusions** These preliminary results suggest that transplant recipients have similar biceps brachii strength but are 19% weaker in their quadriceps compared with healthy controls. While this difference does not reach statistical significance, these findings may be of clinical importance.

**Supported by** Advanced Lung Disease Unit, Royal Perth Hospital and the Lung Institute of Western Australia, Sir Charles Gairdner Hospital.

**Nomination** Physiotherapy and OLIV prize.

**Conflict of Interest** No.

P134

### A NATIONAL SURVEY OF PHYSICIAN MANAGEMENT OF IDIOPATHIC PULMONARY FIBROSIS: WHAT HAS CHANGED IN 12 YEARS?

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**Background** Idiopathic pulmonary fibrosis (IPF) is a disease characterized by progressive lung fibrosis, for which there is no proven therapy. IPF is often difficult to accurately diagnose, with wide variation in management practices. Revised guidelines for the diagnosis and management of IPF were published in 2011.

**Aim** To determine the current IPF management practice amongst physicians, and to compare this to practice in 1999.

**Methods** A survey was distributed to TSANZ members in which participants answered 20 questions addressing demographics, approach to investigation, treatment and long-term follow-up of IPF patients. Responses were compared to results of a similar survey in 1999.

**Results** 133 surveys have been completed to date. 59% of respondents are hospital specialists and 11% in private practice. Over 80% of physicians regularly perform HRCT, spirometry, DLco, autoimmune serology and SpO<sub>2</sub> at baseline assessment. Six-minute walk test is ordered routinely by >40%, compared with 15% in 1999. Most would either not treat a patient with probable IPF (56%) or would refer for participation in a clinical trial (62%). This compares to 1999, when 74% treated immediately with immunosuppression. Nearly half (48%) have changed their practice in the past 1–2 years. Many (90%) now access multidisciplinary teams for additional care.

**Conclusion** There have been significant changes in the management of IPF, notably in the shift towards multidisciplinary review, early referral for clinical trial participation and less immunosuppressive therapy.

**Conflict of Interest** None.

P135

### THE AUSTRALIAN IDIOPATHIC PULMONARY FIBROSIS REGISTRY: A NATIONAL COLLABORATION

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**Background** In Australia, Idiopathic Pulmonary Fibrosis (IPF) research is limited by the small population spread across our large continent. A national Registry will facilitate research to improve outcomes for IPF patients.

**Methods** Principle Investigators, supported by the Australian Lung Foundation, have developed a comprehensive Registry compatible with other international registries. Data from four sources are collated. Patients complete a questionnaire and clinicians complete a two-page survey every 6 months, identifying investigations for entry into the Registry database. Histopathology and HRCT scans are collected for expert multidisciplinary review. Remote-access technology facilitates data collection across remote sites, while ensuring high-level security.

**Results** Launched in April 2012 at the TSANZ Annual Scientific Meeting, the first 10 months of Registry data give some preliminary insight into the epidemiology of IPF in Australia. To date, 94 patients have consented (68 male; mean age  $69 \pm 7$  years). 25 were never smokers, 55 ex-smokers, with 1 current smoker. Baseline pulmonary function included: FVC  $80.3 \pm 20.8\%$ , FEV<sub>1</sub>  $84.4 \pm 20.5\%$ , DLCo  $46.6 \pm 14.1\%$ . Six-minute walk test distance was  $443 \pm 113$  m, with SpO<sub>2</sub> at rest ( $94.9 \pm 2.1\%$ ) and end exercise ( $86.1 \pm 7.2\%$ ).

**Conclusion** The Australian IPF Registry is a collaborative effort to develop and contribute to a unique resource, providing a platform for epidemiological and clinical research and improving future IPF outcomes.

**Conflict of Interest** None.

P137

### THERAPEUTIC SURGICAL RESECTION OF PRIMARY PULMONARY ARTERY SARCOMA

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**Introduction** Primary pulmonary artery (PA) sarcoma is an atypical and rare malignancy. The disease is often extensive and aggressive surgical resection is an infrequent intervention.

**Case Report** A 53-year-old non-smoker female presented with recurring massive haemoptysis and dyspnoea. The CT pulmonary angiogram showed large filling defects in the main pulmonary arterial trunks extending to the segmental branches bilaterally, more prominent on the left. The left pulmonary artery had an unusual distortion with an expansile mass that had increased FDG avidity on PET imaging. Repeated bronchial artery embolizations provided temporary control of her recurring massive haemoptysis. The clinical suspicion of PA sarcoma was eventually confirmed on CT guided core biopsy after two separate failed attempts of endobronchial ultrasound guided biopsy of the left PA mass. Although her disease was extensive, she underwent a left pneumonectomy, debulking of right PA tumour and right endarterectomy at 2 months following her initial presentation.

**Discussion** The indication for surgical resection was to alleviate the recurring symptoms of massive haemoptysis. It also provided histological specimen for definitive diagnosis.

**Conclusion** Extensive disease of primary (PA) sarcoma may be amenable to therapeutic surgical resections.

**Conflict of Interest** None.

P138

### DESATURATED BUT NON-BREATHLESS PULMONARY HYPERTENSION PATIENT, HOW LOW IS TOO LOW?

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**Introduction** The 6-min walk test (6MWT) is reported a safe assessment of exercise capacity in pulmonary arterial hypertension (PAH) associated congenital heart disease (PAH-CHD). However, PAH-CHD patients have a marked decrease in arterial oxygen saturation (SpO<sub>2</sub>) during exercise which, based on standard guidelines, would result in the termination of the 6MWT. Given the clinical value of the 6-min walk distance (6MWD), many centres continue to undertake 6MWT in PAH-CHD patients, albeit with a marked reduction in end exercise SpO<sub>2</sub>. To date there has been no description of the cardiopulmonary response to 6MWT in PAH-CHD patients. We report the gas exchange abnormalities during a 6MWT in a single patient to challenge current literature in PAH-CHD.

**Methods** A 39-year-old woman born with transposition of the great vessels and irreversible PAH (mean pulmonary artery pressure: 87 mm Hg), World Health Organization-Functional Class II & on PAH therapy. Completed a 6MWT whilst the gas exchange measured simultaneously (portable metabolic cart, Cortex). SpO<sub>2</sub> estimated using the average value from two forehead probes. Oxygen carrying capacity (CaO<sub>2</sub>) estimated from the resting Hb (17.8 g/dl) and the SpO<sub>2</sub>.

**Results** 6MWD was 563 m with no rest. Pre exercise SpO<sub>2</sub> and dyspnoea (0–10 Borg scale) were 88% and 0 respectively. End 6MWT: SpO<sub>2</sub>, 42%; dyspnoea, 3; heart rate, 161 bpm; oxygen uptake 17 mL/kg/min, breathing efficiency (V<sub>E</sub>/VCO<sub>2</sub>) 43.4. Her CaO<sub>2</sub> fell from 20 to 12 mL/100 mL.

**Conclusion** This PAH-CHD patient had a marked reduction in the CaO<sub>2</sub> during exercise, characterized by an alarming fall in SpO<sub>2</sub>. Despite this, the individual was able to complete the 6MWT and remain remarkably non-breathless. These data highlight the need to develop specific guidelines for 6MWT in this PAH subgroup.

**Conflict of Interest** No.

P136

### PREDICTING SURVIVAL IN INTERSTITIAL LUNG DISEASE: THE ROLE OF DTPA LUNG CLEARANCE SCANS

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**Introduction** A variety of lung function, radiological and inflammatory markers are used to predict the clinical course of interstitial lung disease (ILD). The perceived value of <sup>99m</sup>Techneium-labelled diethylenetriamine penta-acetic acid (DTPA) clearance as one of these has waxed and waned over 20 years or more. One deficit has been the lack of long term studies addressing the value of DTPA clearance in predicting overall survival.

**Aim** To determine whether DTPA lung clearance predicts survival in ILD.

**Methods** We analyzed DTPA lung clearance scans performed in the assessment of ILD at Concord Hospital from Jan 2000 to Dec 2010. Normal clearance was t<sub>1/2</sub> > 25 min with mono-exponential pattern. Overall survivals for normal and abnormal groups were compared using Kaplan-Meier plots and hazard ratios calculated using standard methodology.

**Results** 219 DTPA scans were performed for initial assessment of ILD in the study period. Diagnoses were idiopathic pulmonary fibrosis in 84(38%), unspecified ILD in 51(23%), connective tissue disease-related ILD in 37(17%) and ILD/COPD in 19(8.6%). Subjects with normal clearance had mean age (SD) 72(13) and with abnormal clearance 70(12). 53% were male. Abnormal DTPA clearance time predicted shorter survival with hazard ratios (95% CI) at 1 year of 0.45 (0.22–0.92), at 3 years 0.53 (0.31–0.90) and at 5 years 0.55 (0.34–0.88).

**Conclusions** Independent of other factors rapid DTPA clearance predicts substantially poorer survival in patients being initially evaluated for ILD.

**Nomination** No.

**Conflict of Interest** No.

P139

**MEASUREMENT PROPERTIES OF THE LEICESTER COUGH QUESTIONNAIRE IN INTERSTITIAL LUNG DISEASE**

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**Aim** To evaluate the reliability and validity of the Leicester Cough Questionnaire (LCQ) in interstitial lung disease (ILD).

**Methods** Participants completed the LCQ, the Short Form 36 Survey and the Chronic Respiratory Questionnaire (CRQ). Relationships between the LCQ and established measures of disease severity and quality of life were evaluated. After 8 weeks reliability was evaluated in stable participants using the Bland Altman method and intra-class correlation coefficients (ICCs). Changes in LCQ were evaluated over 6 months.

**Results** Forty-five participants (29 with idiopathic pulmonary fibrosis, IPF) of mean age 71 (SD 9) years and TLCO 49 (16) %predicted took part. Eighteen percent of participants reported 'troublesome cough'. Correlations between LCQ domains and measures of disease severity were weak and non-significant. Worse scores on the mastery domain of the CRQ were associated with significantly lower LCQ domain scores, but correlations were weak ( $r_s = 0.30-0.33$ ). There were no relationships between LCQ and other quality of life measures. The mean difference between LCQ total scores after eight weeks was 0.29 units, with limits of agreement  $-7.31$  to  $7.07$  units. The ICCs for total and domain scores were fair to moderate, ranging from 0.37 to 0.58. Over the following 6 months there was a significant decrease in FVC, however LCQ scores did not change. Results were similar when only participants with IPF were included.

**Conclusions** In ILD, the LCQ may be less reliable than has been reported in other chronic respiratory diseases and does not have a strong relationship with other quality of life measures.

**Supported by** American Thoracic Society, Pulmonary Fibrosis Foundation.

**Nomination** Nil.

**Conflict of Interest** No.

P141

**AIRWAY HYPER-RESPONSIVENESS TO HYPERTONIC SALINE IN LUNG TRANSPLANT RECIPIENTS**

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Airway hyper-responsiveness to methacholine and hypertonic saline (HS) has been noted in patients following lung transplantation. Moreover it has been suggested that airway hyper-responsiveness may be predictive of subsequent Chronic Lung Allograft Dysfunction (CLAD).

**Aim** The aim of this study was to assess airway hyperresponsiveness at 3 and 9 months post double lung transplant (DLTx) and note any association with onset of CLAD within the first 2 years post lung transplant.

