Conclusion

The Pacific Island patients are younger and have an increased BMI than the other patients. They are also more likely to have accessed the health system later as many of them are immigrants and are unfamiliar with the New Zealand health system for many English is not their first language. They are more likely to have complex disease. Twelve of the Pacific Island group require additional oxygen especially when asleep. All 24 of the Pacific Island patients and 10 Maori patients are in the lowest socio-economic decile but only four of the seven European. This has major implications for compliance and usage of equipment due to increased power costs. The Asian patient has asthma, ASD, and kyphoscoliosis.

Support Nil.
Nomination Nil.
Conflict of Interest Nil.

REPORTED RESPIRATORY SYMPTOMS IN YOUNG ADULTS OF EXTREME PRETERM BIRTH

DEBRA ENEVER1, STEPHANE YERKOVICH1, PETER GRAY2, DANIEL CHAMBERS1
1Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane, Australia, and 2Mater Children’s Hospital, Brisbane, Australia

Introduction

Very little is known about adult health of survivors of extreme preterm birth. The aim of this study was to assess the burden of respiratory symptoms in a cohort of young adults born prematurely compared to sibling controls.

Method

One hundred and fifty six children born prematurely (26–33 weeks gestation) at the Mater Hospital Brisbane between 1989–1990 were mailed questionnaires to assess their respiratory symptoms using a modified version of The European Community Health Survey. Term-born siblings were invited to act as controls.

Results

Thirty six responses were received (23%). The studied cohort consisted of 36 cases (64% female) and 17 controls (59% female). The median age was 19 years (18–21) in the cases and 18 years (16–27) in the control group (p = ns). Shortness of breath (SOB) was reported in 25% of the preterm cases, but nil in the control group (p = 0.044). There was a higher incidence of day/night cough (50% vs. 13%, p = 0.0135) and morning cough (37% vs. 0%, p = 0.0045) in the preterm cases compared to controls. The preterm cases were also more likely to experience a chest infection before the age of five (38% vs. 13% of controls, p = 0.046). SOB was unrelated to a history of asthma, atopy, exposure to smoke or domestic animals as there was no difference between controls and cases.

Conclusion

A higher incidence of SOB was reported in young adults who were born prematurely compared to sibling matched controls, and this appears to be unrelated to asthma and atopy. Further subjects will be enrolled to assess predictors of respiratory symptoms in early adulthood.

Conflict of Interest No.

GAG REFLEX AND SWALLOW RESPONSE TESTING POST BRONCHOSCOPY

KAREN L PIKE, HUBERTUS PA JERSMANN
Department of Thoracic Medicine, Royal Adelaide Hospital, Adelaide, Australia

Background

Currently all protocols for checking patient readiness for oral intake post fibre optic bronchoscopy (FOB) are non-evidence based. There is a need to establish the shortest safe time to implement resumption of oral intake following administration of local anaesthesia for various reasons. We examined return times for the gag reflex and swallow response.

Method

A prospective study of 100 consecutive patients presenting for a FOB, age 18–86, were assessed for optimum time to check the gag and swallowing reflex. The gag was checked pre and post FOB by the touch method (tickle back of throat), swallow was checked post FOB with a sip of water at various times.

Results

After 1 hour 67% and 90% of patients had a gag reflex (n = 82) and swallow response (n = 100) respectively. This increased to 88% and 96% at 1½ hours, 95% and 99% at 2 hours, 100% and 100% at 2½ hours. The amount of sedation or length of procedure did not correlate with the return of the gag reflex or swallow response. None of the patients who swallowed with the gag still absent coughed or aspirated. Eighteen patients did not have a gag reflex pre FOB.

Conclusion

The gag reflex and swallow response are separate. Data shows it is possible to swallow safely without a gag reflex. The time to safe swallow is much shorter than recommended in current protocols. However, we consider it safer to allow oral intake when both reflexes are present, if the gag is present pre FOB. Otherwise the patient should wait for 1½ hours post FOB as 88% have a returned gag reflex, if swallow response is also back.

Nomination None.
Conflict of Interest No.

© 2010 The Author(s)
Journal Compilation © 2010 Asian Pacific Society of Respirology
CHILDREN’S CONCEPTIONS OF THEIR PARENT’S LUNG TRANSPLANT

Tr-win LEISFIELD1, KAY WIGGINS1, P FULBROOK2
1Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane Queensland, Australia, and 2Research and Practice Development, The Prince Charles Hospital, Brisbane Queensland, Australia

The effects of parents’ critical illness on children include strong emotions such as anxiety, sorrow, fear and conflict. There is some research into parents’ perceptions of their child’s transplant but none that focuses on children’s experiences of parents’ lung transplantation. Our aim was to describe children’s concerns and understandings of parent’s transplant surgery.

Method Phenomenography, a qualitative research design was used comprising two phases and two data collection methods: children’s artwork and interviews. In phase one children produced artwork that depicted experiences of their parent’s transplant, accompanied by a brief verbal commentary. These were used in phase two for follow up interviews which were then analysed thematically to determine children’s conceptions of transplant i.e. commonalities and differences.

Results Ten children aged 8–15 participated and used artwork to depict a variety of concepts related to their parent’s transplant. Analysis revealed five commonalities that reflected their conception of their situation: separation, disruption, anxiety and uncertainty, desire for normality and social support. The main difference that emerged was the children’s coping mechanism, which was polarised: adjustment or avoidance.

Conclusions The findings have implications for multidisciplinary family care for those facing critical life events such as lung transplantation. The five themes revealed can be used by nurses and social workers to assess children based upon their own conceptions. The phase one artwork proved to be a very effective medium which provided a platform for children to talk about their experiences. We suggest this strategy may be employed in family care contexts. Our findings are that children respond by adjusting to the situation or avoiding it. A main consideration, when assessing children is to determine their coping response, as each requires a different approach.

Conflict of Interest Nil.

PATIENT PERCEPTIONS AND UNDERSTANDING OF CLINICAL TRIALS

SANDRA BANCROFT, STEPHANIE YERKOVICH, PETER HOPKINS
Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane, Australia

Potential clinical trial participants are provided with trial specific information, but not necessarily what a clinical trial is per se. Therefore the aim of this study was to better understand how our patients perceive clinical trials and how best to deliver information regarding what a clinical trial is.

Methods A short clinical trial information sheet describing what a clinical trial is and a patient satisfaction survey were mailed to 11 patients participating in an idiopathic pulmonary fibrosis clinical trial for at least four months.

Results This ongoing study has had nine (82%) respondents, predominantly male (63%) with a median age 62 years. Prior to starting the trial, 89% of participants felt they understood what was involved in the trial they were consenting to. However, the clinical trial information sheet gave them a better understanding of what a clinical trial is and all respondents stated this information sheet should have been supplied concurrently with a one on one discussion prior to starting the trial. Interestingly only 78% of respondents felt they had better understanding after attending the follow-up training activities begun in 2007.

Conclusions Screening results were reported by 1,442 GPs for 16,061 patients in 2007. Another 1,921 GPs reported screenings for 46,386 patients in 2008. By mid-2009 cumulative totals were 4,639 GPs, 1,308 PNs and 80,002 screenings, with a consistent detection rate of airflow limitation of 12%. Attitudes, knowledge and confidence relating to COPD diagnosis and treatment changed significantly for GPs and PNs. Conclusions It is feasible to enable primary care practitioners to undertake respiratory screening and uncover substantial numbers of new cases for whom treatment is likely to be beneficial. The success of this program warrants system-wide support.

Conflict of Interest Yes.

OSCILLATORY IMPEDENCE IS REPEATABLE IN COPD

S TIMMINS1,2, C WALSH1,2, N BROWN1,2, C SALOME1,2, N BEREND1,3, G KING1,3,1
1Department of Respiratory Medicine, Royal North Shore Hospital, Sydney, Australia, 2Woolcock Institute of Medical Research, and 3University of Sydney, Australia

Introduction Home monitoring in COPD may identify acute exacerbations earlier, enabling prompt treatment, thus improving morbidity and mortality. Reactance (Xr), measured by forced oscillation technique has a potential role in home monitoring. The aim of this study was to determine within- and between-day repeatability of resistance (Rrs), Xr, and spirometry in stable COPD subjects.

Methods Ten COPD subjects underwent seven consecutive home visits consisting of three measures of FOT (1 minute recording) and spirometry before and after 200 mcg ventolin via spacer.

Results Subject characteristics Mean (SD) - Age 74.7 years (7.43), smoking history 48.6 pack years (17.3), post-BD (post-bronchodilator) FEV1 51.1% predicted (16.3), FEV1/FVC ratio 0.4 (0.11). Repeatability measures are reported as intra-class correlation coefficient (ICC) and SD of within subject variance (Sw).

|                        | Within session | Between day |
|------------------------|----------------|-------------|
|                        | ICC            | Sw          | ICC          | Sw          |
| Xr Pre-BD              | 0.96           | 0.046       | 1.0          | 0           |
| Rs Pre-BD              | 0.94           | 0.045       | 0.93         | 0.03        |
| Xr Post-BD             | 0.97           | 0.34        | 0.91         | 0.62        |
| Rs Post-BD             | 0.95           | 0.52        | 0.9          | 0.62        |
| Post-BD FEV1 (%)       | 0.98           | 0.07        | 0.91         | 0.59        |
| Post-BD FVC(%)         | 0.99           | 0.13        | 0.79         | 0.91        |
| Post-BD FEV1/FVC       | 0.99           | 0.13        | 0.93         | 0.03        |

Conclusion In 10 moderate-severe COPD subjects, Xr and Rs exhibit within session and between day repeatability. This is an important first step in our evaluation of Xr as a potential home monitoring technique in COPD.

Support Asthma CRC, Australian Postgraduate Award.

NOMINATION TSANZ Travel Grant, Janet Elder International Travel Award.

Conflict of Interest No.
Lung Cancer SIC Oral Session

GWAS AND CANDIDATE SNPS FOR COPD AND LUNG CANCER COMBINE TO IDENTIFY LUNG CANCER SUSCEPTIBILITY: VALIDATION IN A PROSPECTIVE STUDY

ROBERT P YOUNG1,2, RAY HOPKINS1, BRYAN HAY1, GRAHAM D GAMBLE1
1Department of Medicine, University of Auckland, New Zealand. 2Syngeneic Biosciences Ltd, Auckland, New Zealand

Introduction
Chronic obstructive pulmonary disease (COPD) is the single most important risk factor for lung cancer (affecting 50–90% of those diagnosed). Considerable overlap exists between smokers who develop COPD and/or lung cancer, suggesting involvement of shared pathogenic pathways (inflammation, matrix remodeling and cell death). In a prospective study of high and low risk smokers we have combined SNPs from GWAS and candidate gene studies to develop a susceptibility score for lung cancer (LCSS).

Methods
Seven hundred and twenty eight high risk individuals (chronic smokers, >40 years old, >20 pack years, spirometric confirmed COPD), and 484 smokers without COPD were recruited and followed for a mean of 5 years. Cohorts were matched for smoking history, ethnicity, gender and age, thereby excluding confounding from these variables. All volunteers completed spirometry, modified ATS respiratory questionnaire and gave blood for DNA. iPLEX and Taqman systems were used to genotype the SNP panel. Included SNPs: n(ACHR) d5 SNP rs 16956968 on Chr 1q25, Tert SNP rs 402710 on Chr 5p15.33, BAT3 SNP rs 1052486 on Chr 11q24, CRP rs 2808630 on Chr 1q23.2, ILRAP SNP rs 7626795 Chr3q28, HPRT rs 1489759 on Chr 4q31.22, GYP A2 rs 220507 Chr 4q31.22.

Results
We have identified 52 cases with histology confirmed lung cancer; 41 (79%) were in the high risk (COPD) cohort (6% over 5 years, mean score = 6.3) and 11 (21%) from the low risk cohort, normal lung function (2% over 5 years, mean score 3.4). The healthy unaffected smokers’ mean score was 2.3. This prospective study confirms the risk status assigned by the LCSS with 41 (6%) vs. 11 (2%) lung cancers over the 5 year follow up (OR = 2.6 (% CI 1.3–5.4, p = 0.005). The performance characteristics of the LCSS reported here, confirm its utility, in correctly identifying smokers at greatest lung cancer risk.

Conclusion
In this prospective study, we show that the LCSS identifies those at greatest risk of lung cancer who might benefit from aggressive preventive strategies such as cessation and chemoprevention.

Conflict of Interest
The author is not aware of any conflict of interest.
SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) AND RISK OF LUNG CANCER IN AN AUSTRALIAN CAUCASIAN POPULATION

ME TAN1, RLG SMITH1, MU MARTINS1, SM SAVARANMUHTU1,2, CM WRIGHT1,2, V PELAN1,2, MR DAVIDSON1,2, JSHAW1,2, JJ DE LAAT1, PV ZIMMERMAN1, JE LARSEN1, RB BOWMAN1,2, IA YANG1,2, KM FONG1,2
1The Prince Charles Hospital, and Brisbane, Queensland, Australia, 2The University of Queensland, Brisbane, Australia

Smoking is the principal cause of lung cancer, yet less than 20% of smokers develop the disease, suggesting the role of genetic predisposition. We hypothesised that SNPs predispose susceptible smokers to lung cancer, independent of clinical confounders.

Methods Three databases were queried to find all reports of SNPs associated with susceptibility to non small cell lung cancer (NSCLC). SNPs studied in Caucasian populations were further prioritised based on case/control numbers, minor allele frequency and tag SNPs. MassArray sequencing was used to genotype DNA from smokers with and without NSCLC. Associations with lung cancer status were tested using $^2$ tests. For positive associations, logistic regression was performed using lung function and pack-years as co-variates.

Results Smokers with NSCLC (n = 914) had mean (SD) age 66(10); 53(34); pk-yr, FEV1 78(21)%; pred. Smokers without NSCLC (n = 1,168) had mean (SD) age 62(14); 46(32) pk-yr, FEV1 66(28)% pred. Two high risk genes, CYP1A1 and CHRNA3, were associated with NSCLC in an independent cohort. SNPs in CHRNA3 (rs1696996, p = 0.026 and p = 0.002 respectively). Associations remained significant after controlling for pack-years and FEV1 %predicted.

Conclusion Preliminary results from this cohort suggest that genomic variation may contribute to lung cancer susceptibility, in addition to environmental factors and independent of airflow obstruction. Further genotyping will be undertaken in a larger cohort.

Support The Prince Charles Hospital Foundation, NHMRC CDA (FY) and PF (KF), Cancer Council Queensland, Smart State, DDB.

Conflict of Interest None.

NON-SMALL CELL LUNG CANCER PATIENTS PRESENT AT PROGRESSIVELY EARLIER STAGE WITH INCREASING AGE

DANIELE ZARATE1, SHEK COLOQUIST1, KINAN FONG2, RAYLEEN BOWMAN2
1Queensland Cancer Control Analysis Team, Queensland Health, Brisbane, Queensland, Australia, and 2The Prince Charles Hospital, Brisbane, Queensland, Australia

Purpose We examined age trends in the distribution of stage at diagnosis in patients presenting with non-small cell lung cancer (NSCLC) at tertiary hospitals.

Methods We used the Queensland Integrated Lung Cancer Outcomes Project (QILCOP), a clinical registry which collects information on about 40% of all lung cancer patients in Queensland, to analyse the distribution of clinical (TNM) stage among 2,923 patients diagnosed with NSCLC between 2000 and 2005. Differences in stage distribution across age were analysed using tests of proportions and multivariable logistic regression with stage as the dependent variable and other demographic characteristics as covariates.

Results The median age at diagnosis of patients in the study was 68 years (range 26–95) and 68% were males. The overall proportions of stages I, II, III, and IV were, respectively, 18%, 10%, 9%, 25%, and 32%. The percentage of stage I disease increased with age (p < 0.001), from 19% in those younger than 55 years to 26%, 31%, and 37% in those aged 55–64, 65–75, and 75 years or older, respectively. Age differences in stage distribution remained significant in multivariable analysis controlling for gender, rural residence, and socioeconomic status. Among the other characteristics, only gender differences in stage 55–64, 65–75, and 75 years or older, respectively. Age differences in stage distribution were significant, with stage I cancer being more common in women compared to men (34% vs. 29%, p = 0.02).

Conclusions Older patients with NSCLC are more likely to present with resectable early stage cancer compared to younger patients.

Support Nil.

Nomination Nil.

Conflict of Interest No.

QUEENSLAND LUNG CANCER SCREENING STUDY: FINDINGS FROM THE FIRST 197 PARTICIPANTS’ PREVALENCE LOW DOSE CT SCANS

H MARSHALL, RV BOWMAN, J CROSSIN, M FUENTES, R SLAUGHTER, L PASSMORE, L MCCaul, D COURTENAY, M WEBB, M WINDSOR, IA YANG, PV ZIMMERMAN, T HAYES, S REDMOND, KM FONG
Departments of Thoracic Medicine, Medical Imaging and Thoracic Surgery, The Prince Charles Hospital, Queensland, Australia

Introduction Mortality benefits for LDCT screening are not yet known. The Queensland Lung Cancer Screening Study is screening up to 750 high risk volunteers based on the NLST/ACRIN protocol.

Aims Observational cohort study to assess: disease detection rate; lung nodule work-up; cost; quality of life issues; smoking cessation; biomarker collection feasibility.

Methods Recruitment via local advertisement and press release. Major inclusion criteria: age 60–74 years; smoking history >30 pack years; fit for surgery. Volunteers have one prevalence and two incidence scans and follow-up for three years. LDCT parameters: Phillips Brilliance 64 slice multidetector scanner; low-dose protocol; 0.9mm slice width. Scan reporting: two radiologists independently; independent CAD reading (Phillips Brilliance software); final report is agreed by consensus.

Results See Table 1 to be updated.

Table 1. Results, median (range) unless stated

| Male/ female, n | 138/59 |
|----------------|--------|
| Age, years     | 64.7 (60.1–74.5) |
| FEV1 % predicted | 52.0 (51.3–100.0) |
| Current smokers, n (%) | 89 (45.2) |
| Smoking history, pack-years | 55.0 (30–220) |
| Participants with nodule >4 mm diameter, n (%) | 102 (51.7) |
| Nodule diameter (mm) <4.0 or 4–10 or >10.0, n | 391/ 214/ 15 |
| Participants with Pleural plaques, n (%) | 66 (33.5) |
| Participants with radiological emphysema, n (%) | 119 (60.4) |

Conclusions A high prevalence of indeterminate nodules has been found, recruitment continues.

Support Queensland Smart State Grant and NACARD.

Conflict of Interest No.

IMPROVED LOCAL CONTROL OF MALIGNANT PLEURAL MESOTHELIOMA USING TECHNOLOGICAL ADVANCES IN RADIOTHERAPY

MALCOLM FEIGEN1, MRA WADA1, SZE TING LEE2, CATHERINE LAWFORD1, KATHRYN CHURCHER1,2, CHRISTOPHER HAMILTON1
1Radiation Oncology Centre, Austin Health, Heidelberg West, Victoria, Australia, and 2Centre for PET, Radiation Oncology Centre, Austin Health, Heidelberg West, Victoria, Australia

Australia has the world’s highest incidence of mesothelioma, a disease which has no proven effective therapy. The median survival of less than 12 months and five year survival of 5% have not changed in two decades. Radical resection has a high attrition rate with most cases recurring locally, and few patients have durable responses to chemotherapy. Symptoms are related to local disease which compresses the lung and causes severe chest pain from enlarging tumour masses.

Aim To improve local control of mesothelioma by high dose radiotherapy using advanced technologies that precisely define the active tumour and reduce toxicity to normal tissues.

Methods All patients had FDG PET scans co-registered with a simulation CT scan to define the target volume, and follow-up PET scans were analysed to assess the residual total glycolytic volumes (TGV) after radiotherapy. Acute and long term toxicities were assessed.

Results Between 2003 and 2009 thirty patients with incompletely resected pleural mesothelioma were treated with radiation doses of 30 to 60 Gy to par or all of one hemithorax. All patients who received chemotherapy had progressed prior to radiotherapy. In 2006 we introduced a program using a new technique called intensity-modulated radiotherapy (IMRT). TGVs reduced by 60% after radiotherapy, median survival was extended to 24 months and there were no major radiation toxicities, the most common being grade 2 pneumonitis. Relapses were frequent on extended follow-up, the majority in areas outside the radiotherapy field.

Conclusions IMRT is effective in maximising local control in mesothelioma patients who have had extrapleural pneumonectomies, and for selected patients with an intact lung. Toxicities are manageable and locoregional control is very good. High dose radiotherapy is recommended for most mesothelioma patients for long term palliation and control of locoregional progression.

Conflict of Interest No.
CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: ASSESSING PULMONARY ENDARTHROCTOMY OUTCOMES WITH MRI

B NG1, P HOPKINS1, K MCNEIL1, D CHAMBERS1, F KERMEEN1, R SLAUGHTER2, J DUNNING3
1Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane, Australia, 2Centre of Excellence for Cardiovascular MRI, The Prince Charles Hospital, Brisbane, Australia, and 3Department of Cardiothoracic Surgery, Papworth Hospital, UK

Magnetic resonance imaging (MRI) is a useful modality for assessing chronic thromboembolic pulmonary hypertension (CTEPH) before pulmonary endarterectomy (PEA). Cardiac MRI provides more accurate right ventricular (RV) data than echocardiography. MRI angiography demonstrates vascular changes reliably to a segmental level and MR perfusion shows disease distribution.