**Methods** 50 DLTx recipients were recruited, 8 lost to follow-up. Patients underwent spirometry on regular basis as part of their clinical management to identify the onset of BOS. Subjects had hypertonic saline challenges at 3 and 9 months post-transplant, using a modified protocol with a cumulative dose of 60 mL, or a 15% drop being the endpoint. DRS (cumulative dose/% fall) was calculated as a marker of sensitivity to inhaled hypertonic saline. At 2 years post Tx, 18 had developed some level of allograft dysfunction (CLAD  $\geq 0$  p), 24 developed no CLAD. Of 18 CLAD patients, 14 had hypertonic saline challenge at 3 months. Of the 24 non-CLAD patients, 19 had HS at 3 months. For the CLAD group the (mean  $\pm$  SEM) DRS =  $8.9 \pm 4.5$ , non-CLAD average DRS =  $21.5 \pm 4.9$  at 3 months ( $p = 0.05$ ). There was no statistical difference in DRS between those patients who developed the Bronchiolitis Obliterans Syndrome (BOS) form and CLAD and non-BOS form of CLAD. 8 patients deceased at 2 years, 5 had HS challenges at 3 months of which 4 were positive.

**Conclusions** Patients who develop allograft rejection have greater bronchial hyperresponsiveness early post lung transplant.

**Support** NHMRC Grants: 486101, 491103.

**Conflict of Interest** None.

P140

**POSITIVE SERUM PRECIPITINS MAY BE A NON-SPECIFIC FINDING IN PATIENTS WITH INTERSTITIAL LUNG DISEASE**

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**Background** The significance of positive serum precipitins is controversial, as it does not distinguish patients with hypersensitivity pneumonitis from simple contact individuals.

**Aim** To investigate the role of serum precipitins across interstitial lung disease (ILD).

**Methods** Consecutive patients attending the RPAH ILD clinic (Sept 2010-Sept 2012) with serum precipitins were included. Diagnoses from multidisciplinary review were recorded. Clinical data and serum precipitins results were collected by an investigator blinded to the ILD diagnosis. Serum precipitins results included: budgie (Ge90) & pigeon (Ge91) (Jul 2011-Sep 2012) and farmer's lung mix (GMX7) (Jan-Sept 2012) specific IgG measured on the Immunocap 250, and AVP for pigeon, budgie, poultry, and farmer's lung (Sept 2010-Dec 2011).

**Results** 109 ILD patients (mean age  $62 \pm 13$  years; male 55) had baseline serum precipitins. The mean FVC was  $77.8 \pm 22.6\%$  and DLco  $51.9 \pm 22.4\%$ . Diagnoses included: idiopathic interstitial pneumonia (IIP  $n = 38$ ); connective tissue disease (CTD) related ILD ( $n = 29$ ); hypersensitivity pneumonitis (HP  $n = 17$ ); sarcoidosis ( $n = 10$ ) and other ILD ( $n = 15$ ). 22 (20%) patients had positive serum precipitins: budgie (Ge90  $n = 10$ ; AVP  $n = 1$ ); pigeon (Ge91  $n = 15$ ; AVP  $n = 2$ ), farmer's (GMX7  $n = 3$ ; AVP  $n = 1$ ) and poultry AVP ( $n = 1$ ). Of those with positive serum precipitins, diagnoses included: (IIP,  $n = 8$ ); CTD ILD ( $n = 7$ ); HP ( $n = 3$ ); sarcoidosis ( $n = 1$ ) and other ILD ( $n = 3$ ). There was no relationship between the diagnosis of HP and a positive serum precipitins result ( $p = 0.8$ ).

**Conclusion** Serum precipitins may be non-specific for the diagnosis of HP in ILD patients.

**Conflict of Interest** None.

P142

**INHOMOGENEITY OF VENTILATION IN THE SMALL CONDUCTING AIRWAYS IS ASSOCIATED WITH LUNG REPAIR IN PATIENTS FOLLOWING LUNG TRANSPLANTATION**

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**Background** Lung transplantation is regarded as an effective treatment for people with end-stage lung disease. We have previously reported that Cara Cell secretory protein (CCsp) was associated with the degree of ventilation heterogeneity that occurs in the small conducting airways early post lung transplant. What is not clear is if this association is a result of patients who then go on to develop allograft dysfunction (CLAD).

**Methods** Double lung transplant patients had measures of spirometry and acinar (Sacin) and conductive (Scnd) measures of ventilation heterogeneity from the multiple breath washout technique (MBW) at regular intervals over a 24 month period. IL8 and CCsp were estimated from BAL taken at the time of lung function measures. Patients were then divided in to those that developed CLAD and those who remained well.

**Results** 39 patients were recruited. Over study period 18 patients developed CLAD. In the patients that developed CLAD there was a significant relationship between Scnd and CCsp/L-8 ( $R^2 = 0.386$   $p < 0.05$ ). However there was no relationship between Scnd and CCsp/L-8 at any other time period. Furthermore there was no relation between Scnd and CCsp/L-8 in the patients who did not develop CLAD.

**Conclusion** Ventilation heterogeneity in the conducting airways is associated a marker of lung repair in patients at 3 months after lung transplantation who then develop CLAD.

**Support** NHMRC Grants: 486101, 491103.

**Conflict of Interest** None.

P143

### AN UNUSUAL CASE OF GASTROINTESTINAL BLEEDING POST HEART–LUNG TRANSPLANTATION

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**Introduction** A non-respiratory presentation of a systemic condition in a heart-lung transplant recipient.

**Case Report** A 32-year-old female received a heart-lung transplant (HLTx) in 2006 for Eisenmenger's Syndrome. Both donor and recipient were Cytomegalovirus negative, however an Epstein Barr Virus (EBV) mismatch was present. In 2012, the patient presented with bright red painless rectal bleeding. Blood investigations revealed severe iron deficiency anemia, elevated urea & lactate dehydrogenase and abnormal liver function tests. Pulmonary Function tests, CXR & CT Chest/neck were stable and normal. CT abdomen revealed multiple hypo dense liver lesions and an adrenal lesion. MRI Rectum confirmed a large rectal mass filling the entire lumen. PET scan showed high FDG uptake in the rectal mass, liver, multiple bony sites and mesenteric nodes. Sigmoidoscopy confirmed a large, smooth, purplish rectal mass. Rectal mass biopsy showed only necrotic debris, and liver biopsy was performed. In situ hybridization for liver and rectal biopsy was positive for EBV confirming multifocal post-transplant lymphoproliferative disorder (PTLD).

**Discussion** PTLD is usually EBV-related and B-cell type and occurs most commonly in the first 2 years post-transplant. Late disease and extra-thoracic involvement is associated with worse outcome. Reduction in immunosuppression is the mainstay of treatment, together with combinations of Rituximab and conventional chemo-radiotherapy.

**Conclusions** PTLD is an important multifaceted disease post HLTx and should be considered in the differential diagnosis of a variety of thoracic and extra-thoracic presentations.

**Conflict of Interest** No.

P145

### PAEDIATRIC LUNG TRANSPLANT OUTCOMES VARY WITH MYCOBACTERIUM ABSCESSUS COMPLEX SPECIES

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**Aims** *Mycobacterium abscessus* complex, is an emerging pathogen in young patients with end stage cystic fibrosis (CF). Approach to suitability for lung transplant listing varies widely. Published post-transplant outcome data are conflicting, and do not differentiate species within the *M. abscessus* complex (*M. abscessus (sensu stricto)*, *M. massiliense* and *M. bolletii*). We describe recent single centre experience and attempt to relate outcome to species type.

**Methods** Retrospective identification of five subjects transplanted since 2003 with active *M. abscessus* infection at the time of transplant at Great Ormond Street Hospital. All non tuberculous mycobacterium (NTM) isolates were identified to separate species level. Management included wide lymph node excision with amikacin pleural cavity washout before organ implantation (where possible), and extended intravenous antibiotic and ongoing oral/nebulized prophylactic NTM antibiotic regimen.

**Results** Survival was 80% at both 1 year and to date (follow-up 2.5–7.5 years). Post-transplant mortality and ongoing morbidity occurred with 2/3 subjects with pre-transplant *M. abscessus (sensu stricto)* whilst no post-transplant NTM associated morbidity occurred with *M. massiliense* and *M. bolletii*.

**Conclusion** Acceptable post-transplant outcomes can be achieved in children colonized with *M. abscessus* complex. Increased morbidity and mortality seems to be associated with *M. abscessus (sensu stricto)* infection and not other species within the *M. abscessus* complex. Other factors may include completeness of lymph node excision, pleural adhesions and activity of infection (failure to achieve smear negativity). Multicentre collaborative studies are required to clarify whether risk stratification between species and strains is appropriate when considering suitability for lung transplantation.

**Support** PR was funded by a generous donation from David Mackintosh.

**Conflict of Interest** The authors have no conflicts of interest.

P144

### ST VINCENT'S LYMPHANGIOLEIOMYOMATOSIS (LAM) CLINIC: A SERVICE FOR AN ORPHAN LUNG DISEASE

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**Aims** The St Vincent's LAM clinic provides a specialized diagnostic, assessment and treatment service to women with suspected or confirmed LAM. Here we describe the LAM clinic, including patient demographics and treatment data.

**Methods** Clinical information was prospectively collected using a standardized format. LAM was diagnosed & classified according to ERS LAM guidelines.

**Results** 82 patients (77 females, 5 males) are under follow-up. 3 have undergone lung transplantation; 2 others are deceased. 15 have been treated with doxycycline as part of the Doxycycline in LAM study; 13 are currently on treatment with everolimus.

Sporadic LAM (sLAM)	34
Tuberous sclerosis complex related LAM (TSC-LAM)	10
Tuberous sclerosis complex without LAM	20
Renal angiomyolipomas*	17
Multifocal micronodular pneumocyte hyperplasia (MMPH)*	3
Predominantly abdominal lymphangioleiomyoma*	6
Emphysema	
Likely related to smoking	3
Unrelated to smoking	2
Birt Hogg Dube (BHD) syndrome	7
Other diagnoses: extrinsic allergic alveolitis (1), solitary PEComa (1), metastatic leiomyosarcoma (1), tracheobronchial papillomatosis (1), succinate dehydrogenase B deficiency.	

**Conclusions** A specialized clinic allows tailored treatment for women with LAM.

**Supported by** St Vincent's Hospital.

**Conflicts of Interest** None.

P146

### EFFECTS OF EXERCISE TRAINING ON EXERCISE CAPACITY AND QUALITY OF LIFE IN PULMONARY ARTERIAL HYPERTENSION

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**Aim** To investigate the effects of exercise training on exercise capacity and health-related quality of life (HRQoL) in individuals with pulmonary arterial hypertension (PAH).

**Methods** Participants with PAH were assessed for exercise capacity and HRQoL at baseline, and at 12 and 24 weeks. Exercise group participants attended supervised exercise training 3 times/week for 12 weeks followed by a 12-week home exercise program.

**Results** 5 exercise (5 F) and 5 control (4 F) group participants, aged 50 ± 11 years (mean ± SD) were recruited. Exercise capacity data for the exercise group, at baseline and 12 weeks, are outlined in the table. The exercise group maintained these improvements in exercise capacity at 24 weeks. No significant changes in HRQoL were observed in the exercise group at 12 or 24 weeks. The control group was stable throughout the period.

**Conclusion** The results suggest aerobic capacity was improved following training and, importantly, the benefits were maintained with a home exercise program.

Exercise group	Peak V <sub>O</sub> <sub>2</sub> (L/min)	V <sub>O</sub> <sub>2</sub> at AT (L/min)	Endurance time (min)	6MWD (m)
Baseline	1.11 (1.09–1.14)	0.63 (0.54–0.65)	7.3 (6.3–8.4)	560 (483–610)
12 weeks	1.25 (1.23–1.42) <sup>†</sup>	0.79 (0.75–0.84) <sup>†*</sup>	21.3 (18.4–23.1) <sup>†*</sup>	650 (623–679)

Data presented as median (interquartile range); V<sub>O</sub><sub>2</sub>, oxygen uptake; AT, anaerobic threshold; 6MWD, 6-min walk distance; <sup>†</sup>p < 0.05 compared to baseline.