Aim To examine the relationship between changes in MRI parameters with clinical and haemodynamic outcomes post-PEA.

Methods RV end-diastolic volume (RVEDV), RV ejection fraction (RVEF), vessel abnormalities and lobar perfusion defects were determined with MRI before and after PEA. Changes in New York Heart Association (NYHA) functional class, six minute walk distance (6MWD), mean pulmonary artery pressure (mPAP) and cardiac output (CO) were collected retrospectively from patient charts.

Results Nineteen patients assessed pre-PEA were of mean ± SD age 57 ± 12 years, NYHA class 2.8 ± 0.7, 6MWD 414 ± 103 metres and mPAP 42±10 mmHg. Immediately post-PEA, mPAP fell by 13 ± 7 mmHg which was related to changes in RVEDV of 26 ± 15% (r² = 0.38, p = 0.006). At 6–12 months post-PEA, 6MWD improvement (115 ± 99 metre) was related to changes in RVEF of 28±49% (r² = 0.40, p = 0.007) but angiographic changes had a weak relationship with NYHA class shift (r² = 0.22, p = 0.034). Perfusion generally improved after PEA relating weakly with RVEDV (r² = 0.3, p = 0.032) but not clinical outcomes.

Conclusions This study shows that improvements in MRI parameters (RV data more than angiographic findings) after PEA correspond to clinical and haemodynamic outcomes. We have demonstrated a useful imaging test for monitoring patients post-PEA with no radiation exposure.

Conflict of Interest Nil.

OLIV SIG Oral Session 1

THE IL-6 FAMILY OF CYTOKINES MODULATE BLEOMYCIN-INDUCED LUNG FIBROSIS

HL LAU1,2, J R O’DONOGHUE1, M ERNST1, G ANDERSON2, J JONES3, S MUTSAERS1,2
1Lung Institute of Western Australia, 2PathWest Laboratory Medicine Western Australia, 3University of Western Australia, 4Ludwig Institute for Cancer Research, Victoria, Australia, and 5University of Melbourne, Victoria, Australia

Idiopathic pulmonary fibrosis (IPF) is characterised by marked collagen deposition. The receptor subunit gp130 has been associated with the progression of fibrosis. The interleukin (IL)-6 family of cytokines all require gp130 to initiate signal transduction to activate either the extracellular regulated kinase (ERK) or signal transducer and activator of transcription (STAT) pathways. The IL-6 family of cytokines consist of IL-6, IL-11, oncostatin M (OSM), leukemia inhibitory factor (LIF), cardiotoxin-1 (CT-1), ciliary neurotrophic factor (CNTF), IL-27 and IL-31. Previous studies in our laboratory have demonstrated that exaggerated gp130-STAT3 signalling is fundamental to the development of bleomycin-induced lung fibrosis in a murine model. We hypothesise that pulmonary fibrosis is mediated by IL-6 family cytokine/gp130-STAT3 signalling. The aim of the current study was to identify which of the IL-6 family cytokines are important in the development of bleomycin-induced pulmonary fibrosis. Bleomycin or control saline was administered intranestrally to individual IL-6 knockout (IL-6−/−) mice and dual IL-6 and IL-11 s-receptor knockout (IL-6−/−IL-11−/−R−/−) mice. Collagen production was examined by histology and HPLC in lung tissue 30 days post treatment. No significant increase in collagen was observed in bleomycin treated IL-6−/− or IL-6−/−IL-11−/−R−/− mice implicating a role for IL-6 in the development of pulmonary fibrosis. Interestingly, the histology of IL-6−/−IL-11−/−R−/− mice displayed marked emphysema with no induced IL-6−/− mice suggesting this is an IL-11-mediated response. The role of IL-6 family cytokines in proliferation, myofibroblast differentiation and collagen expression were examined using fibroblasts isolated from wildtype (WT) and genetically engineered mice containing point mutations to prevent gp130-ERK1/2 signalling (gp130375) or gp130-STAT3/1 signalling (gp130310). Overall, there was no significant increase in proliferation 48 hours post cytokine stimulation as assessed by WST-1 reagent. IL-6 and IL-11 did not stimulate v-SMA or collagen expression above control, measured by real time PCR. In conclusion, increasing evidence suggests that IL-6 plays an important role in the development of bleomycin-induced pulmonary fibrosis but this does not appear to be induced by direct effects of IL-6 on fibroblast proliferation, differentiation or collagen production.

Supported NH&MRC.

Nomination No.

Conflict of Interest No.

INCREASED NKT CELLS ARE A MAJOR SOURCE OF PRO-INFLAMMATORY CYTOKINES AND GRANZYMES IN LUNG TRANSPLANT PATIENTS

GREG HODGE1, SIMON HODGE1, PAUL REYNOLDS1, MARK HOLMES1,2
1Department of Thoracic Medicine, Royal Adelaide Hospital, Adelaide, South Australia, Australia, and 2South Australian Lung Transplant Service, Adelaide, Australia

NKT cells are a small but significant population of T lymphocytes (+1%), however their role in lung transplant is undetermined. We have previously shown lung transplant rejection was associated with an increase in peripheral blood T cell production of IFN-gamma, TNF-alpha and granulocyte B. NKT cells are a source of these pro-inflammatory mediators and as such may be involved in lung transplant pathology. Almost all immunosuppressive agents are targets of T-cell function including pro-inflammatory cytokines, however their effect on NKT cell function is largely unknown. To investigate this, we analysed NKT cell numbers, cytokine and granulocyte and PFC profiles in the peripheral blood of a group of stable lung transplant patients and control subjects using multiparameter flow cytometry. There was a significant increase in NKT cells in transplant patients compared with control subjects (1.9 ± 0.8 vs. 0.4 ± 0.2% respectively). There was an increase in the numbers of NKT cells producing IFN-gamma, TNF-alpha, granulocyte A, granulocyte B and granulysin in transplant patients compared with controls (1.9 ± 0.8 vs. 0.4 ± 0.2%, 4.2 ± 3.8 vs. 0.5 ± 0.3%, 0.5 ± 0.3 vs. 0.0 ± 0.0%, 0.7 ± 0.7 vs. 0.0 ± 0.0%, respectively). NKT cells are increased and are a major source of pro-inflammatory cytokines and granulocytes in the peripheral blood of lung transplant patients and are associated with graft rejection. Drugs that reduce NKT cells and associated pro-inflammatory mediators may improve patient morbidity.

Support NH&MRC.

Nomination Nil.

Conflict of Interest No.

Support NH&MRC.

Nomination No.

Conflict of Interest No.
TACROLIMUS DELAYS PROGRESSION OF BRONCHIOLITIS OBLITERANS SYNDROME (BOS) IN LUNG TRANSPLANTATION

Stephan T Yerkoovich, Peter MA Hopkins, Daniel C Chambers

Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane, Australia

BOS remains the major barrier to long-term survival following lung transplantation. While the risk factors for development of BOS are well described, factors influencing progression of BOS once it is established have been less well studied.

Methods
We retrospectively reviewed factors (demographics, type of transplant, rejection load (sum of A scores), calcium inhibitor, hypogammaglobulinaemia, respiratory viral infection) which may influence BOS progression using Kaplan-Meier survival curves and Cox proportional-hazards models.

Results
Seventy-six patients (median age 49.8 years (range 13.6-63.2), 45% female, 26% CF and 53% COPD) had reached BOS1 at 34.3 months (median, range 2.4-129.9) post-transplant and were included. For 47 patients (62%) who progressed from BOS1 to BOS3 the median time to progression was 6.4 months (range 0.6-67.2). On univariate analysis the only factor which predicted more rapid progression was younger age (<45 years, p = 0.009), while tacrolimus based immunosuppression protected against progression (p = 0.0002). There was a trend for a diagnosis of CF (p = 0.084) and being female (p = 0.055) to lead to more rapid BOS progression, however when all these factors were combined in a Cox-proportional hazards model, only the use of tacrolimus delayed BOS progression (risk 0.26, p < 0.0001) and younger age (risk 2.8, p = 0.001) was confirmed as a risk factor for rapid progression. Other studied factors did not influence BOS progression.

Conclusions
Once a patient has developed BOS1, tacrolimus delays progression to BOS3. Younger patients with cystic fibrosis are at higher risk of more rapid progression.

Conflict of Interest
No.

COMPARTMENTALISED REDUCTION OF MANNOSE BINDING LECTIN CORRELATES WITH BRONCHIOLITIS OBLITERANS SYNDROME

Sandra Hodge1, Jessica Ahern1, Melissa Dean2, Gregg Hodge1, Mark Holmes1

Queensland, Australia, and Australian Red Cross Blood Service, Brisbane, Australia

Mannose binding lectin (MBL) is a key mediator of innate immunity and efferocytosis (clearance of apoptotic cells) and is thus important in protecting against tissue damage. Reduced MBL is implicated in airways disease including infection, COPD and BOS, however, ‘normal’ plasma levels of MBL are highly variable due genetic polymorphisms complicating correlation with disease processes. We have previously shown reduced MBL and defective efferocytosis in BAL from patients with post-transplant BOS, but there are conflicting reports of the link between low plasma MBL levels, increased complement activation and graft rejection. To compare MBL levels in the peripheral blood and BAL compartments, we investigated MBL in paired plasma and BAL from 46 lung transplant recipients (10 stable; 36 stable with infection) which may influence BOS progression using Kaplan-Meier survival curves and Cox proportional-hazards models.

Results
Seventy-six patients (median age 49.8 years (range 13.6-63.2), 45% female, 26% CF and 53% COPD) had reached BOS1 at 34.3 months (median, range 2.4-129.9) post-transplant and were included. For 47 patients (62%) who progressed from BOS1 to BOS3 the median time to progression was 6.4 months (range 0.6-67.2). On univariate analysis the only factor which predicted more rapid progression was younger age (<45 years, p = 0.009), while tacrolimus based immunosuppression protected against progression (p = 0.0002). There was a trend for a diagnosis of CF (p = 0.084) and being female (p = 0.055) to lead to more rapid BOS progression, however when all these factors were combined in a Cox-proportional hazards model, only the use of tacrolimus delayed BOS progression (risk 0.26, p < 0.0001) and younger age (risk 2.8, p = 0.001) was confirmed as a risk factor for rapid progression. Other studied factors did not influence BOS progression.

Conclusions
Once a patient has developed BOS1, tacrolimus delays progression to BOS3. Younger patients with cystic fibrosis are at higher risk of more rapid progression.

Conflict of Interest
No.

DEAD SPACE REDUCES EXERTIONAL DYSPNEA IN SIMULATED LUNG RESTRICTION WITH MATCHED VENTILATION

Luke Garske,1,2 Ryan Lal,2 Norm Morris2, Troy Cross2, Lewis Adams2

1 Respiratory Medicine, Princess Alexandra Hospital, Brisbane, Queensland, Australia, and 2 School of Physiotherapy and Exercise Science, Griffith University, Gold Coast, Queensland, Australia

In normal subjects, external dead space with exercise is associated with a slower deeper breathing pattern compared at the same ventilation. With simulated lung restriction and constant intensity exercises, we tested the hypothesis that dead space combined with reduced exercise intensity to match ventilation, would alter pattern of breathing, reduce Inspiratory Reserve Volume (IRV) and thus increase dyspnea.