**Conflict of Interest** No.

**Supported by** The Advanced Lung Disease Unit, RPH and LIWA.

**Nomination** Physiotherapy Prize, OLIV Prize.

P147

### COMPARISON OF PHYSIOLOGICAL AND SYMPTOM OUTCOMES TO LABORATORY AND FIELD-BASED EXERCISE TESTS IN PAH

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**Aim** To compare physiological and symptom outcomes between laboratory and field-based exercise tests in individuals with pulmonary arterial hypertension (PAH).

**Methods** 10 individuals (9 F) with PAH, aged 50 ± 11 years (mean ± SD) in World Health Organization functional class II and III, performed two unencouraged 6-min walk tests (6MWT), an incremental cardiopulmonary exercise test (CPET) and a constant workload cycle ergometer test (CWLT) during three visits separated by ≥24 h. Heart rate (HR) and oxygen saturation (SpO<sub>2</sub>) were recorded every minute during each test. Breath-by-breath gas analysis was performed during both cycle ergometry tests. Fatigue and dyspnoea were assessed at test end.

**Results** Peak HR ( $p \leq 0.014$ ), leg fatigue ( $p \leq 0.027$ ) and general fatigue ( $p \leq 0.025$ ) were lower on the 6MWT, when compared to the CPET and CWLT. Nadir SpO<sub>2</sub> was lower on the 6MWT (94 ± 2%), compared to the CPET (96 ± 4%) and CWLT (96 ± 3%), however this difference did not reach statistical significance. There were no significant differences in dyspnoea scores across the 3 tests. Peak HR, nadir SpO<sub>2</sub> and symptom scores were not significantly different on the CPET and CWLT. Peak oxygen uptake averaged 5 ± 6% higher on the CWLT ( $p = 0.034$ ) compared to the CPET. The CPET and CWLT yielded similar ventilatory responses.

**Conclusion** In the PAH population, the unencouraged 6MWT elicits sub-maximal responses compared to the CPET and CWLT.

**Conflict of Interest** No.

**Supported by** The Advanced Lung Disease Unit, RPH and LIWA.

**Nomination** Physiotherapy Prize, OLIV Prize.

P148

### CREATING INDICATIONS FOR IV THERAPY FOR PULMONARY ARTERY HYPERTENSION (PAH) IN NEW ZEALAND

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Treatment for PAH in NZ is restricted to dual oral/nebulized combination (CT) therapy.

**Aim** To assess the severity of patients on CT and to develop criteria for IV therapy in NZ.

**Methods** To compare the 6MW and haemodynamics at start of monotherapy (MT) and CT and to assess who would be suitable for IV therapy and/or LT.

**Results** 147 patients with Dana Point Class I, IV and V PH were included. 108 were female, mean age at diagnosis was 49 years (SD = 17 years). Mean time to diagnosis was 102 weeks. 52 (35%) had IPAH, 43 (29%) CTD and 27 (18.2%) had CTEPH. Overall survival was 91% at 1 year and 67% at 5 years. 121 patients received PH specific therapy; 72 MT, 49 CT and 6 CCB therapy. Mean time to CT was 76 weeks. The 6MW and RHC results at the initiation of MT and CT are below. There was no significant difference between the RHC variables and 6MW between initiations of MT and CT. There was however a significant worsening of WHO class from Class III to Class IV\*\*.

	6MW	RA	mPA	CO	PVR
Monotherapy	339 (190)	8 (7.75)	50 (13)	3.8 (1.3)	10.2 (5.1)
Combination therapy	324 (185)	11 (8.5)	56 (16)	3.8 (1.4)	12.36 (7.07)

\*Results are given as median (IQR); \*\* $p = 0.009$  Wilcoxon Signed Rank Test.

**Conclusion** Criteria for IV therapy: WHO IV, 6MW < 300\*, ↑RA or ↑RHC haemodynamics on CT for 6 months. There are 32/49 patients (12 are LT candidates) alive on CT at 1/9/12 who are candidates for IV therapy. They have severe disease at initiation of therapy and there is a need for IV therapy in NZ.

\*Unless limited by other factors e.g. gout, obesity, immobility.

**Support** Nil.

**Conflict of Interest** Nil.

## PAEDIATRIC SIG: POSTER SESSION

P149

### A SINGLE DOSE OF AZITHROMYCIN DID NOT IMPROVE CLINICAL OUTCOMES IN CHILDREN ≤18 MONTHS HOSPITALIZED WITH ACUTE BRONCHIOLITIS: A DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED TRIAL

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**Introduction** Bronchiolitis is the most common reason for hospital admission in infants. Macrolides have potential benefit in a setting such as ours with high bacterial carriage and infection rates resulting in prolonged illness. We aimed to determine if a single large dose of azithromycin reduced acute morbidity of children hospitalized with bronchiolitis.

**Methods** Double-blind, placebo-controlled randomized trial. Children ≤18 months admitted to 2 Northern Australian hospitals during 2008–2011 were eligible. Children were stratified by site, ethnicity and age, and randomized 1:1 to receive either a single dose (30 mg/kg) of either azithromycin or placebo. Primary outcome was length of stay (LOS). Secondary outcomes were duration of oxygen (O<sub>2</sub>) and respiratory readmissions ≤6 months after discharge.

**Results** 97 children were randomized (median age 5.3 months (IQR 3.0–9.4)). Median LOS was similar in both groups; azithromycin = 54 hours group, placebo = 58 hours group (difference 4 hours 95% CI –8, 13,  $p = 0.6$ ). O<sub>2</sub> was also not significantly different between groups; Azithromycin = 35 hours; placebo = 42 hours (difference 7 hours, 95% CI –9, 13,  $p = 0.7$ ). Readmissions did not differ between group (OR = 0.9, 95% CI 0.3, 2,  $p = 0.83$ ).

**Conclusion** A single large dose of azithromycin did not significantly reduce LOS, duration of O<sub>2</sub> or readmissions in hospitalized children with bronchiolitis. Further research is required to determine whether a longer duration of azithromycin is effective in improving clinical outcomes.

**Supported by** Financial Markets Foundation for Children & Channel 7 Foundation.

**Conflict of Interest** None.

**Nomination** No.

P150

### CLINICAL PROFILE OF CHILDREN WITH NON-CF BRONCHIECTASIS UNDERGOING BRONCHOSCOPY AND HRCT IN THE NORTHERN TERRITORY

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**Introduction** The burden of respiratory disease in the Northern Territory (NT), in particular for Indigenous children is high. Non-CF bronchiectasis is associated with very high rates of childhood pneumonia and other acute respiratory infections (e.g. bronchiolitis). We aim to define the clinical profile of children being investigated for non-CF bronchiectasis.

**Methods** Prospective cohort study of children aged 3 months to 10 years undergoing bronchoscopy and high resolution computed tomography (HRCT) at Royal Darwin Hospital are eligible. Demographic, clinical and medical history were obtained.

**Results** From November 2007 to October 2012, 145 children have been enrolled (median age 28 mths (IQR 20–48)). Indigenous children represent over 90% of the cohort (Table). The proportion of referred children who have bronchiectasis remains very high, ranging from 100% in 2007 to 84% in 2011.

	Indigenous N = 134	Non-indigenous N = 11	Total N = 145
Clinical results			
HRCT confirmed	125 (94%)	6 (55%)	131 (91%)
Suppurative airways	92 (69%)	3 (27%)	95 (66%)
Current wet cough	63 (47%)	2 (18%)	65 (45%)
Respiratory hospitalizations (≥2 in the last 12 months)	41 (31%)	3 (27%)	44 (30%)

**Conclusion** The burden of non-CF bronchiectasis in the NT remains high; in particular for Indigenous children. There is an ongoing need for education so children can be referred earlier for prompt diagnosis and management.

**Supported by** NHMRC project grant 1019834 and NHMRC CRE 1040830.

**Conflict of Interest** None.

**Nomination** No.

P151

## H. INFLUENZAE-SPECIFIC ANTIBODY RESPONSES IN CHILDREN WITH CHRONIC SUPPURATIVE LUNG DISEASE

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**Introduction** *Haemophilus influenzae* (HI) is commonly associated with chronic suppurative lung disease (CSLD) yet limited data exists regarding humoral immunity to this pathogen.

**Aim** To determine if children with CSLD have a suboptimal systemic antibody response to HI compared to healthy controls (HC).

**Method** Plasma IgG<sub>1</sub> and IgG<sub>4</sub> levels to recombinant HI outer membrane proteins, P4 and P6, were measured in children (aged 8–154 months) with CSLD (n = 40; median age 25 months) and healthy children (n = 32; median age 58 months) using Dissociation-Enhanced Lanthanide Fluorescent Immunoassay (DELFLIA®). Arbitrary fluorescence units (afu) between groups were compared.

**Results** Compared to healthy children, children with CSLD had significantly lower IgG<sub>4</sub> titres to P4 and P6. These differences remained when corrected for age. There was no significant difference in IgG<sub>1</sub> levels between the groups.

Median afu <sub>(IQR)</sub>	IgG <sub>1</sub>		IgG <sub>4</sub>	
	P4	P6	P4	P6
CSLD, n = 40	1670 <sub>(800–5010)</sub>	12200 <sub>(3950–29400)</sub>	1080 <sub>(279–2270)</sub>	2580 <sub>(1530–5080)</sub>
HC, n = 32	2850 <sub>(927–7840)</sub>	6860 <sub>(2060–24800)</sub>	2880 <sub>(889–6270)</sub>	8700 <sub>(2190–17000)</sub>
p	0.179	0.274	0.007	0.006

**Conclusion** We found that CSLD was associated with suboptimal levels of HI-specific IgG<sub>4</sub>. Further studies are underway to elucidate the role of humoral immunity in the aetiology of HI infection in children with CSLD.

**Supported by** NHMRC (SP: postgraduate scholarship 1038415; CRE grant 1040830); Financial Markets Foundation for Children.

**Conflict of Interest** No.

P153

## THE HIGH-RISK HOME ENVIRONMENT OF YOUNG CHILDREN ADMITTED TO HOSPITAL WITH SEVERE LRTI

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**Aim** To assess the home environment of young children admitted with a severe lower respiratory tract infection (LRTI) as part of an intervention programme to reduce the risk of ongoing respiratory disease.

**Methods** 400 children < 2 years of age admitted with severe LRTI (pneumonia or bronchiolitis) to KidzFirst Hospital between March 2011 & September 2012 were randomized to an 'intervention' programme (n = 203) which included a housing assessment or 'control' (n = 197) to continue usual care.

**Results** 210 housing assessments have been conducted for 181 families with repeated assessments (27 × 2, 1 × 3) required due to 15.5% moving within 1 year. 25% part/owned their home compared to 66.9% from the national NZ 2006 census. 44% were in private rental, 31% in Housing NZ houses and 7% were in temporary arrangements. 26 households (12.4%) warranted a new referral to either Housing NZ and/or Snug Homes (a regional home insulation initiative) for assistance. In 5% the child slept on a mattress on the floor, 59% in a bed with only 37% in cots (most appropriate for age group) and nil had bassinets. Mould was present in the sleeping room in 15%, and 92% were sharing the sleeping room with parents and/or siblings. In the first follow-up visit, 20% of the children were not up to date with the recommended immunization schedule.

**Conclusions** A poor home environment is likely to be one risk factor for these children who have had at least one hospital admission for a severe LRTI by 2 years of age.

**Supported by** Health Research Council NZ grant 10/510.

**Conflict of Interest** No.

P152

## YOUNG CHILDREN ADMITTED WITH LRTI HAVE ONGOING RESPIRATORY MORBIDITY AND OTHER HEALTH DEFICIENCIES

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**Aim** To trial an intervention programme to reduce the development of chronic respiratory disease in high risk children subsequent to hospital admission for an early, severe lower respiratory tract infection (LRTI).