Methods
Eleven healthy male subjects, aged 28-61 (SD) years completed separate visits with (a) no restriction and (b) chest wall strapping to reduce FVC by 30 (7) %. For each visit, subjects performed two 10 minute constant exercise tests with numeric rating scale for dyspnea (a) at 90% of anaerobic threshold (AT), and (b) with 600 ml dead space at a lower exercise intensity required to match ventilation.

Results
Mean (SD) values after 4 minutes exercise were:

| Condition | No restriction | Restriction | Dead space |
|-----------|---------------|-------------|------------|
| Work, W   | 135(28)       | 135(28)     | 58(36)     |
| Ventilation, l/min | 49.1(7.7) | 55.3(8.0) | 54.3(7.2) |
| RR, breath/min | 20.7(4.6) | 32.8(7.3) | 31.0(6.7) |
| TV, l     | 1.38(0.30)    | 1.30(0.30)  | 1.40(0.34) |
| Dyresnea (0-10) | 2.7(1) | 4.5(1.7) | 3.4(1.7) |

Conclusions
In the unrestricted condition, dead space with matched ventilation resulted in a 6% increase in tidal volume. With simulated restriction, dead space did not significantly alter pattern of breathing, with moderately reduced dyspnea. Dyspnea intensity with simulated lung restriction may depend on the relative contribution of different ventilatory stimuli. IRV was similar in all conditions.

Grant support Nil.
Conflict of Interest Nil.

GLOSSOPHARYNGEAL BREATHING ALTERS DISTRIBUTION OF PULMONARY PERFUSION AND THORACIC STRUCTURE IN BREATH-HOLD DIVERS

Leigh Seccombe1, Steven Chung1, Christine Jenkion1, Clayton Frater1, Doug Mackey1, Mark Pearson2, Louise Emmett3, Matthew Peters3

1 Departments of Thoracic Medicine, and 2 Nuclear Medicine, Concord Repatriation General Hospital, Concord, New South Wales, Australia

Introduction
Glossophaerengal breathing (GBP) is used by competitive breath-hold divers to increase lung gas content above TLC to improve performance. This occurs by both lung expansion and gas compression. Whilst GBP is known to induce hypotension and tachycardia, little is known about the changes that occur to both the pulmonary circulation and the structural integrity of the thorax. The aim of this study was to investigate these changes within an elite cohort.

Methods
Six male breath-hold divers were studied. Exhaled VC was measured before and after GBP. Subjects were studied in the supine position at baseline TLC and after maximal GBP above TLC at least 72 hours apart. Tc 99m labelled macro-aggregated albumin was injected and a computed tomography (CT) of the thorax was performed during breath-hold. Dynamic and single photon emission CT (SPECT) images were generated and analysed by two blinded Nuclear Medicine Physicists for perfusion intensity (Wilcoxon signed rank test) and dynamic regional blood flow. A paired t-test was used to assess physiological parameters. Registered CT images were used to determine structural change in the thorax.

Results
Five subjects increased exhaled VC with GBP (mean (SD)) by 1.4 (0.3) L (p < 0.001). There was a reduction in perfusion intensity following GBP in the anterior (p < 0.03) and inferior (p < 0.01) lung segments. There was no change in the timing of blood flow. 69% of the increase in expired lung volume above baseline TLC was via thoracic expansion (p < 0.03 L (p < 0.05)) with a caudal displacement of the diaphragm. One subject who was not proficient at GBP had no change in expired volume, CT appearance or lung perfusion.

Conclusion
We have demonstrated areas of hyper expanded, underperfused lung associated with GBP above TLC. Possible mechanisms include increased alveolar pressure, decrease in arterial pressure or distortion of the pulmonary capillary bed.

Conflict of Interest Nil.

© 2010 The Author(s)
Journal Compilation © 2010 Asian Pacific Society of Respirology
DEEP INSPIRATION AVOIDANCE INCREASES VENTILATION HETEROGENEITY & INCREASES AIRWAY CLOSURE

David CHAPMAN1,2,3, Norbert BEREND1,2,3, Greg KING2,3,4, Cheryl SALOME1,2,3
1Woolcock Institute of Medical Research, Sydney, New South Wales, Australia, 2University of Sydney, New South Wales, Australia, 3CRC for Asthma, Sydney New South Wales, Australia, and 4Department of Respiratory Medicine, Royal North Shore Hospital, New South Wales, Australia

Heterogeneous ventilation leads to airway hyperresponsiveness in asthma. Deep inspiration (DI) avoidance may increase responsiveness in non-asthmatics by increasing ventilation heterogeneity. Aim To determine the effect of DI avoidance on ventilation heterogeneity in non-asthmatics.

Methods Ten non-asthmatics had incremental methacholine (Mch) challenges (0.8 to 200 μmol). The PD20FEV1, or maximal dose of 102.2 μmol, was used in single dose challenges. Multiple breath nitrogen washout (MBNW) was performed before 20 minute of DI avoidance and repeated immediately (no DI) or after 5 DI. Subjects repeated DI avoidance before inhalation of single Mch dose with no DI or SDI. Spirometry was measured before DI avoidance and after Mch. Ventilation heterogeneity in conducting (SCond) and acinar (SAcin) airways was calculated from MBNW. Airway narrowing was measured by % fall (FEV1/FVC) and airway closure by % fall VFC. Data are reported as mean ± s.d.

Results Baseline FEV1 (% pred) was 102.4 ± 7.2. The difference in SAcin (no DI - SDI) correlated with the difference in % fall VFC (%p = 0.07), but not with the difference in % fall FEV1 (%p = 0.23).

Conclusions DI avoidance in non-asthmatics increases ventilation heterogeneity in acinar airways, which may lead to increased airway closure during challenge.

Support NHMRC, Ross Trust Fund, Asthma NSW and CRC for asthma.

Nomination Nil.

Conflict of Interest Nil.

THE UTILITY OF AIRWAY DISTENSIBILITY AS A MEASURE OF AIRWAY MECHANICS IN ASTHMA

VJ KELLY1,2,3, NJ BROWN2,3, GG KING2,3, BR THOMPSON1,2,3,4
1Department of Physiology, Monash University, Victoria, Australia, 2CRCAA, New South Wales, Australia, 3The Woolcock Institute of Medical Research, New South Wales, Australia, and 4Alfred, The Alfred Hospital, Victoria, Australia

Background We have developed a sensitive method to determine conductance-lung volume (conductance profile) and distensibility-lung volume (distensibility profile) relationships using the forced oscillation technique (FOT). Using this method, we aimed to assess the effect of a short-acting bronchodilator (BD) on these profiles in asthma.

Methods Twenty two asthmatics and 20 healthy controls completed distensibility measurements (FOT) and lung function tests before and after BD. The conductance and distensibility profiles were described continuously and determined at specific lung volumes, residual volume (RV), FRC, TLC and midway between FRC and TLC (MD). Results Following administration of BD: The conductance profile in the asthma group was shifted upwards, and the distensibility profile was altered such that significant increases in distensibility were observed at RV (p < 0.001) and FRC (p < 0.01), but not at MID or TLC. In contrast, no changes were seen in the conductance or distensibility profiles in the control group. Post-BD distensibility in asthma remained reduced compared to controls.

Conclusion Using a sensitive method for determining conductance and distensibility profiles, we found that both conductance and distensibility are reduced in asthma across a range from low to high lung volumes. Both these profiles are altered in asthma after BD but not in controls. We propose that in asthma the remaining deficit in distensibility after BD will provide unique insight into altered airway mechanical function due to airway remodeling.

Support NHMRC and CRCAA.

Nomination Nil.

Conflict of Interest Nil.

WIDESPREAD AIRWAY CLOSURE IN NON-ASTHMATIC SUBJECTS MEASURED BY VENTILATION IMAGING

Catherine E WALSH1,4, Elizabeth BAILEY2, Cheryl M SALOME1,4, Norbert BEREND1,4, Gregory G KING2,3,4
1Woolcock Institute of Medical Research and University of Sydney, New South Wales, Australia, 2Department of Respiratory Medicine, Royal North Shore Hospital, St Leonards, New South Wales, Australia, 3Nuclear Medicine Department, Royal North Shore Hospital, St Leonards, New South Wales, Australia, and 4CRC for Asthma and Airways, New South Wales, Australia

Introduction In asthma, airway hyperresponsiveness is associated with airway closure and ventilation heterogeneity. The aim of this study was to determine if non-asthmatic subjects develop airway closure after high dose methacholine challenge (Mch) and if ventilation heterogeneity was related to the magnitude of airway closure.

Methods Six non-asthmatic subjects (two male, age (mean ± SD) = 28.7 ± 8 years) had ventilation single photon emission computed tomography/computed tomography (VSPECT/CT) scans, using [99mTc]-Technegas before and after Mch. Airway closure was measured by loss of ventilation on the images. Multiple breath nitrogen washout was performed at baseline to determine ventilation heterogeneity (Scond). Dose response slope (DRS) was calculated from Mch to measure airway responsiveness.

Results At baseline FEV1 was 109 ± 12% pred. Airway Closure was 19.7 ± 32% (mean ± range). Scond was 0.045 ± 0.022 L1 and DRS was 3.2 ± 0.2. After Mch, Airway Closure increased (25.6 ± 21–68%, p = 0.04), and correlated with DRS (r2 = 0.82, p = 0.013). Scond did not relate to Airway Closure (r2 = 0.19, p = 0.378).

Conclusions Airway closure occurs after high dose Mch in non-asthmatic subjects and correlates with DRS. VSPECT/CT images show the airway closure to be non-basal and diffuse. Consequently, widespread airway closure is not only a feature of asthma, but rather also occurs in non-asthmatic airways with increased sensitivity. Ventilation heterogeneity does not relate to airway closure in non-asthmatic subjects.

Support The Barbara Dunn Trust Fund and NHMRC #1457346.

Conflict of Interest No.
CIGARETTE SMOKE ATTENUATES ALVEOLAR MACROPHAGE FUNCTION BY SELECTIVELY INDUCING PROTEIN CARBONYLATION

STEVEN BOZINOVSKI1, ROSS VLAHOS1, Y LIN ZHANG1, GARY P ANDERSON1,2
1Department of Pharmacology, and 2Medicine, The University of Melbourne, Australia

Cigarette smoke exposure is a major risk factor in susceptibility to serious respiratory infections, particularly in children. Although smoke exposure is known to alter immunity to infection, the underlying molecular mechanisms are not well understood.

Aim Identify regulatory mechanisms that drive impaired macrophage function.

Methods The MH-S alveolar macrophage cell line was exposed to a short 15 minute pulse of Cigarette Smoke Extract (CSE) prior to challenge with LPS or FITC-E.coli.

Results CSE blocked phagocytosis of E.coli and inhibited LPS activation of canonical and alternative TLR4 pathways. Both NFkB translation and transactivation pathways were compromised as CSE inhibited IkB degradation and p65 phosphorylation. CSE also blocked AP-1 activity by inhibiting p38, but not JNK or Erk1/2. We next excluded LPS tolerance mechanisms involving receptor internalisation or induction of negative regulators. As free radical species are abundant in CSE we investigated their role using the potent scavenger, reduced glutathione (GSH). Since GSH restored all responses, we screened a panel of oxidative/nitrosative stress markers and identified carbonylation as the only CSE inducible marker. Oxyblot analysis confirmed that CSE potently introduced carbonyl groups to many proteins (30–100 kDa range) in a dose and time dependent manner that inversely correlated with TNF-alpha expression. CSE treated macrophages also displayed heavily carbonylated pseudopodia that was reversed by GSH as determined by immunocytochemistry (ICC).

Conclusion Macrophage sensing and ingestion of pathogen is compromised by protein carbonylation of the outer membrane vesicle phagocytic receptors cluster and also penetrates cytoplasmic regions where signalling moieties reside. Therefore, targeting single pathways will not restore macrophage function due to the global nature of CSE mediated carbonylation.

Support NHMRC.

Conflict of Interest Nil.

TO 032

TRANSFORMING GROWTH FACTOR-β (TGF-β) INDUCES GLUCOCORTICOID-RESISTANCE IN HUMAN AIRWAY EPITHELIAL CELLS

S SALEM, T HARRIS, J MS LIAN, M YS LI, M SCHULIGA, AG STEWART
Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia

Background Asthma shows varying levels of resistance to effective treatment by glucocorticoids. In studies on TGFβ-induced epithelial mesenchymal cell transition (EMT) using the A549 type II human epithelial cell line, the regulatory effect of the glucocorticoid, dexamethasone (Dex, 0.1–1000 nM) on interleukin-1α (IL-1α)-induced interleukin-8 (IL-8) generation was markedly reduced in the presence of TGFβ at 400 pM (n = 7; p < 0.05).

Aim Our studies were designed to characterise the mechanism of the glucocorticoid resistance.

Results The resistance induced by TGFβ was concentration dependent (4–400 pM); a glucocorticoid class effect as it also occurred with budesonide; independent of EMT; it was observed within 4 hours, whereas EMT requires 3 days; also observed in the central airway epithelial cell line, BEAS-2B and passaged, primary bronchial epithelial (NHBE) cells. Treatment of A549 cells with SB431542, a TGFβ receptor type 1 kinase inhibitor, restored the Dex inhibitory effect on IL-8 release (from control 17 ± 7% to 45 ± 7%, inhibition in SB431542 1 μM, n = 9; p < 0.05). In A549 cells transfected with a glucocorticoid response element (GRE)-driven reporter gene, TGFβ (40 pM) inhibited the GRE response to Dex (0.1–1000 nM) by more than 80%. In addition, TGFβ impaired Dex regulation of the GRE-dependent gene, IκB.

Conclusion TGFβ is a candidate mediator of glucocorticoid resistance.

Support Nil.

Nomination Nil.

Conflict of Interest Nil.

TO 031

PGE2 SELECTIVELY UP-REGULATES PROSTAGLANDIN E2 SYNTHASE AND EP RECEPTORS IN HUMAN EPITHELIAL CELLS

S BALTIC, MP DUNN, LP CHUNG, PJ THOMPSON
Lung Institute of Western Australia, University of Western Australia, Australia

PGE2 plays a protective role in asthma by inhibiting airway inflammation. It is predominantly produced by epithelial cells in response to pro-inflammatory stimuli and acts as an autocrine and paracrine mediator. Prostanoids have been shown to regulate expression of enzymes involved in their metabolism, as well as expression of their receptors and that regulation is tissue- and cell-specific. Despite its importance, however, mechanisms underlying the regulation of expression of enzymes involved in PGE2 metabolism and its receptors in human lung epithelial cells have remained elusive. Therefore, we hypothesised that PGE2 regulates expression of PGE2 synthase 1 (PGES1) and its receptors (E-Prostanoid (EP) 1–4) in human airway epithelial cells.

Methods Real Time RT PCR and FACS analysis were used to assess mRNA and protein expression, respectively in human airway epithelial cells 16 HBE before and after PGE2 stimulation.

Results PGE2 up-regulates PGES1 in time and concentration dependent manner. In addition, EP receptors (EP1, EP2 and EP4) were up-regulated following PGE2 stimulation at mRNA level. However, these receptors show different dynamics in expression. While EP1 reaches peak in mRNA expression at 6 hour, peak expression for EP2 and EP4 is at 12 hour post stimulation. In terms of protein expression, preliminary results show transient increase of EP1 and EP2 receptors, while EP3 receptor is down-regulated at 24 hour following PGE2 stimulation.

Conclusion PGE2 differentially up-regulates PGES1 and EP receptors in human lung epithelial cells. This may in turn alter PGE2 production and autocrine activation with potential implication on the function of epithelial cells, which is important in modulation of immune response in asthma and lung inflammatory diseases.

Conflict of Interest Nil.

TO 030

MONOCYTE DERIVED DENDRITIC CELLS FROM COPD PATIENTS AND THEIR THERAPEUTIC POTENTIAL

Xiaoyan HE, SG Gangireddy, PGIBSON, PWARK
Department of Respiratory and Sleep Medicine, HMRI, University of Newcastle, New South Wales, Australia

Monocyte derived Dendritic Cells (DCs) have been recognised for their potential role in immune responses and their functional relevance with regard to adaptive immune responses although more detailed knowledge of DC biology in human airways is required. The objective of this study was to modify the monocyte derived DCs from peripheral blood and direct the cells via exposure to pro-inflammatory conditions as seen in COPD, with a view to identifying novel targets for cellular therapy. We characterised monocyte-derived DCs in culture and evaluated the effects of human rhinovirus infected bronchial epithelial cells, pI:C (polyinosine-polycytidyllic acid) and BC (bacterial extract) on directing DC differentiation, and in particular, an impaired CD8 effector function in COPD patients. Our DC culture results showed that both MHC-I and MHC-II expression on DCs from COPD were significantly down-regulated compared to healthy controls, which could affect MHC restricted Ag presentation, and lead to a failure to activate responder T cells. Furthermore, we tested the capability of monocyte-precursors to differentiate into functional DCs. Only a very small percentage of cultured monocytes from patients with COPD was capable of differentiating into mature DCs, compared with healthy controls. During DC activation, there was up-regulation of co-stimulatory (CD80/86) and maturation markers (MHCs), enabling DCs to activate naive T cells into mature DCs, compared with healthy controls. Our preliminary data indicated that this activation leads to the generation of effector T cells, further study is needed. Defective DC activation of T cells may underlie poor T cell responsiveness in COPD in response to inflammation and may, in part, determine the response to therapy. Our data suggest a promising role in vitro for pharmacologic treatment as a means of generating functional DCs and will further stimulate speculation regarding their potential clinical application.

Support NHMRC Australia.

Conflict of Interest No.
A ZAFAR USMANI1, JEN NI CHENG2, BRIAN J SMITH1,3, KRISTIN V CARSON3

1Department of Respiratory Medicine, 2Department of Medicine, and 3Clinical Practice Unit, The Queen Elizabeth Hospital, Adelaide, SA, Australia

Introduction Chronic obstructive pulmonary disease (COPD) is characterised by worsened airflow obstruction, exercise performance and overall health. It is also associated with much morbidity, mortality and health care costs. We sought to evaluate the effectiveness of outreach nursing programmes for COPD patients.

Methods We carried out a search in the Cochrane Airways Group Specialised Register of Trials (December 2008). We also reviewed study references and made enquiries to authors regarding other studies. Only randomised control trials were included. The intervention was a nurse visiting COPD patients in their homes, providing support, education, monitoring patient status and providing liaison with physicians. Studies in which the intervention was physical training were not included.

Results Eight RCTs/COTs were included. Pharmacotherapy showed nil significant effect to control anxiety (SMD of -0.33, p value 0.16, n = 76), however, showed significant benefit in controlling depression symptoms (SMD -0.57, p value 0.02, n = 76) in COPD over short-term. On the other hand, CBt was found to be beneficial in controlling both anxiety (MD -5.0, p value 0.04, n = 30) as well as depression (MD -7.30, p value 0.02, n = 30) in COPD over short term.

Conclusion CBt is superior as compared to pharmacotherapy over short-term to control anxiety and depression in COPD.

Support Australasian Cochrane Airways Group.

Nomination Nil.

Conflicts of Interest No.

Cystic Fibrosis SIG Oral Session 1

CLONAL PSEUDOMONAS AERUGINOSA (PA) IN AUSTRALIANS WITH CYSTIC FIBROSIS (CF)

TJ KIDD 1, 2, KA RAMSAY Y1, 2, H HUI1, PTP SYE1, GB MARKS3, CE WAINWRIGHT4, PJ GLASBON5, BR ROSE2, C HARBOUR1, K GRAPRAK6, SC BELL 7, 8 AND ACPINCF INVESTIGATOR STUDY GROUP

1School of Medicine, University of Queensland, Australia, 2QCMRI, Royal Children’s Hospital, Brisbane, Australia, 3Sydney University, Australia, 4Royal Prince Alfred Hospital Campdown, New South Wales, Australia, 5Woolcock Institute, Sydney, Australia, 6Royal Children’s Hospital, Melbourne, Australia, and 7The Prince Charles Hospital, Brisbane, Australia

Background The emergence of clonal Pa and associated risk of cross-infection is a major cause for concern in CF centres in several countries, including Australia. Two clonal Pa strains (AES1 and AES2) have been detected in several eastern Australian CF centres, but the overall prevalence of these and other strains throughout Australia remains unknown.

Methods A cross-sectional study involving 18 CF centres (8 paediatric, 9 adult, 1 combined) was performed. In total, 638 sputum-producing children and adults with documented Pa infection provided two sputum samples, 6 months apart, and 3 Pa isolates from each sample were genotyped by repPCR-based cluster analysis.

Results Collectively, AES1 and/or AES2 strains were identified in 44% of Pa infected CF patients and found in all participating CF centres. Several other minor clonal strains were also identified in many centres. Only 25% of patients were infected with unique (non-clonal) Pa strains and 8% of patients were infected with more than one clonal strain.

Conclusion Clonal Pa strains are common in Australian patients with CF. There is marked variation in prevalence of both major and minor clonal strains between CF centres and within states. Longitudinal analysis of the clinical impact of clonal Pa infection is urgently required so as to allow an evidence-based approach to patient management and infection control.