**Methods** Children < 2 years of age admitted with severe LRTI (pneumonia or bronchiolitis) with no established co-morbidities to KidzFirst Hospital, between March 2011 & September 2012 were randomized to enrol in an 'intervention' programme or 'control' with continued usual care. Based on a cystic fibrosis model, intervention involves regular community clinic reviews to institute good health behaviour, ensure full recovery from the index admission and institute early treatment for deviation from normal health.

**Results** 2146 children < 2 years were admitted with a respiratory illness, 667 met the eligibility criteria and 400 (60%) consented to enrol, mean age 8 months (range 10 days to 2 years). Ethnicities included 55.3% Pacifica, 31.8% Māori, 9.3% European, and 4% 'other'. 228 had pneumonia (mean age 10 months) and 91 had severe bronchiolitis (mean age 4.4 months). There were no differences in age, ethnicity or LRTI diagnosis between the two groups. Regards intervention; 62.6% attended their first follow-up within 45 days, 26.6% greater than 45 days. 20% required immunization catch up, 32% had ongoing respiratory illness, 30% ENT problems and 48% skin infection/eczema, with 28% having >2 areas of concern.

**Conclusions** Successful enrolment into a randomized trial of a model of care in children at high risk of ongoing respiratory illness was achieved with significant health deficiencies needing management in their initial follow-up.

**Supported by** HRC NZ grant 10/510 & Lotteries Grant 230954.

**Conflict of Interest** No.

P154

## CHRONIC COUGH FOLLOWING ACUTE RESPIRATORY ILLNESS IN CHILDREN

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**Introduction** Despite chronic cough being a substantial cause of childhood morbidity and associated costs, data on its prevalence following acute respiratory illness (ARI) in children are scarce.

**Aim** To determine the prevalence of chronic cough (>4 weeks duration) amongst children following presentation to a tertiary paediatric emergency department (ED) with ARI.

**Methods** A cohort study of children aged <15 years attending the Royal Children's Hospital ED, Brisbane with cough as a symptom. Children participate for 28 (± 3) days following enrolment. Demographic, epidemiological, risk factor, microbiological and clinical data are collected at enrolment. Daily diary cards and weekly contacts are used to ascertain cough persistence. Children with persistent cough at day 28 are reviewed by a paediatric respiratory physician.

**Results** We report preliminary data on 248 children (median age 30.3 months, range 1.02 months to 13.9 years, male: 62.1%) enrolled between December 2011 and August 2012, contributing a total of 5663 child-days of follow-up. The prevalence of chronic cough at day 28 was 20% (95% CI 14.8, 24.7); wet cough (37%), dry cough (22%), variable cough (18%), unsure (22%).

**Conclusions** The prevalence of chronic cough in these children following ARI is the highest yet reported. Our ongoing study will comprehensively describe the natural history, aetiology and outcomes of cough during and after ARI.

**Supported by** Queensland Children's Medical Research Institute.

**Conflict of Interest** No.

P155

**PROTRACTED BACTERIAL BRONCHITIS IN CHILDREN: RESULTS OF A LARGE PROSPECTIVE COHORT STUDY**

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**Introduction** Protracted Bacterial Bronchitis (PBB) is a major cause of chronic cough in children. Our previous clinical description of PBB was based on a small cohort of children (n = 45). We aimed to improve understanding of PBB by delineating the clinical and laboratory features in a larger cohort. Our secondary aim was to determine rates of viral detection in children with PBB. **Methods** Children undergoing bronchoscopy were prospectively recruited and PBB determined based on previous criteria. A subset had NPA taken for extended viral studies by PCR. All had monthly follow-up and completed cough diaries during periods of illness. **Results** Amongst 120 children with PBB, 87 (72.5%) were male, median age = 19.5 mo, median cough duration = 26 weeks, household tobacco smoke exposure proportion = 37.5%. At 1-year follow-up, 72 of 82 (87.8%) had recurrent PBB (≥3 episodes/year). Median CD56 & CD16 (Natural Killer) cells were elevated relative to the normal range. Virus/es were detected on NPA in 49 of 62 (79%), with 21 (33.9%) positive for two or more viruses. **Conclusion** PBB was more common in males and those exposed to tobacco smoke. PBB was also associated with high rates of viral co-detection and elevated numbers of NK cells in blood. **Support** Financial Markets Foundation for Children (project), Allen & Hanburys, QCMRI and NHMRC (for DW), NHMRC (for JU and AC). **Conflict of Interest** None.

P157

**DEFINING THE PARENTAL BURDEN OF ACUTE COUGH IN CHILDREN**

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Despite the prevalence of acute cough in children (<2 weeks duration), the burden to parents and families is largely unknown. The objectives of this study were to determine the parental burden of children's acute cough, and to evaluate psychological and other influences on the reported burden of acute cough in children. **Methods** Parents of children with a current acute cough (<2 weeks) at enrolment completed 4 questionnaires (state trait anxiety inventory (STAI); short form health survey (SF-8); depression, anxiety and stress 21-item scale (DASS<sub>21</sub>); and our preliminary 48-item parent acute cough specific quality of life (PAC-QOL<sub>48</sub>) questionnaire). In PAC-QOL<sub>48</sub>, lower scores reflect worse QOL. **Results** Median age of the 104 children enrolled was 2.63 (IQR 1.42, 4.79) years, 54 were boys. Median length of cough at enrolment was 3 (IQR 2, 5) days. Median total PAC-QOL<sub>48</sub> score of parents enrolled at presentation to the emergency department (n = 70) was significantly worse than of parents enrolled through the community (n = 24) (p < 0.01). More than half (n = 55) had sought medical assistance more than once for the current acute coughing illness. PAC-QOL<sub>48</sub> score was significantly negatively correlated to verbal category descriptive and visual analogue scale cough scores (Spearman r = -0.26, p = 0.05 and r = -0.46, p = 0.01 respectively) and DASS<sub>21</sub> total score (r = -0.36, p = 0.01), but not to child's age. **Conclusions** Consistent with data on chronic cough, stress was the predominant factor of parental burden. This study highlights the ongoing need for clinicians to be cognizant of parental worries and concerns when their children are coughing, and for further research into safe and effective therapies for acute cough in children. **Supported by** Queensland Children's Medical Research Institute. **Conflict of Interest** No.

P156

**CLINICAL AND BAL FINDINGS IN 100 CHILDREN WITH CHRONIC WET COUGH UNDERGOING BRONCHOSCOPY IN BRISBANE**

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**Aim** To describe the clinical and BAL findings of 100 children with chronic wet cough who underwent bronchoscopy in Brisbane. **Methods** Children < 18 years referred for bronchoscopy were prospectively recruited. Data collection included demographics, bronchoscopy indication, BAL results and diagnostic results. **Results** Of the 100 children with wet cough, 63% were male. Median age at recruitment was 2.24 years (IQR 1.27, 4.64).

Diagnosis	TCC (IQR)	Neutrophil % (IQR)	Macrophage % (IQR)	Lymphocyte % (IQR)
PBB (65%)	250 (123,475)	32 (15,57)	50 (28,72)	9 (5,13)
CSLD (20%)	280 (162,652)	45 (7,73)	49 (15,80)	5 (2,13)
Other* (15%)	160 (60,340)	6 (4,14)	71 (57,89)	15 (7,23)
P value	0.110	0.001	0.027	0.012

Other diagnoses: Malacia (n = 13), Uncertain Diagnosis (n = 2). Median eosinophil % for each group was 0. **Conclusions** PBB is the most common cause of chronic wet cough in children. However clinicians should be cognizant of other aetiology of wet cough. **Conflict of Interest** No.

P158

**ATMOSPHERIC PRESSURE AND SPONTANEOUS PNEUMOTHORAX IN A PAEDIATRIC COHORT**

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**Aim** To determine whether an association between incidence of Spontaneous Pneumothorax (SP) and atmospheric pressures (Patm) can be found in a paediatric cohort. **Methods** Cases of SP from two tertiary paediatric hospitals (n = 70), collected as part of a larger multicenter retrospective study of paediatric SP management (n = 223, 9 sites, presenting 2003–2010) were included in the analysis. Relationships between SP and meteorological data across the entire study period (Australian Bureau of Meteorology; mean Patm, change in Patm and documented thunderstorms) were investigated. **Results** SP cases included both primary (38/70, 54%) and secondary pneumothorax cases (32/70, 46%). Mean (SD; range) age 13.87 (3.60; 2–17).

Patm on non-SP days	Patm on SP days	Max Δ Patm on non-SP days	Max Δ Patm on SP days	SP occurring on 3 days pre-SP	SP occurring on days of storms
1017 (6.7)	1018 (6)	5.03(2.60)	4.95 (2.56)	7.70 (3.29)	3/70 (4.3%)
	p = 0.36*		p = 0.80*		p = 0.18*

Data presented as mean (SD). \*Vs non-SP days. **Discussion** No significant association was found between SP occurrence and Patm change or thunderstorm occurrence in our paediatric cohort. **Nomination** TSANZ Travel Grant. **Conflict of Interest** No.



P159

### BREASTFEEDING PROTECTS AGAINST CHILDHOOD SNORING

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**Aim** To investigate the association between breastfeeding practices and snoring at age 8.

**Methods** Data were collected from a cohort of children with a family history of asthma who were recruited antenatally, CAPS (Childhood Asthma Prevention Study). Breastfeeding practices of the mothers were prospectively recorded by nurses for 1 year. Snoring status and sleep apnoea were measured at age 8 by parental recall. A directed acyclic graph (DAG) was created including all possible covariates at birth and age 8 to determine the minimal sufficient set of confounders needed to measure the total (traditional confounding) and direct associations.

**Results** 450 (73% of the initial cohort) children were tested at age 8 years. Breastfeeding for longer than one month was associated with a reduced prevalence of habitual snoring at age 8 (adjusted OR 0.48, 95% CI 0.29 to 0.81) and duration of breastfeeding was inversely associated with the prevalence of habitual snoring (adjusted OR 0.79, 95% CI 0.62 to 1.00). Breastfeeding for longer than 1 month was protective for witnessed sleep apnoea (adjusted OR 0.17, 95% CI 0.04 to 0.71). The protective associations were not mediated by BMI, current asthma, atopy or rhinitis at age 8 years.

**Conclusion** Breastfeeding protects against snoring and witnessed sleep apnoea in childhood.

**Supported by** NHMRC.

**Nomination** Ann Woolcock Young Investigator Award, TSANZ Travel Grant.

**Conflict of Interest** No.

P161

### IN PRESCHOOL CHILDREN WITH SEVERE ACUTE WHEEZE, HUMAN RHINOVIRUS GROUP C IS THE MOST COMMON VIRAL INFECTION AND SHOWS A MARKED ASSOCIATION WITH ATOPY

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**Aim** To determine the relationship between HRV-C and other common viruses and atopy in preschool children presenting with acute wheezing.

**Methods** 214 children aged 0–5 years presenting to Emergency with an acute wheezing illness were prospectively recruited. A control group of 75 children were recruited from the community. Skin prick tests (SPT) were performed and nasal aspirates and blood were collected. Viral RNA was extracted, reverse transcribed and tested for all common respiratory viruses. Additionally, a two-step PCR of the HRV 5' NCR was sequenced for typing.

**Results** Of the successfully typed HRV samples, 82/167 (49.1%) cases and 6/72 (8.3%) controls had HRV-C. Among cases, HRV-C was the most common virus and showed a marked and significant association with atopy. This was shown through all measures when HRV-C positive cases were compared to cases without HRV-C (see table below).