Funding Support NHMRC, TPCH Foundation, ACFRT, Rotary Australia.

Nomination Nil.

Conflict of Interest No.

DEFICIENCY OF THE GLUTATHIONE ANTI-OXIDANT DEFENCE SYSTEM IN YOUNG CHILDREN WITH CYSTIC FIBROSIS (CF)

PETER D SLY1, CATHERINE L GANGELL1, ANTHONY KETTLE2 ON BEHALF OF AREST CF CHILDREN WITH CYSTIC FIBROSIS (CF)

1Telton Institute for Child Health Research, Perth, Australia, and 2Free Radical Research Group, Department of Pathology, University of Otago, Christchurch, New Zealand

Reduced glutathione (GSH), a major component of anti-oxidant defence, is transported into the lung via CFTR. GSH protects against Myeloperoxidase (MPO)-induced oxidative stress by undergoing oxidation to GSSG and GSA. Excess MPO induces chlorination of tyrosine (3-CL-Tyr) via the production of hypochlorous acid. We undertook a cross-sectional survey of young children with CF participating in our early surveillance program that includes annual bronchoalveolar lavage (BAL) and chest CT scan. Markers of neutrophilic inflammation and of the GSH system were determined in BAL and the presence of bronchiectasis (B) and air trapping (AT) determined on chest CT. 188 samples from children with CF (mean age 3.35 years) and nine samples from children without CF (mean age 6.13 years) undergoing investigation for chronic respiratory symptoms (NCF) were studied. CF samples had more neutrophils than NCF samples (mean 42.6 vs. 3.0 x 10⁹/ml fluid retrieved), more MPO (239.4 vs. 0.31 ng/ml, p = 0.001), lower levels of GSH (1393.7 vs. 3285.1 nm, p < 0.001) and a trend for a lower GSH/GSSG (46.2 vs. 95.2, p = 0.07). Within the CF samples levels of MPO correlated with GSSG (p = 0.01) and GSA (p < 0.001) and a 3-C-Try correlated with GSSG (p = 0.005) and GSA (p = 0.01) indicating neutrophilic inflammation exceeding anti-oxidant defence capability. However, after controlling for age and the presence of free neutrophil elastase, there were no relationships between GSH, GSSG or GSA and either B or AT. While our data demonstrate GSH deficiency and defective anti-oxidant defence, these are not related to structural lung disease. Longitudinal studies will be required to determine the impact of GSH deficiency in the initiation and progression of lung disease in CF.

Support - NHMRC, ACFRT, MCRI and PMH Foundation (Aust).

Conflict of Interest No.

© 2010 The Author(s).

The Thoracic Society of Australia & New Zealand Annual Scientific Meeting 2010
A SURVEY OF P. AERUGINOSA DETECTION AND ERADICATION PRACTICES AMONGST PAEDIATRIC CF CENTRES IN AUSTRALASIA

TA DOUGLAS1,2, C GANELL1, C DUNFORD1, PD SLY1,3 ON BEHALF OF ACREST CF 1Princess Margaret Hospital for Children, and 2Telethon Institute for Child Health Research, Perth, Western Australia, Australia

Introduction There are no Australasian guidelines for the detection and eradication of Pseudomonas aeruginosa in preschool children with CF. The optimal eradication regimen for preschool children remains uncertain.

Aims To develop Australasian guidelines for P. aeruginosa detection and eradication in preschool children with CF based on a national multi-centre randomized controlled trial.

Methods An electronic web-based questionnaire was sent to every tertiary paediatric CF centre in Australia to determine current detection and eradication practices.

Results All eleven centres completed the survey. A combination of positive oropharyngeal culture (OPC) and confirmatory bronchoalveolar lavage (BAL) culture was the most common method of P. aeruginosa detection (55%), with surveillance frequencies varying; annually (n = 3, 27%), every clinic visit (3, 27%) and clinically indicated (4, 36.4%). Eradication treatment was instigated on one positive culture (OPC n = 5, BAL culture n = 5 centres) for P. aeruginosa at any bacterial density (50%) or bacterial density >105 cfu/ml (40% of centres). Eradication regimens varied between centres with most (51%) using intravenous antibiotics either alone (n = 1); in combination with 3–12 months nebulised antibiotics (n = 3); or with 1–3 months nebulised and oral antibiotics (n = 5). Choice of regimen was influenced by clinical status in three centres. Two centres used combinations of inhaled and oral antibiotics alone. Failure to eradicate resulted in a change in treatment in 64% of centres. Inhaled tobramycin 80 mg (28 days and 12 months) was considered the least acceptable regimen for preschool children in terms of efficacy and burden of care with most centres. Inhaled tobramycin 80 mg (28 days and 12 months) was considered the least acceptable regimen for preschool children in terms of efficacy and burden of care.

Conclusion This survey supports a call for evidenced based Australasian guidelines for the detection and eradication of P. aeruginosa in preschool children. Comparative trials of the most favoured eradication regimens would enhance this process.

Conflict of Interest No.

Support Nil.

Nomination Nil.

A RETROSPECTIVE REVIEW OF PATHOGENS INFECTING THE LUNGS OF ADULTS WITH CYSTIC FIBROSIS

KA RAMSAY1,2, TJ KIDD1,2, MW FRANCE1, PJ MASEL2, SC BELL1,3 1School of Medicine, University of Queensland, Queensland, Australia, 2Telethon Laboratory, QCMRI, Royal Children’s Hospital, and 3Adult Cystic Fibrosis Centre, The Prince Charles Hospital, Brisbane, Australia

Background Changing microbiology patterns in Australian adults with CF is not well understood. To determine the prevalence over an eight year period of bacterial pathogens infecting the lungs of adult patients with CF attending an Adult CF Centre.

Method A retrospective study of expectorated sputum cultures at TPCH was undertaken. The results from all sputum’s collected from 2001 through to 2008 were included. The pathology information management system was used to collect the data.

Results Over the eight year period a total of 359 adult CF patients (female 42.7%) were treated at TPCH. Overall, the most prevalent bacterial pathogen encountered was Pseudomonas aeruginosa (Pa) (74.0%) and this decreased by ~1% per year from 2002 to 2008. Conversely, the rate of patients remaining free of Pa infection has increased (18.2% to 27.0%). Methicillin Sensitive Staphylococcus aureus (MSSA) was detected in 38% of patients and remained stable over time. Fungal infection with Aspergillus species was common and has decreased by 9% over the eight years. Infection with Sten. maltophilia and Ac. xylosoxidans remained constant, and detected in less than 10% of patients. The prevalence of MRSA decreased over the study (9.3% to 3.4%). The number of sputum samples collected decreased from 7.5/patient/year in 2001 to 5.0 patient/year in 2008. The proportion of patients who submitted >1 sputum sample was similar each year. In 2008, 72.2% of patients had >2 and 52.9% had >4 sputum samples submitted.

Conclusion The most prevalent organism in this large adult CF setting was Pa. Decreasing rates of Pa and MRSA have been seen. The percentage of adults with ≥1 respiratory sample collected for culture per year is below that reported in the US but many of these patients are non-sputum producers or rarely attend clinic.

Funding Support NHMRC, TPCH Foundation.

Nomination Nil.

Conflict of Interest No.

CLOSTRIDIUM DIFFICILE COLITIS IS ASSOCIATED WITH CIPROFLOXACIN AND PROTON PUMP INHIBITOR USE IN CYSTIC FIBROSIS PATIENTS

ANNA TAI1, TIMOTHY KIDD2,3, KAY RAMSAY1,2, ANGELA MATSON1, SCOTT BELL1,2, KAREN HERD1, ANTHONY BURKE1, MEGAN FRANCE1, KAREN HERD1, ANGELA MATSON1, SCOTT BELL1,2

1Adult Cystic Fibrosis Centre, The Prince Charles Hospital, Brisbane, Australia, 2School of Medicine, University of Queensland, Brisbane, Australia, and 3QCMRI, Queensland Children’s Medical Research Institute, Royal Children’s Hospital, Brisbane, Australia

Background Clostridium difficile colitis remains a rare but potentially life threatening complication in CF patients particularly in the post lung transplant setting.

Aim (1) To review the incidence of C. difficile colitis among non-transplant and post-lung transplant CF patients attending our centre. (2) To identify the clinical features in CF patients presenting with CDAD.

Method Retrospective study on C. difficile toxin status in all fecal samples collected in CF patients between 2000 to 2009 was reviewed. Patients with positive C. difficile toxin were identified as index cases, those with negative samples were selected as control cases.

Results Two hundred and twenty-three fecal samples were collected from 74 CF patients. Nineteen CDAD cases were identified in 15 patients including 13 non-transplant and two post-transplant patients. Nineteen had mild colitis and two had fulminant colitis. Incidence density of CDAD in non-transplanted CF patients (2.8/100 000 patient-days) is comparable to the transplant group (two episodes/100 000 patient-days). Time to diagnose CDAD among post-transplant patients is shorter than non-transplant patients (1 vs. 6 days). A significantly higher proportion in the CDAD group had recent Ciprofloxacin when compared to controls (38.5% vs. 0%, p-value: 0.0006). A significantly higher proportion of patients in the CDAD group are currently on gastric suppression therapy than control group (92% vs. 59%, p-value: 0.03).

Conclusion The incidence density of CDAD is comparable between pre and post transplant CF patients. CDAD is more common among patients with prolonged Ciprofloxacin treatment and concurrent gastric acid suppression. Improving patient awareness by optimizing patient education particularly during prescription of Ciprofloxacin or gastric acid suppression treatment can prompt early presentation and management of CDAD.

Conflict of Interest No.
OUTCOME IN MAJOR (MASSIVE AND SUB-MASSIVE) PULMONARY EMBOLISM

G KARMAKAR1, D MILNE2, M WILSHER1
1Green Lane Respiratory Services, and 2Department of Radiology, Auckland City Hospital, Auckland, New Zealand

Introduction

Major (massive or submassive) pulmonary embolism (PE) is a potentially lethal condition particularly if associated with cardiogenic shock. Thrombolysis is accepted as standard treatment for massive PE with hypotension, but it carries substantial risk of bleeding and risk may outweigh the benefit in submassive PE. The objective of this study was to examine risk factors for and the outcome of major PE in this institution.

Methods

We collected data retrospectively from all patients with MPE requiring ICU admission in Auckland City Hospital (ACH) over a 5 year period. The primary outcome variable was mortality with secondary variables including precipitating factors and morbidity.

Results

Twenty-eight subjects (12 massive PE) were identified. Eight of 12 with massive PE were thrombolysed and four were treated conservatively with 30 day mortality of 50% and 25% respectively. Twelve of 16 patients with submassive PE received thrombolysis with no mortality. Significant bleeding complications were reported in four of 20 thrombolysed patients. Prior surgery without DVT prophylaxis was identified as a precipitant in 10 patients.

Conclusions

Massive PE carries significant mortality irrespective of thrombolysis but such treatment appears safe in submassive PE. In spite of evidence of efficacy, failure to offer prophylaxis of DVT in the perioperative setting appears an ongoing risk factor for major PE.

Conflict of Interest
Nil.

RSV AND HUMAN METAPNEUMOVIRUS ARE NOT ASSOCIATED WITH OBLITERATIVE BRONCHIOLITIS OR INFERO SURVIVAL POST LUNG TRANSPLANTATION

PETER MA HOPKINS, FORNA D KERMEEN, HELEN SEALE, TRISH M LEISFIELD, STEPHANIE T YERKOVICH, DANIEL C CHAMBERS
Queensland Centre for Pulmonary Transplantation and Vascular Disease, the Prince Charles Hospital, Brisbane, Queensland, Australia

Purpose

Seasonal onset of Bronchiolitis obliterans syndrome (BOS) in lung transplant recipients suggests respiratory viral infection as an initiating agent. Respiratory syncytial virus (RSV) and its relative human Metapneumovirus (hMPV) are associated with acute graft dysfunction, although limited data exists on the subsequent risk of BOS and survival longer term. Our aim was to describe the long term outcome of a hMPV and RSV cohort from a single institution.

Methods and Materials

Lung transplant patients between January 2002 and March 2008 with symptoms of respiratory viral infection underwent nasopharyngeal aspirates (NPA). Individuals with hMPV or RSV and allograft dysfunction received a minimum of 7 days intravenous ribavirin and pulse steroids. Intragam (human immunoglobulin, CSL) was reserved for intractable graft dysfunction.

Results

Fifty-one patients had 459 visits for NPA studies with 58 samples (12.7%) PCR positive for RSV n = 34 and hMPV n = 24. Fourteen patients experienced mild upper respiratory tract symptoms only. Median decline in FEV1 relative to baseline for hMPV at followup 27.5 ± 15 months was 1.8% (-7.47–2.59, CI), compared with 11% (-13.89–4.68, CI, p < 0.05) for RSV at followup 23.6 ± 16. There was no significant effect on time for BOS 1 to BOS 3 progression or survival compared with the non viral cohort n = 114. Kaplan–Meier BOS free probability for the RSV and hMPV group confirmed no difference from the non viral cohort (p = 0.559 and 0.777 respectively)

Conclusion

With an aggressive treatment regimen incorporating ribavirin, RSV and hMPV are relatively benign infections and cause no long term impact on allograft function.

Conflict of Interest
No.

REPORT OF THE AUSTRALASIAN REGISTRY NETWORK FOR ORPHAN LUNG DISEASE (ARNOLD) - THE FIRST QUARTER

ADAM JAFFE1, ADAM LAVERY2, DANIEL CHAMBERS3, MARGARET WILSHER4, JACOB TSWIS5, ELI GABBAY6, JAN GLASPOLE7
1Sydney Children’s Hospital, Randwick, 2Great Ormond Street Hospital for Children, London, 3Queensland Centre for Pulmonary Transplantation & Vascular Disease, 4Auckland City Hospital, Auckland, 5Starship Children’s Hospital, Auckland, 6Royal Perth Hospital, Perth, and 7The Alfred Hospital, Melbourne, Australia

Introduction

There is a need to improve general understanding of the epidemiology, pathophysiology, outcome and therapies for rare (orphan) lung diseases.

Aims

1) To establish an electronic reporting registry of orphan lung diseases in Australia. 2) To provide a useful resource for physicians and patients.

Methods

A website (www.arnold.org.au) was developed containing information on 30 orphan lung diseases, useful links and an on-line patient discussion forum. TSANZ members were invited to participate in reporting cases electronically by a quarterly email reminder.

Results

Ethical approval in New Zealand is still awaited. The first email was sent on 01/07/2009 to 707 TSANZ members (537 physicians, 101 advanced trainees, 69 OLV SIG members). Seventy-eight responses were received; 48 had no cases to report. Of the 30 reported cases, 11 had patient details: TOF (one, old), Congenital cystic lung lesions (two, both new), Lobar emphysema (one, new). Growth in CPAM (two, both new), Haemossodesis (one), Wegener’s (one), Churg-Strauss (one, new), OB (one, new), COP (seven, one old, six no details). Drug eosinophilia (one), Extrinsic allergic alveolitis (four, one new, three no details), PAP (one), Papillomatosis (two), PCD (one, old). The forum has three registered members and no posted discussions.

Conclusion

ARNOLD provides a means by which data on patients with rare lung diseases can be collected. The reporting of patient details needs to be improved. The site also acts as an information resource and a potential support network for patients and families that requires more publicity.

Funded by The Australian Lung Foundation

Conflict of Interest
None.

AMERIALIZATION OF MONOCROTALINE INDUCED PULMONARY ARTERIAL HYPERTENSION BY TARGETED UPREGULATION OF BONE MORPHOGENETIC PROTEIN RECEPTOR TYPE-2 IN THE PULMONARY ENDOTHELIUM

ANN M REYNOLDS1, MARK D HOLMES1, NICHOLAS W MORELL2, SERGEI DANILOV3, PAUL N REYNOLDS3
1Department of Thoracic Medicine, Royal Adelaide Hospital, Hanson Institute, Adelaide, SA, Australia, 2University of Cambridge, Cambridge, UK, and 3University of Illinois at Chicago, USA

Mutations in the bone morphogenetic protein receptor type 2 (BMPR2) are implicated in pulmonary arterial hypertension (PAH). Thus, gene therapy using a normal BMPR2 gene could be therapeutic. We previously developed a unique system for the upregulation of pulmonary endothelial BMPR2 gene expression in rats using adeno viral (Ad) vectors linked to a pulmonary endothelial targeting conjugate (Fab-S99); and showed that this ameliorated hypoxia-induced PAH. The development of vascular inflammation and remodelling following monocrotaline (MCT) administration is an alternative well-established animal model of PAH. We hypothesised that our novel treatment could reverse PAH in response to MCT.

Methods

Sprague-Dawley rats were assigned to three groups (two MCT injected and one saline control). Ten days after MCT, rats were given a tail vein injection of Ad Tre Luc (irrelevant viral control) or Ad BMPR2, each with Fab-S99. After a further 8–10 days, PAH was assessed.

Results

Numbers in parenthesis indicate % difference. Compared to MCT treated rats that received control vector, those receiving BMPR2 gene delivery had significantly lower right ventricular systolic pressures (36%), lower pulmonary vascular resistance (47%), less right ventricular hypertrophy (21%) and improved cardiac output (21%) and cardiac index (25%) (P < 0.05, ANOVA and Holm-Sidak multiple comparison test).

Conclusion

In our in vivo model system, over-expression of pulmonary endothelial BMPR2 ameliorated further development of MCT-induced pulmonary hypertension, suggesting this approach may have value in PAH secondary to inflammatory vascular remodelling.

Support

NHMRC and NHF.

Conflict of Interest
None.

Nomination
Nil.

© 2010 The Author(s)

Journal Compilation © 2010 Asian Pacific Society of Respirology
THE COMBINED AUSTRALIAN EXPERIENCE WITH HUMAN SWINE INFLUENZA H1N1 IN LUNG TRANSPLANT RECIPIENTS

B NG1, A GLANVILLE2, J D COSTA2, G SNELL2, M MUSK1, M HOLMES2, D CHAMBERS2, P HOPKINS1

1The Prince Charles Hospital, Queensland, Australia, 2St Vincents Hospital, New South Wales, Australia, 3The Alfred Hospital, Victoria, Australia, 4Royal Perth Hospital, Western Australia, Australia, and 5Royal Adelaide Hospital, South Australia, Australia

Australia was affected by the Human Swine Influenza (H1N1) pandemic during the winter season. Incidence was estimated at 20% of the population with 178 deaths. Respiratory viruses have been shown to cause significant allograft dysfunction in lung transplant (LT) recipients.

Aim To report on the impact of H1N1 on LT recipients in Australia.

Methods A retrospective audit across the five LT programs in Australia between May and September 2009 of confirmed H1N1 cases. Data collected included demographics, clinical presentation, management and outcomes.

Results Twenty-three H1N1 cases of mean ± SD age 41.7 ± 7 years were confirmed from 826 known LT recipients (incidence 2.8%). Cases peaked in New South Wales (n = 10) and Queensland (n = 6) consistent with epidemiology in the general community. Clinical manifestations included allograft dysfunction in 17 of 23 (73.9%), upper respiratory tract symptoms only 26.1%, fever 52.6%, myalgias 68.4%, hypoxia 26.3% and radiological infiltrates 42.1%. Mean hospitalisation was 11 ± 9.1 days. Cases were diagnosed in the hospital setting (n = 16) and in the community (n = 7). Other risk factors included obesity n = 7, diabetes n = 4 and malignancy n = 3. Transplant consisted of osteoarticular 75 mg bd initially for 5 days in all 23 cases, extension beyond 5 days n = 14 (mean 8 ± 1.4 days) due to ongoing symptoms, steroid therapy n = 17, mechanical ventilation n = 1 and non-invasive support n = 2.5 patients (21.7%) have not returned to baseline lung function and there were four deaths (BOS grade three n = 3 and grade 0 n = 1 prior to diagnosis).

Conclusions The incidence of H1N1 in the Australian LT population was less than that estimated for the broader community but mirrored the geographical distribution. The majority experienced allograft dysfunction with most deaths recorded in those with preexisting BOS grade 3. We recommend H1N1 vaccine (Panvax, CSL) for all LT recipients. Conflict of Interest No.

THE INNATE IMMUNE RESPONSE TO RHINOVIRUS IN BRONCHIAL EPITHELIAL CELLS IS PRIMORDIALLY CONTROLLED BY SIGNALLING INITIATED VIA MDA-5

SREYAVAMASINGE1, GANGIREDDY1, KRISTY PARSONS2, MELINDA TOOZE1, PETER AB WARK1,2

1Centre for Asthma and Respiratory Disease, Hunter Medical Research Institute, University of Newcastle, New South Wales, Australia, and 2Department of Respiratory and Sleep Medicine John Hunter Hospital New South Wales, Australia

Rhinoviruses (RV) are the major cause of a common cold and the most common acute triggers of asthma and Chronic obstructive pulmonary disease (COPD). Bronchial epithelial cell (BEC) are the primary site of RV infection which induces antiviral Type I and Type III interferons (IFN). Much is unknown as to what factors determine the molecular mechanisms of the BEC antiviral response to RV infection.

Aim To characterise innate antiviral response to RV infection in BEC's

Methods We investigated the expression patterns and roles of TLR-3, MDA-5 and RIG-I by using the siRNA knockdown for each. Type I interferon responses were measured, with the release of IFN-β and phosphorylation(p) of STAT-1 by western blot and IFN stimulated gene CXCL10. Following successful knockdown, BEAS-2B cells were infected with RV-1B and RV-43 (MOI = 20) We also used BX795, a potent and relatively specific inhibitor of TIK1 and IKK and p38 inhibitor SB220025 to further elucidate innate signalling pathways.