	Cases HRV-C +ve	Cases HRV-C -ve	p value
Atopic (>1 SPT +ve)	63.1% (n = 41/65)	38.7% (n = 24/62)	p = 0.006
Mean no. SPT +ve	1.85 (n = 65)	0.81 (n = 62)	p = 0.001
Mean cumulative SPT wheal size (mm)	11.48 (n = 65)	4.98 (n = 62)	p = 0.002
Mean total IgE	207.16 (n = 60)	153.40 (n = 43)	p = 0.011
Mean dust mite IgE	23.05 (n = 60)	15.82 (n = 43)	p = 0.040

**Conclusions** HRV-C was the most common virus causing severe acute wheezing exacerbations in young children and shows a significant relationship with atopy. These findings have strong implications regarding the relationship between atopy and asthma.

**Supported by** NHMRC.

**Conflict of Interest** No.

**Nomination** Nil.

P160

### SURFACE EMG SIGNALS OF THE DIAPHRAGM IS A DIFFERENT MEASURE TO OAH1 IN CHILDREN'S SLEEP STUDY – A PILOT STUDY

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**Aim** To determine if the surface EMG signals from the diaphragm (sEMG<sub>dia</sub>) and hence work of breathing is different between normal snorers, children with increased work of breathing (WOB) and children with obstructive sleep apnoea (OSA).

**Methods** Sleep studies were divided into three groups: 1. 'Normal snorers' who had an obstructive apnoea hypopnoea index (OAH1) < 1/h; 2. 'WOB' group who had OAH1 < 1/h but visually increased WOB; 3. 'OSA' group who had OAH1 > 1/h. In each child, two excerpts consisting of 10 consecutive breaths during each stage of sleep (light sleep, deep sleep, and REM sleep) were exported from the Compumedics Profusion 2 system to the Spike2 data acquisition and analysis system for analysis of sEMG<sub>dia</sub>.

**Results** The two 'Normal snorers' had lower sEMG<sub>dia</sub> of 5.05 uV (median, IQR 4.01–5.32) compared to the two children with OSA (sEMG<sub>dia</sub> 21.85 uV, 13.18–26.85) (P < 0.001). The one child in WOB group had significantly increased respiratory effort compared to normal snorers, with sEMG<sub>dia</sub> 9.80 uV (7.47–12.00) (P = 0.013). The three groups' (normal, WOB, and OSA) sEMG<sub>dia</sub> are statistically different. (P < 0.001) OAH1 did not correlate with sEMG<sub>dia</sub>.

**Conclusions** sEMG<sub>dia</sub> hence work of breathing can be elevated even in children with normal sleep study (OAH1 < 1/h). sEMG<sub>dia</sub> appears to be a different measure to OAH1 in evaluating children for sleep-disordered breathing. Further study is needed.

**Supported by** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

P162

### MARKERS OF PAEDIATRIC ASTHMA AND INFLAMMATORY BOWEL DISEASE IN THE BREATH

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**Background** Exhaled breath condensate (EBC) collection is a simple, non-invasive method for measuring biomarkers in lung diseases such as asthma. Inflammatory bowel disease (IBD) frequently affects the lungs, thus it was hypothesized that IBD disease biomarkers (mucin, trefoil factor 2 (TFF2)) would be found in EBC.

**Aims** To investigate the levels of EBC inflammatory and oxidative stress biomarkers, comparing normal subjects with those with asthma and IBD.

**Methods** In this cross-sectional study, spirometry and FENO were measured as were EBC pH, 8-isoprostane, trefoil factor 2 (TFF2) and mucin levels.

**Results** Subjects included 30 with asthma (A), 30 IBD, 20 controls (C). EBC pH was significantly lower in IBD and asthma (IBD: 6.59 ± 0.18; A: 7.04 ± 0.11; C: 7.5 ± 0.09, p < 0.004). EBC 8-isoprostane (pg/mL) was highest in asthma (A: 16.59 ± 1.47; C: 12.92 ± 1.35; IBD: 10.96 ± 2.11, p = 0.046). TFF2 and mucin were detected in EBC but the levels between the groups were not significantly different.

**Conclusion** Markers of inflammation are detectable in the breath of those with IBD, as well as asthma.

**Conflict of Interest** No.

P163

### ASTHMA MEDICATION EXPERIENCES OF CHILDREN IN AUSTRALIA AND INDIA – A COMPARATIVE QUALITATIVE STUDY

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**Introduction and Aim** This study compared asthma medication experiences of children with asthma and their parents/carers in Australia and India.

**Methods** Semi structured qualitative interviews in a purposive convenience sample of parent/carer – child asthma pairs in Sydney, n = 26 (Australia) and New Delhi, n = 20 (India). Interviews were tape recorded, transcribed verbatim and thematically analyzed.

**Results** Common issues reported in both countries included poor parent/child understanding of medications, fears about long term medication use, inadequate inhaler technique, non adherence and issues with cost of medication. Child self image, resistance to medication use, lack of responsibility in medication taking and the child's non inclusiveness in the consult were common themes that emerged from child interviews. Some unique issues emerged from the Indian interviews such as fatalistic attitudes, lack of expressed desire for self autonomy and stigma particularly in the case of female children.

**Discussion** This is one of the first research studies exploring the cross cultural viewpoint of children with asthma and their parent/carers about their medications. It is possible that simple models of culturally relevant patient/carer education, empowerment and child inclusion in medical consultations could be designed to enhance the quality use of asthma medications in children.

**Conflict of Interest** None.

P164

### THE RELATIONSHIP BETWEEN EARLY-LIFE FACTORS AND ADULT BRONCHIAL HYPER-RESPONSIVENESS DEPENDS ON CHILDHOOD ASTHMA STATUS

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**Aim** To examine the relationship between childhood exposures and BHR in middle-age.

**Methods** 778 middle-age participants from the 2005 follow-up survey of the Tasmanian Longitudinal Health Study underwent BHR testing to methacholine.

**Results** BHR prevalence was 11.5% (95% CI 7.3–17.6), higher in females (16.1%) than males (6.4%, p = 0.01). Childhood asthma was strongly associated with BHR (OR 3.9; 2.0–7.5). Females without childhood asthma had greater odds of BHR (5.6; 1.9–16.4) than females with childhood asthma (1.4; 0.74–2.8, p<sub>interaction</sub> 0.031). Childhood hay fever was positively associated with BHR in those with childhood asthma (2.5; 1.5–5.2) but negatively associated in those without childhood asthma (0.15; 0.03–0.64, p<sub>interaction</sub> 0.001). Childhood hay fever was also positively associated with the log-dose response slope in those with childhood asthma ( $\beta = 0.505$ , p = 0.05) but not associated in those without childhood asthma ( $\beta = -0.320$ , p = 0.16, p<sub>interaction</sub> 0.019). Exclusive breast feeding was negatively but weakly associated with BHR in those without childhood asthma (0.37; 0.13–1.06) but not associated in those with childhood asthma (1.7; 0.9–3.3, p<sub>interaction</sub> 0.013).

**Conclusions** The relationship between childhood hay fever, sex, exclusive breast feeding and middle-age BHR was modified by childhood asthma status.

**Support** NHMRC.

**Conflict of Interest** No.

### PULMONARY PHYSIOLOGY & SLEEP SIG: POSTER SESSION

P165

#### THE DANGERS OF OXYGEN THERAPY IN THOSE WITH REDUCED VENTILATORY DRIVE

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**Introduction** The dangers of the use of high-flow oxygen in those with reduced ventilatory drive is well-recognized in hospital practice. We present a patient with Ondine's curse (central alveolar hypoventilation syndrome), who developed problems associated with high-flow oxygen administration.

**Case Presentation** A 78-year-old male developed Ondine's curse from a brainstem stroke. He subsequently required nocturnal assisted ventilation via bilevel positive airway pressure during the night due to hypoventilation and insensitivity to hypercapnia. On four occasions his mask became dislodged at night, he was found apnoeic and was transferred to hospital on high-flow oxygen. On presentation, the PaCO<sub>2</sub> levels were 92.7, 96.1, 97.0 and 124.0 mm Hg, and corresponding PaO<sub>2</sub> values were 154.0, 77.6, 34.5 and 27.8 mm Hg, respectively. A Medic-Alert bracelet worn after the first episode, indicating 'CO<sub>2</sub> retainer- give only 24% O<sub>2</sub>', did not appear to alter the FiO<sub>2</sub> delivered consistently. On his last presentation, pre-hospital oxygen was delivered at a FiO<sub>2</sub> of 100% giving an arterial pH of 7.066, PaCO<sub>2</sub> 66.9 mm Hg and PaO<sub>2</sub> 99.2 mm Hg. He was in complete apnoea on arrival and unfortunately died despite resuscitative efforts.

**Discussion** Ondine's curse is a rare form of central ventilatory dysfunction, but this is also seen in others with CO<sub>2</sub> retention, who will hypoventilate if their hypoxia is over-corrected. Patients should only be given supplemental oxygen to maintain a low-normal SpO<sub>2</sub> and to titrate the FiO<sub>2</sub> down once SpO<sub>2</sub> is in the normal range, particularly in pre-hospital medicine where PaCO<sub>2</sub> cannot be measured.

**Conflict of Interest** None.

P166

#### CHANGES IN AIRWAY BLOOD FLOW ARE RELATED TO CHANGES IN VENTILATION DURING EXERCISE IN HEART FAILURE

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**Introduction** We have previously demonstrated that in heart failure (HF), airway blood flow (Q<sub>aw</sub>) is related to increased airway obstruction. In healthy subjects, Q<sub>aw</sub> increases during exercise, however to date there has been no examination of changes in Q<sub>aw</sub> during exercise for HF. The purpose of the current study was to report the changes in Q<sub>aw</sub> during exercise in a group of HF patients.

**Method** Eleven New York Heart Association (NYHA) Class II-III (60 ± 9 year, 10 male) subjects completed Q<sub>aw</sub> measurements at rest, during 10 min of exercise at 35W and in recovery. Q<sub>aw</sub> was estimated from the uptake of the soluble gas dimethyl ether. During rest, exercise and recovery, measurements of cardiac output (Q), VO<sub>2</sub> and V<sub>E</sub> were made using open circuit spirometry. All data are presented as mean ± SD.

**Results** Changes in Q<sub>aw</sub>, Q, VO<sub>2</sub> and V<sub>E</sub> are reported in Table 1. For each measure, there was a significant increase (P < 0.01) during exercise.

**Table 1** Responses at rest, exercise and during recovery

	Rest	Exercise	Recovery
Q <sub>aw</sub> (μL/mL/min)	49.9 ± 15.8	80.1 ± 28.0*	48.5 ± 21.6
Q (L/min)	5.4 ± 0.5	7.3 ± 1.1*	5.4 ± 1.0
VO <sub>2</sub> (L/min)	0.38 ± 0.10	0.94 ± 0.11*	0.36 ± 0.08
V <sub>E</sub> (L/min)	14.6 ± 2.5	27.4 ± 5.1*	13.8 ± 2.6

Changes in Q<sub>aw</sub> were significantly related to changes in VE (r = -0.71, p < 0.02).

**Discussion** Similar to what we have previously seen in healthy subjects, Q<sub>aw</sub> increased significantly during exercise in HF. This increase appears to be inversely related to changes in ventilation, with a greater rise in Q<sub>aw</sub> being associated with lower increases in ventilation.

**Support** NIH HL71478 and Griffith University.

**Conflict of Interest** Nil.

P167

P169

WITHDRAWN

**DYSFUNCTIONAL BREATHING IS COMMON IN PATIENTS BEING INVESTIGATED FOR SLEEP APNOEA**

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**Aim** Dyspnoea is a common complaint in patients with suspected obstructive sleep apnoea (OSA). This study was to test for an association between OSA and dysfunctional breathing.

**Methods** Patients attending for sleep studies completed a Nijmegen Questionnaire, a validated tool for dysfunctional breathing. These data were then correlated with the Apnoea-Hypopnoea Index (AHI), sex, body mass index (BMI) and Epworth Sleepiness Score (ESS).

**Results** Of 136 participants, (median age 58, 68.4% male), 30 (22%) had Nijmegen scores of 23 or more, indicating a positive result. There were no statistically significant differences between groups of patients at any threshold of AHI, and Pearson's correlation coefficient was -1.04%. However, dysfunctional breathing was significantly more common in females than males (40% vs 13%,  $p = 0.0016$ ), with an odds ratio of 4.024 (95%CI 1.595–10.251). Patients with an ESS  $\geq 16$  were significantly more likely to have dysfunctional breathing than those who scored  $<16$  (55 vs 24%,  $p = 0.0181$ ), with an odds ratio of 4.933 (95%CI 1.157–21.567). Pearson's correlation coefficient was 28.14%.

**Conclusions** Dysfunctional breathing is common in patients being investigated for OSA, but was not predicted by the severity of OSA. Dysfunctional breathing was significantly associated with female sex and high Epworth Sleepiness Score. The mechanism underlying these observations is unclear and warrants further study.

**Funding** None.

**Nomination** None.

**Conflict of Interest** No.

P168

WITHDRAWN

P170

**CLINICAL AUDIT: OBSTRUCTIVE SLEEP APNOEA, CPAP COMPLIANCE AND OUTCOMES**F AMEER<sup>1,2</sup>, D MARANTOS<sup>1</sup>

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**Aim** To evaluate the CPAP adherence and its impact on symptom control. Secondary outcomes were Hypertension/ Diabetic control in patients with Obstructive Sleep Apnoea.

**Methods** Retrospective review of patients case notes and CPAP compliance data, with diagnosis of OSA who were followed up in the last 2 years in the respiratory and sleep out patient. Data were collected using a questionnaire for patients' demographics, co-morbidities and their CPAP compliance and effectiveness. Compliance data were presented as mean values.

**Results** 46 patients were included, of which 60 % ( $n = 28$ ) had good compliance ( $>4$  h/night – for 80% of the nights). Compliant group had good symptoms control, however, of these, less than 50% of patients achieved good blood pressure and glycaemic control ( $n = 13$ ). Compliant population had more medical comorbidities as compared with the poor compliance group ( $n = 8$ ) who largely suffered with psychiatric illness. Poor compliance population were younger (mean age 49 years) than the compliant group (mean age 65 years).

**Conclusions** It is important to improve long term compliance amongst all patients. Psychological co morbidities should be addressed and treated concomitantly. The younger population is more vulnerable and need close monitoring of their compliance. Education, help with improved mask interface and family support are vital for a better compliance.

**Grant Support** None

**Conflict of Interest** No.

P171

**OVERLAP SYNDROME—PREVALENCE, CHARACTERISTICS AND PREDICTORS**A THASNEEM<sup>1</sup>, JL SIMPSON<sup>2</sup>, S PRADEEPAN<sup>1</sup><sup>1</sup>Respiratory and Sleep Medicine, John Hunter Hospital, NSW 2305, and<sup>2</sup>Hunter Medical Research Institute, NSW 2305

Overlap syndrome (OS) is defined as the co-existence of Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnoea (OSA) in the same patient. OS patients are at a higher risk of nocturnal hypoxemia and are likely to suffer increased morbidity and mortality.

**Aim** To identify the prevalence of OS, characteristics and predictors of OSA in COPD patients referred for sleep study at John Hunter Hospital.

**Methods** Retrospective audit of COPD patients referred to our centre for sleep study over the last 3 years. Physical characteristics, smoking history, reasons for referral, pulmonary function tests and sleep studies were analyzed.

**Results** Of the 76 patients with COPD (FEV<sub>1</sub>/FVC < 70%) who underwent diagnostic Polysomnography, 54 patients had sleep apnoea (Apnoea Hypopnoea Index; AHI > 5). No significant difference was observed in age and sex between the groups. Body Mass Index (36 v 31, P = 0.048), FEV<sub>1</sub>% predicted (54% v 43%, P = 0.030) and FEV<sub>1</sub>/FVC (54% v 46%, P = 0.007) were significantly higher in patients with OS compared to patients with COPD alone. OS patients had significantly lower nocturnal nadir oxygen saturation (67.4%) when compared to patients with COPD (82%, P = 0.021). FEV<sub>1</sub>/FVC was an independent predictor of AHI using multiple linear regression.

**Conclusion** High prevalence (71%) of OSA was observed in patients with COPD referred to our centre for sleep study. Patients with less severe airflow obstruction have higher AHI and more severe OSA. OS was associated with significant nocturnal hypoxemia.

**Conflict of Interest** Nil.

P173

**UTILITY OF PUBLICLY FUNDED INVESTIGATION SERVICES FOR OBSTRUCTIVE SLEEP APNOEA**

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**Introduction** In designing health care services, it is logical to match funding for diagnostic services with that for later treatment. In NSW, there is a wait-time but no cost barrier to access publicly funded polysomnography (PSG) for Obstructive Sleep Apnoea (OSA). In contrast, for confirmed OSA, many patients have no access to public funding for treatment or must self-fund initial treatment to prove adherence. The end result can be confirmed disease leading to no intervention and a longer waiting list for first studies.

**Aim** To evaluate the efficiency of our Sleep Medicine diagnostic service in selecting patients for PSG and the frequency with which patients with OSA were established on and maintained CPAP treatment.

**Methods** We audited 432 patients who had an initial PSG in 2008. We determined the number who were diagnosed with OSA and proceeded to a CPAP titration study. From this subset, we established how many were started on CPAP and maintained treatment at 1 year. For this purpose, patients were severity-stratified on RDI alone.

**Results** 33% of patients had a normal study (RDI < 5), 22% of PSG confirmed mild (RDI 5–15), 21% moderate (RDI 15–30), 12% severe (RDI 30–60) and 12% very severe (RDI > 60) OSA. The rate of subsequent CPAP titration studies were 38% for mild, 51% for moderate, and 74%/88% for severe/very severe respectively. For patients accessible to follow-up, rates of CPAP use at 1 year were 25% in mild and 77% in moderate. Rates were higher in more severe OSA but follow-up is incomplete to this point. Cost was the most commonly quoted reason for not commencing treatment.

**Conclusions** There is a case for focussing this publicly funded service on patients more likely to have severe OSA and for public expenditure now allocated to diagnostic services to be put toward treatment implementation.

**Conflict of Interest** No.

P172

**MANDATORY REPORTING HARMS PUBLIC ROAD SAFETY**

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**Aim** To determine whether public road safety is harmed by current mandatory reporting laws in South Australia (doctors are required to report to Transport SA (TSA) any patient whom they believed 'would be likely to endanger the public' should they drive a motor vehicle).

**Methods** Paper based surveys were given to 150 consecutive English speaking patients at each of 3 public hospital clinical sleep laboratories in South Australia (n = 379; response rate 84.2%; age 20–86).

**Results** While 54.4% of responders were in favour of the mandatory reporting law, only 56.9% were aware of the law. 8.2% indicated that as a consequence of the law they would behave inappropriately towards their doctor by: avoiding going altogether (3.1%); doctor shopping (1.0%); or lying to their doctor (4.1%). 5 patients indicated that had they known about the law they would probably not have had a sleep study and a further 12 indicated that they would lie or doctor shop as a consequence of finding out about the law. 10 patients also knew of 1 or more family or friends who were avoiding having a sleep study as a consequence of the law. 26.2% were not aware of their own legal requirement to report themselves to TSA if they had a medical condition that would affect their ability to drive safely. However 93.9% would report themselves to TSA if encouraged to do so by their doctor (either directly 21.3% or indirectly 72.6%), 0.9% if encouraged solely by their families, and only 5.2% indicating that they would not report themselves to TSA under any circumstances.

**Conclusions** Given that TSA is as or more likely to be made aware of unsafe drivers by the drivers themselves than by their doctors (93.9% vs 91.8%), and that the mandatory reporting law is directly responsible for some patients avoiding diagnosis altogether it is likely that public safety would be improved if the mandatory legislation was removed and more effort put into educating drivers about their own responsibilities.

**Conflict of Interest** No.

P174

**RESPIRATORY INFECTIOUS DISEASES SIG: POSTER SESSION****EXACERBATION OF CHRONIC CIGARETTE SMOKE INDUCED LUNG DISEASE BY RHINOVIRUS**AN LARCOMBE<sup>1</sup>, R WONG<sup>1</sup>, T IOSIFIDIS<sup>1</sup>, RE FOONG<sup>1</sup>, LJ BERRY<sup>1</sup>, PD SLY<sup>2</sup><sup>1</sup>Division of Clinical Sciences, Telethon Institute for Child Health Research & Centre for Child Health Research, University of Western Australia, WA 6008, and <sup>2</sup>Queensland Children's Medical Research Institute, University of Queensland, Qld. 4072

**Aim** Symptoms of the common cold precede many chronic obstructive pulmonary disease (COPD) exacerbations. Respiratory viruses are detected in up to 60% of COPD exacerbations, and rhinoviruses account for approximately half of these. This study aimed to assess the effects of rhinovirus infection on exacerbation of chronic cigarette smoke induced lung disease with an emphasis on comparing male and female mice.

**Methods** Adult male and female BALB/c mice were exposed to 6 cigarettes/day, 5 days/week for 12 weeks. After the final exposure, mice were infected with  $5 \times 10^6$  TCID<sub>50</sub> of purified rhinovirus (HRV1A). Appropriate controls were used throughout. 72 h after infection we assessed lung viral titre, pulmonary inflammation, lung mechanics and lung structure.

**Results** Cigarette smoke (CS) exposure did not significantly alter viral load in either sex (p > 0.308 in both cases), but it did increase total pulmonary inflammation in both sexes (p < 0.045 in both cases). HRV1A infection increased neutrophilia in both sexes. In male mice, the combination of both insults exacerbated neutrophilia (p < 0.001). CS exposure and HRV1A infection significantly altered lung volume and baseline lung mechanics in male mice, but there were limited effects of either exposure in female mice.

**Conclusions** Exacerbation of chronic CS induced lung disease by rhinovirus infection was significantly different between male and female mice. This has important implications for the extrapolation of data from mouse models of chronic CS exposure and rhinovirus infection to humans.

**Supported by** University of Western Australia Research Development Award, Australian Research Council Discovery Project.

**Conflict of Interest** No.

P175

### GRANULOMAS, CANCER AND PULMONARY EMBOLISM: THE MANY GUISES OF DISSEMINATED PULMONARY NOCARDIOSIS. A CASE SERIES

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Pulmonary nocardiosis is an uncommon respiratory tract infection caused by the actinomycete, *Nocardia*, often affecting patients with impaired cell mediated immunity. The diagnosis is challenging and effective treatment is frequently delayed because the organism is difficult to culture. Pulmonary manifestations include nodules, consolidation and pleural effusions and disseminated nocardiosis has a high mortality rate. We present two cases of disseminated pulmonary nocardiosis that mimicked more common respiratory conditions. The first case presented with hilar lymphadenopathy, an endobronchial lesion and granulomatous inflammation on biopsy thought to be sarcoidosis, he was commenced on high dose corticosteroid. The diagnosis was eventually made following a stormy course with left main bronchus obstruction and intracranial disease. The patient recovered with trimethoprim-sulfamethoxazole-based treatment. The second case presented with severe pleuritic chest pain whilst on high dose corticosteroid and was found to have pulmonary emboli and an associated pleural effusion but symptoms failed to improve with anticoagulation. Pleural plaques, mediastinal lymphadenopathy and a superior vena cava syndrome rose the possibility of malignancy however subsequent thoracocentesis and bronchial lavage grew *Nocardia*. Pulmonary nocardiosis can present like more common respiratory disorders and should be considered in those patients that fail to improve, especially in the context of corticosteroid use.

**Grant Support** No.**Conflict of Interest** No.

P177

### RESPIRATORY PRESENTATIONS OF STRONGYLOIDIASIS IN A LOW PREVALENCE SETTING

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**Introduction** Strongyloidiasis, caused by infection with *Strongyloides stercoralis*, affects millions worldwide with highest endemicity in tropical and subtropical regions. Although strongyloidiasis has a good prognosis when treated promptly, it can be fatal in cases of concomitant immunosuppression, delayed diagnosis, and dissemination. This case series highlights the varied modes of disease manifestation in a low prevalence setting.

**Case Series** Four patients were treated for strongyloidiasis after peripheral blood eosinophilia was noted and who subsequently tested positive for strongyloides serology but had a negative stool culture for ova, cysts, and parasites. Each patient presented with a different respiratory manifestation (pneumothorax, pleural effusion, chest infection, asthma-like symptoms). In addition, all four patients had either skin lesions and/or abdominal symptoms. Contrary to the epidemiological data, three out of the four patients were from a low prevalence background (born and living in countries with low endemicity for strongyloidiasis). Their past travel history to Southeast Asia and Papua New Guinea suggests a disease association with tropical zones. All patients were treated with ivermectin and their signs and symptoms gradually resolved.

**Conclusion** Although strongyloidiasis has a good prognosis when treated promptly, its disseminated form has a high mortality rate. It is important for clinicians to recognize the varied manifestations of this disease in order to make correct diagnosis and provide timely treatment.

**Conflict of Interest** No.

P176

### WHEEZING CHILDREN WITH HUMAN RHINOVIRUS SPECIES C HAVE A HISTORY OF RESPIRATORY VIRAL INFECTIONS

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**Rationale** Human rhinovirus species C (HRV-C) is associated with the majority of hospital admissions for acute wheezing illnesses in children and more severe exacerbations than other respiratory viruses and HRV species.

**Aim** To determine whether children wheezing with HRV-C are more susceptible to common respiratory viruses prior to and/or after an acute episode.

**Methods** Children (n = 231) were recruited on presentation to hospital with an acute wheezing exacerbation and their respiratory infection was ascertained from respiratory samples. Clinical data on infections (respiratory syncytial virus, adenovirus, influenza virus or parainfluenza virus) were collected retrospectively for other respiratory presentations to hospital prior to and after recruitment. Nonparametric tests were used to compare children that had an HRV-C with other viruses detected at recruitment.

**Results** Children were predominantly male (60.17%) with a mean age of 3.7 years (range 0.09–14.98 years). Of the children who presented to hospital more than once, those with HRV-C detected at recruitment had more respiratory infections prior to this wheezing episode (mean 0.43, SD 0.59) than children with other viruses at recruitment (mean 0.0, SD 0.0, n = 33, p = 0.023). Children with HRV-C detected at recruitment had similar numbers of infections after the exacerbation (mean 0.33, SD 0.62) as children infected with other viruses at recruitment (mean 0.25, SD 0.45, n = 27, p > 0.05). Age had no significant bearing on infections prior to or after recruitment.

**Conclusion** Children with HRV-C detected during an acute wheezing episode have a significant history of common respiratory viral infections.

**Supported by** NHMRC.**Nomination** Nil.**Conflict of Interest** No.

P178

### A CASE OF IDIOPATHIC EOSINOPHILIC PLEURITIS

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We present an unusual case of recurrent idiopathic eosinophilic pleural effusion. A 56-year-old woman presented with a three-week history of dyspnoea on exertion and left-sided pleuritic chest pain. She had suffered from a dry cough for over a year, headaches, and intermittent diarrhoea. She had a background of mild asthma and a long history of recurrent sinusitis. Inhaled budesonide was her only regular medication. She was found to have an eosinophilic, exudative left pleural effusion, peripheral eosinophilia, and an elevated serum immunoglobulin E level. There had been no recent overseas travel. Clinical and microbiological evidence of infection was lacking. Pleural fluid cytology was negative for malignant cells. Aside from the pleural effusion and a small pericardial effusion, imaging of the chest, abdomen, pelvis, and brain were normal. Pulmonary emboli were excluded by CT pulmonary angiogram. Cardiac function was normal on echocardiography. Screening for auto-antibodies associated with vasculitic disorders was unremarkable. The left effusion recurred after drainage. Thoracoscopic pleural and lung biopsies demonstrated florid eosinophilic pleuritis with normal lung parenchyma. Pleurodesis was performed. A right pleural effusion subsequently developed. On starting steroid therapy, symptoms and the right pleural effusion resolved. The pathological process causing this constellation of features is unclear. The combination of steroid-responsive eosinophilic pleuritis and peripheral eosinophilia without parenchymal lung disease is unusual.

**Conflicts of Interest** None.

P179

### STREPTOCOCCUS PNEUMONIAE, BUT NOT OTHER BACTERIAL EMPYEMA PATHOGENS, INDUCES MESOTHELIAL CELL DEATH

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Empyema is a common disease. The effects of empyema pathogens on the predominant (mesothelial) cells in the pleural cavity are unknown.

**Aim** To study the effects of common bacterial empyema pathogens on mesothelial cell viability.

**Methods** Benign mesothelial cells (MeT-5A) were treated with live or heat-killed *Streptococcus* species or *Staphylococcus aureus* for up to 24 hr and viability determined by LIVE/DEAD fixable stain.

**Results** All live *S. pneumoniae* reference strains (ATCC) tested caused near complete mesothelial cell death ( $p < 0.01$ ) in a time- and dose-dependent fashion. The results were reproducible in 23 of 25 *S. pneumoniae* isolates cultured from pleural fluid and/or blood of patients with pneumococcal disease. In contrast, *S. milleri* group species and *S. aureus* induced negligible killing of mesothelial cells. *S. pneumoniae*-induced cell death was mediated by secreted bacterial products as filtered conditioned media reproduced the lethal effects on mesothelial cells. Conversely, heat-killed *S. pneumoniae* did not induce cell death. The lethal effects on mesothelial cells could also be reproduced using recombinant pneumolysin, a pneumococcal cytolytic toxin.

**Conclusion** Of the most common bacterial empyema pathogens, only *S. pneumoniae* caused pleural mesothelial cell death *in vitro* via secreted products. The role of pneumolysin warrants investigation.

**Supported by** Cultural Affairs and Missions Sector, Egyptian government; Lung Institute of Western Australia; Westcare (Western Australia).

**Nomination** Nil.

**Conflict of Interest** No.

P181

### VACCINE IMPACT ON CARRIAGE AND LOWER AIRWAY INFECTION IN AUSTRALIAN INDIGENOUS CHILDREN WITH BRONCHIECTASIS

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**Background** 7-valent pneumococcal conjugate vaccine (PCV7) was introduced for Northern Territory Indigenous children in 2001 and replaced by 10-valent pneumococcal *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV10) in 2009 and PCV13 in 2011.

**Aim** To determine whether vaccine type influenced nasopharyngeal (NP) carriage and lower airway infection (LAI) in Indigenous children with bronchiectasis.

**Methods** Children presenting for high-resolution computed tomography (HRCT) and bronchoscopy were eligible for enrolment. NP swabs and bronchoalveolar lavage (BAL) fluid were collected under anaesthetic, stored at  $-80^{\circ}\text{C}$  and processed as previously described. LAI was defined as  $>10^4$  cfu/mL BAL fluid. Data were recorded on vaccines administered since birth. Proportions were compared using the two-sample proportion calculator in Stata 12.1.

**Results** From July 2007 to July 2012, 123 Indigenous children aged 5.2 to 154.6 (median 27.6) months with HRCT-confirmed bronchiectasis were enrolled; 75 (61%) were male. While 92 children had received  $\geq 2$  doses of PCV7 (86 had  $\geq 3$  doses), only 28 had  $\geq 2$  doses of PHiD-CV10 (22 had  $\geq 3$  doses). *Streptococcus pneumoniae* NP carriage in PCV7 children was 41% and in PHiD-CV10 children 32%; nontypeable *H. influenzae* (NTHi) carriage was 52% and 43% respectively. *S. pneumoniae* LAI in PCV7 children was 17% and in PHiD-CV10 children 25%; NTHi LAI was 33% and 25% respectively. Low numbers precluded any significance.

**Conclusions** There are currently insufficient data to draw conclusions regarding vaccine impact. Studies are ongoing to assess the impact of PCVs on respiratory microbiology and clinical outcomes in this population.

**Supported by** NHMRC Project Grant 545223.

**Conflict of Interest** Study partially supported by GlaxoSmithKline.

P180

### OPTIMAL UTILITY OF BAL FLUID GALACTOMANNAN IN DIAGNOSING INVASIVE PULMONARY ASPERGILLOSIS IN IMMUNOCOMPROMISED PATIENTS

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**Introduction** Invasive pulmonary aspergillosis (IPA) is a significant cause of morbidity and mortality in immunocompromised (IC) patients. Correct diagnosis is important, but can be delayed or difficult, and differentiating between colonization and invasive disease complex. Galactomannan (GM) is a major constituent of *Aspergillus* cell walls released during hyphal growth, indicating active replication. BAL GM has been shown to be a useful additional diagnostic tool for IPA. However, sensitivity and specificity using different Optical Density (OD) cut off points vary across different IC populations.

**Aim** To evaluate the ideal OD cut off of BAL GM in diagnosis of IPA in IC patients.

**Methods** IC patients who underwent bronchoscopy between October 2010 and 2012 were recruited. BAL GM was analyzed using ELISA. Results obtained using OD  $\geq 1.5$  and 0.5 were compared, using direct microscopy and positive cultures for *Aspergillus* as the gold standard.

**Results** 157 bronchoscopies performed. 79 solid-organ transplant recipients, 57 haematological malignancies, 9 HIV, 12 others. At OD  $\geq 1.5$ , GM/FC+ = 11/18. Sensitivity 50%, specificity 92%, PPV 61%. NPV 94%. At OD  $\geq 0.5$  GM/FC+ = 11/78. Sensitivity remained 50% but specificity reduced to 48%, PPV 14%, NPV 50%.

**Conclusions** Using BAL GM cut-off OD  $\geq 1.5$  provides optimal specificity without reduction in sensitivity in IC patients.

**Conflict of Interest** No.

P182

### COMMUNITY-ACQUIRED PNEUMONIA, CHANGES IN FUNCTIONAL ABILITY OVER TIME

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**Aim** To determine the functional ability of older adults admitted to hospital with community acquired pneumonia and to investigate changes during and at 3-month post hospital admission.

**Methods** A prospective longitudinal observational study was undertaken with patients admitted to The Prince Charles Hospital with community acquired pneumonia. Participants underwent comprehensive multidisciplinary geriatric assessments during inpatient stay, and at 3 months following discharge from hospital. Measures included the Modified Barthel Index (MBI), Frenchay Activities Index, the short portable MSQ and RUDAS.

**Results** Fifty-four people with pneumonia have been recruited to date; 61% male ( $n = 33$ ), age 79 (SD 7) years, with an average length of stay 6.4 days (SD 4). On admission, average (SD) MBI was 95 (7) and Frenchay was 23 (10). By discharge, MBI had decreased to 93 (12). At 3 months MBI was 91 (14) and Frenchay 22 (12). Cognitive ability, tracked over time, remained relatively unchanged.

**Conclusions** It appears that by discharge participants experienced reduced functional ability with further reductions evident by 3 month follow-up, although preliminary analysis only has been undertaken. The project is ongoing and additional information will be presented.

**Supported by** The Prince Charles Hospital Foundation.

**Conflict of Interest** No.

P183

### DOES THE INTERFERON GAMMA BECOME NEGATIVE AFTER TREATMENT FOR LATENT TB INFECTION (LTBI)? DO WE NEED TO RETEST IT POST-TREATMENT?

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**Introduction** Interferon Gamma release assays (IGRA) are approved as diagnostics for Mycobacterium Tuberculosis (MTB) infection. It's been reported that these assays have usefulness in monitoring disease activity post infection in patients with either Latent TB infection (LTBI) or active Tuberculosis.

**Study Objectives** To answer the question 'Does IGRA become negative after treatment for LTBI. Does it therefore need to be retested routinely after treatment for LTBI.'

**Methods** This is a retrospective study that looked at 84 patients referred to the TB clinic at the Canberra Hospital Respiratory department for medical evaluation for LTBI based on suspected exposure to TB index case and/or positive tuberculin skin test (TST) from June 2005 to May 2012. Inclusion criteria – adults with a positive IGRA and clear Chest X-ray prior to starting treatment for LTBI. Patients were treated with Isoniazid and pyridoxine using modified direct observation therapy. IGRA was then retested after treatment.

**Results** 24 patients were included in the study. 45.8% (11/24) patients were from Australia and New Zealand and 54.2% (13/24) were from other countries. 54.2% (13/24) were male and 45.8% (11/24) were female. The median age for this cohort of patients was 34.5 years. 70.8% (17/24) patients had a post-treatment IGRA test while 29.2% (7/24) did not. Of those who had a post treatment IGRA test, 70.6% (12/17) remained positive and 29.4% (5/17) returned a negative result.

**Conclusion** There is no benefit of routinely retesting the IGRA after treatment for LTBI. There is need for a better test to monitor the response to prophylactic treatment for LTBI.

**Support** None.

**Conflict of Interest** None.

P185

### DEVELOPMENT OF AN INTEGRATED MODEL OF CARE TO FACILITATE EARLY DISCHARGE FROM ACUTE CARE FOR PNEUMONIA PATIENTS AT NORTHERN HEALTH

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**Introduction** In 2009–10 NH implemented a number of quality improvement interventions to decrease length of stay (LOS) for patients admitted to acute care with moderate to severe pneumonia, these included: (1) Active monitoring and feedback to clinicians of adherence to best practice guidelines for medical management and (2) Commencement of a multidisciplinary (nursing & physiotherapy) early supported discharge service (aim acute care LOS 4 days).

**Aim** To evaluate whether the combination of medical and multidisciplinary interventions would improve guideline adherence and decrease LOS.

**Methods** Data were collected prospectively from 2009–2012 on guideline adherence and multidisciplinary management of pneumonia. Key indicators were: time to commencing antibiotics, duration of IV antibiotics (aim 3 days), coverage for atypical organisms, proportion enrolled in the supported discharge intervention and LOS.

**Results** Audit and feedback to the medical units concerning adherence to guidelines for pneumonia management improved appropriate antibiotic prescribing. Despite this, a substantial proportion remained on intravenous treatment for greater than 3 days and this proved to be a barrier to the successful implementation of the early supported discharge intervention. The greatest improvement in LOS was seen in those with (DRG E62B) moderate to severe pneumonia without complications (mean LOS usual care 5.1 (SD 2.6) days and supported discharge 3.3 (SD 1.9), (p = 0.009).

**Conclusion** Quality improvement activities that involve active feedback to clinicians improved adherence to guidelines for antibiotic prescribing, however barriers remained in decreasing the duration of intravenous treatment and patients being referred for supported early discharge and home-based follow-up.

**Support** Funded by Northern Health.

**Conflict of Interest** Nil.

## RESPIRATORY NURSES SIG: POSTER SESSION

P184

### WEBEX PROVES A WINNER FOR NSW PULMONARY REHABILITATION EDUCATION

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**Background** A NSW Pulmonary Rehabilitation (PR) Survey identified a significant proportion of multidisciplinary clinicians engaged in provision of PR services had limited experience and had not participated in PR specific education and training. Access to PR education and training was identified as a priority workforce need for rural and remote clinicians.

**Method** A free webex based PR Education Series was developed by the Agency for Clinical Innovation and trialled in NSW. An online survey was conducted following each session (n = 6) and the perceived impacts of the overall webex series on local clinical teams was assessed following the third and sixth sessions.

**Results** A total of 208 clinicians accessed one or more sessions with 2/3 employed in regional and rural NSW. Access to webex for all sessions was rated easy (>80%) and information was rated as valuable (>94%). Participants perceived that the webex series had a positive impact locally on clinical skills (74%), clinical practice (59%), interest in respiratory care (68%), multidisciplinary approach to care (57%) and referrals to pulmonary rehabilitation (14%). The cost per 1-h session per clinician was \$3.

**Conclusion** We have demonstrated that webex based education is an effective and efficient format for providing PR education and has positive impacts for local clinical teams in NSW.

**Support** Nil.

**Conflict of Interest** Nil.

P186

### A RANDOMIZED TRIAL OF SUBCUTANEOUS VS INTRADERMAL LIGNOCAINE ON PATIENT SCORES DURING ABG

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**Aim** To determine whether the administration of local anaesthetic via an intradermal route is more effective than a subcutaneous route or standard practice (no local anaesthetic) in reducing pain experienced by patients having arterial blood gas puncture in a nurse-led oxygen clinic.

**Methods** 135 patients underwent randomization to receive 1% (0.25 mL) intradermal lignocaine (54 patients), subcutaneous lignocaine (1% 0.25 mL) (54 patients) or no lignocaine (27 patients) prior to ABG punctures. Patients were masked to intradermal or subcutaneous administration. We used the graphic rating interval scale of zero (no pain) to 10 (worst pain ever) to measure patient assessed pain scores, nurse assessed patient pain score and the level of difficulty experienced for a successful arterial blood gas puncture.

**Results** Patients rated intradermal local anaesthetic (LA) less painful compared to subcutaneous LA, with a relative pain reduction of 20%, (p = 0.05). Patients rated subcutaneous LA less painful than no LA with a relative pain reduction of 36%, (p < 0.0001). Patients rated Intradermal LA less painful than no LA with a relative pain reduction of 47%, (p < 0.0001).

**Conclusion** Local anaesthesia with intradermal and subcutaneous lignocaine reduced procedure-related pain scores rated by patients in the outpatient oxygen clinic. There was a trend to lower patient pain scores with LA administered via the intradermal route compared to the subcutaneous route.

**Supported by** Nil.

**Nomination** Nil.

**Conflict of Interest** No.

P187

**CASE STUDY: IDIOPATHIC PULMONARY ALVEOLAR PROTEINOSIS**

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**Background** Idiopathic pulmonary alveolar proteinosis (IPAP) is an autoimmune disease with neutralizing antibody against GM CSF. It is a rare lung disease (estimated incidence 1–3 per million) characterized by accumulation of phospholipoproteinaceous fluid in the alveoli with cough and dyspnoea on exertion the most common symptoms. Whole lung lavage remains the treatment of choice for this condition.

**Aim** This presentation describes our units' experience case-managing an unusually severe case.

**Case Study** S. (age 36 years) presented in 2007, a diagnosis of IPAP as made in 1999 and she had endured 17 previous lung lavage procedures. Pulmonary function indicated a mild restrictive pattern with moderately impaired gas transfer. During 2007 she became more symptomatic and further lavages were performed, despite these her condition continued to deteriorate. In early 2009 Sonia was hypoxic on minimal exertion desaturating from 93% to 84% RA in 2 min with nocturnal hypoxaemia (<88% for 58.9% of the night). As her condition was deteriorating despite traditional treatment expert opinion was sought from a research haematologist. Lung transplantation was not an option, and he suggested alternate treatments such as GM CSF or possibly the monoclonal antibody (Rituximab). These treatments are not readily available in Australia so a cost benefit analysis was prepared by the respiratory team to justify the hospital funding the expense. In early 2010 the RMH was involved in a Rituximab clinical trial and S. was given two IV infusions 6 months apart, 12-months post treatment her CT scan indicated no residual signs of IPAP. Her most recent lung function (FEV<sub>1</sub> 69%, FVC 71%, DLCO 52%), walking distance >500 metres on RA without significant desaturation (98% RA-94%RA).

**Conclusion** Her case study is an illustration of the role a respiratory nurse can play as a patient advocate, and the role they can play in the development of treatment strategies in the absence of clinical trials.

**Support** Nil.

**Conflict of Interest** Nil.

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**NURSING IN A RESPIRATORY HIGH-DEPENDENCY UNIT: PROFESSIONAL REWARDS**

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Although relatively common in Europe, there are very few Respiratory High Dependency Units (RHDU) in Australia. The Princess Alexandra Hospital RHDU consists of four allocated beds within the Respiratory Ward. The RHDU provides specialized medical and nursing care for patients with complex respiratory conditions. Between 1.10.11 and 30.9.12, 270 patients were admitted to the RHDU. 186 patients had Respiratory Failure (RF) (52 Type 1 RF, Type 2 RF 134), 123 required Non-invasive ventilation (NIV), 17 required CPAP, 10 had tracheostomies and 19 had Intercostal Catheters (ICCs). The mean Therapeutic Intervention Score System in the RHDU was 14.5 ± 3.5 compared to 5.8 ± 2.3 on the Respiratory ward. Despite the high acuity of these patients, overall mortality within the RHDU was 3.7%, with 88% of patients surviving to discharge from hospital. Team nursing is paramount to the successful care of the RHDU patient. One RHDU trained Clinical Nurse and one Registered Nurse are allocated to the RHDU per shift (1:2 nurse to patient ratio). Staff retention rates are high. RHDU nursing requires specialized knowledge and skills, including NIV and CPAP, arterial blood gas and capillary blood gas collection and testing with a point of care analyser, phlebotomy, intravenous cannulation and management of tracheostomies and ICCs. Staff undergo a comprehensive written and practical competency in all of these specialized nursing skills, followed by regular on the job review and feedback.

**Conclusion** The model of RHDU management of high acuity respiratory patients is successful. The RHDU offers nursing staff a dynamic and challenging work environment, contributing to high staff satisfaction and retention. Staff have the opportunity to work in a supportive environment and utilize specialty nursing skills, thus contributing to good patient outcomes in this patient group.

**Support** Nil.

**Conflict of Interest** Nil.

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**IMPLEMENTATION OF BRIEF SMOKING INTERVENTION (BSI) IMPROVES THE USE OF NICOTINE REPLACEMENT THERAPY (NRT) IN HOSPITALIZED INPATIENTS**

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**Background** A structured programme was implemented in the respiratory ward of a tertiary hospital during 2011 to train ward nurses on assessing smoking status, nicotine dependence and provide brief smoking advice in association with Nicotine Replacement Therapy (NRT) to all identified smokers on the ward.

**Aim** Determine the proportion of hospital patients identified as smokers and how many of these smokers received NRT in the respiratory ward vs other wards.

**Method** Retrospective chart audit was conducted in 11 medical and surgical acute wards over 8 days identifying documentation of smoking status and if NRT was commenced.

**Results** 211 patients were audited. Smokers 44 (21%), non smokers 148 (70%), not recorded 19 (9%). On the respiratory ward 5/25 (20%) were identified as smokers; 2 (40%) received NRT, 2 (40%) refused NRT, 1 (20%) no documented offer. Of remaining wards 39/206 (19%); 12 (31%) received NRT during their hospital stay, 2 (5%) refused NRT, 25 (64%) no documented offer was evident. A higher proportion (80%) was offered NRT in the respiratory ward than the other wards (36%).

**Conclusion** In all wards inpatient smoking status was assessed, although the offer of NRT was better on the respiratory ward compared to other wards. Implementation of a ward based BSI programme should be extended to all wards.

**Conflict of Interest** No.