Results RV infection alone led to induction of, pSTAT-1, CXCL10 and release of IFN-α. Silencing of TLR-3 and RIG-I alone had no effect. When combined both siRNA for TLR-3 and MDA-5 had no additional effect. Treatment of BECs with BX795 inhibited the production of Type I IFN but only partially inhibited IFN-γ release. Blockade of p38MAPK however led to substantial blocking of IFN-α release and also led to a marked reduction in the typeIIIFN response.

Conclusion We found that following infection with RV, BECs Type I IFN responses, pSTAT-1 induction as well as release of IFN-α was dependent on MDA-5. Blockade of TLR-1/9KK by BX795 reduced Type I IFN responses, but IFN-γ release was only partially inhibited Blockade of p38MAPK resulted in suppression of both IFN-γ and type IFN, suggesting this pathway is crucial in the antiviral response to RV infection. Conflict of Interest None. Funding NHMRC Australia

Respiratory Infectious Diseases SIG Oral Session 1

ONE YEAR OF WEEKLY AZITHROMYCIN PROVIDES NO BENEFIT FOR INDIGENOUS AUSTRALIANS LIVING WITH COPD IN REMOTE AUSTRALIA

GIANNEK MAGUIRE1,2, BARBARA MOLANUS3, MARIA TCHAN2, BART CURRIE2

1School of Medicine & Dentistry, James Cook University, Queensland, Australia, and 2Menzies School of Health Research, Darwin, Northern Territory, Australia

COPD is an important contributor to the mortality and disability ‘gap’ between Indigenous and non-Indigenous Australians. We have previously demonstrated that the concentration of respiratory bacterial pathogens in sputum is associated with acute exacerbation frequency and airway inflammation. We aimed to determine if regular azithromycin would reduce acute exacerbation frequency and health care utilisation in this setting.

Methods A randomised placebo-controlled trial of one year of weekly supervised 1 g azithromycin in 105 adult (>18 years) Indigenous Australians with COPD (FEV1 <80% pred and FEV1/FVC ratio <0.7, <12% improvement with bronchodilators, no evidence of bronchectasis) living in nine remote communities in the northern ‘Top end’ of the Northern Territory. Endpoints included self-reported acute exacerbations (AE) and respiratory and all cause health care utilisation.

Results Five hundred and thirteen remote residents were screened with 105 enrolled in the trial. Randomisation was successful. Weekly azithromycin was not associated with any difference in self-reported acute exacerbation frequency and respiratory and all cause health care utilisation overall both on an intention-to-treat basis and when controlling for adherence. The study had a power of 76% to detect a halving of AE frequency with azithromycin.

Conclusions We have not shown any benefit from long-term azithromycin for Indigenous Australians with COPD. Despite limited numbers the study had sufficient power to detect a clinically significant effect. The priorities for dealing with the burden COPD places on Indigenous Australian health should be addressing poverty, housing and tobacco, ensuring vaccination coverage, and high quality, accessible and appropriate diagnosis (especially spirometry) and management of established disease.

Support NHMRC and CRC for Aboriginal Health. Nomination Nil. Conflict of Interest No.
CIGARETTE SMOKE EXTRACT IMPAIRS EPITHELIAL CELL ANTIVRAL RESPONSE TO RHINOVIRUS INFECTION

KIRSTY PARSONS1, MELINDA TOOZE1, SRINIVASA GANGIREDDY1, PETER AB WARK1,2
1Centre for Asthma and Respiratory Disease, Hunter Medical Research Institute, University of Newcastle, New South Wales, Australia, and 2Department of Respiratory and Sleep Medicine, John Hunter Hospital, New South Wales, Australia

Subjects with chronic obstructive pulmonary disease (COPD) are exposed to frequent infections and increased risk of severe exacerbations. Infection with rhinovirus (RV) is known to trigger acute exacerbations and subjects with COPD and asthma are particularly susceptible.

Aim To assess the response of bronchial epithelial cells to RV infection following exposure to CSE.

Methods A human bronchial epithelial cell (BEC) line (Calu-3) and primary (pBEC) were grown to confluence. Cells were then exposed for 24 hour to CSE (10% no filter). Cells were then infected with RV43 or RV1-B (MOI = 20) or treated with poly(I:C) (100 μg/ml). Virus replication was measured by cell titration assay. Following infection, IL-6, CXCL-8, CXCL-10, IFN-α, RIG-I, RIG-I and MDA-5 mRNA induction was measured by qPCR. IL-6, CXCL-8, CXCL-10 were measured using cytometric bead array and flow cytometry. Supernatants and whole cell lysates were collected for interferon IFN-α and IFN-β. Similarly, CXCL-8 and IL-6 showed suppression with CSE exposure in pBECs, though not to the same extent as the antiviral response. Paradoxically, CSE exposure reduced IFN-α response.

Conclusions Exposure of BECs to CSE appears to specifically impair the innate antiviral response of infected BECs as well exacerbate the inflammatory response to infection.

Support NHMRC Australia.

Conflict of Interest None.

PATIENTS WITH NON-TUBERCULOUS MYCOBACTERIAL LUNG DISEASE (NTMLD) DO NOT EXHIBIT POOR TH1 CELLULAR RESPONSES

ANDREW LIM1, CATIE ALLISON1, GRANT WATERER2, PATRICK PRICE1
1School of Pathology and Laboratory Medicine, and 2School of Medicine and Pharmacology, University of Western Australia, Nedlands, Western Australia, Australia

Introduction and Aims The incidence of NTMLD is increasing markedly in Australia. It is not known why patients with NTMLD are susceptible to these organisms, as most patients do not have identifiable risk factors or a documented immune defect. As cell-mediated immunity is crucial for control of mycobacterial disease, we assessed whether NTMLD is associated with diminished Th1 immune responses.

Methods Our study cohort consisted of 27 patients with NTMLD at different stages of treatment, 15 offspring of 12 patients and 21 unrelated healthy controls. Plasma levels of CXCL10 and IL-18 were analysed on all subjects by Cytometric Bead Array or ELISA. In a subset of subjects, PBMC were assessed for production of IFNg, IL-5, IL-17 and IL-10 in response to stimulation with mitogen (SEB) and purified protein derivative (PPD). All data was analysed using non-parametric statistical tests.

Results Plasma levels of both CXCL10 and IL-18 were higher in NTM patients compared with unrelated controls and/or offspring (p < 0.001). CXCL10 levels were lower in patients who responded well to treatment compared to those who responded poorly (p = 0.03). Compared with healthy controls, PBMC from NTM patients produced similar levels of IFNg, IL-5 and IL-10, less IL-17 (p < 0.05) in response to SEB, but more IL-10 in response to PPD (p < 0.01).

Conclusions NTMLD is not associated with diminished Th1 responses. Elevated levels of CXCL10 indicate ongoing IFNg release in vivo. NTM patients may have a bias towards an IL-10 production in response to mycobacterial antigens and/or harbour an intrinsic defect in Th1 immunity.

Support The Medical Research Foundation, Royal Perth Hospital and by a Research Development Award from the University of Western Australia.

Nomination Nil.

Conflict of Interest No.

REDUCED ANTI-VIRAL RESPONSES: WHY PREGNANT WOMEN HAVE INCREASED SUSCEPTIBILITY TO RESPIRATORY VIRUS INFECTION

REBECCA FORBES1, PETER GIBSON1,2, VANESSA MURPHY3, PETER WARK1,2
1Centre for Asthma and Respiratory Diseases, University of Newcastle, and 2School of Medicine and Pharmacology, University of Western Australia, Nedlands, Western Australia

Introduction Pregnant women have increased susceptibility to respiratory virus infection. Human rhinovirus (HRV) and influenza are the most common respiratory viruses isolated during pregnancy. Both cause exaggerations in pregnant asthmatics and are high risk factors for respiratory related maternal and neonatal morbidity and mortality. Understanding the innate and adaptive immunological processes underlying respiratory virus infection in pregnancy will lead to improved treatments, resulting in better health outcomes for both mother and baby.

Methods Cross-sectional study of 12 pregnant asthmatics, 10 pregnant non-asthmatics, 8 non-pregnant asthmatics and 10 healthy non-pregnant women. Blood mononuclear cells were then infected with RV-43 or RV1–B (MOI = 20) or treated with polyI:polyC (100 μg/ml). Virus replication was measured by cell titration assay. Following infection, IL-6, CXCL-8, CXCL-10, IFN-α, RIG-I, RIG-I and MDA-5 mRNA induction was measured by qPCR. IL-6, CXCL-8, CXCL-10 were measured using cytometric bead array and flow cytometry. Supernatants and whole cell lysates were collected for interferon IFN-α and IFN-β. Similarly, CXCL-8 and IL-6 showed suppression with CSE exposure in pBECs, though not to the same extent as the antiviral response. Paradoxically, CSE exposure reduced IFN-α response.

Conclusions Exposure of BECs to CSE appears to specifically impair the innate antiviral response of infected BECs as well exacerbate the inflammatory response to infection.

Support NHMRC Australia.

Conflict of Interest None.

LUNG ALLOGRAFT SMALL AIRWAY EPITHELIUM IS MORE SUSCEPTIBLE TO EPITHELIAL-MESENCHYMAL TRANSITION (EMT)

B BANERJEE1,2, A KICIC1,3,4, MM MUSK2, SM STICK1,3,4, DC CHAMBERS5
1University of Western Australia, Crawley, Western Australia, Australia, 2WA Lung Transplant Unit, RPH, Western Australia, Australia, 3TICHR, Subiaco, Western Australia, Australia, 4Respiratory Medicine, PMH, Subiaco, Western Australia, Australia, and 5Queensland Centre for Pulmonary Transplantation & Vascular Disease, Brisbane, Queensland, Australia

BOS is primarily a disease of the small airways of the allograft lung.

Aim To test hypothesis that this may reflect more florid EMT in the small airway.

Methods Small (SAEC) & large (LAEC) airway epithelial cell cultures were established (n = 5, 2 UIP, 1 CHD, 1 LAM, 1 CF, 1 male, aged 44 (25–54), 0 BOS) from bronchial brushings. EMT was induced with TGF-β1 (50 ng/ml) and cells & supernatant were collected over 96 hours. EMT was assessed by morphology, expression of epithelial (ZO-1, CK-19) & mesenchymal markers (Vimentin, EDA-Fn) & matrix metalloproteinase (MMP) 2 and 9 activity.

Results There was significantly increased expression of mesenchymal proteins & reduced expression of epithelial proteins (p < 0.05 for all) in both SAEC & LAEC. EMT was more evident in SAEC compared to LAEC (Vimentin 1.97 fold higher (p = 0.02), EDA-Fn 2.03 fold higher (p < 0.02), ZO-1 2.43 fold lower (p = 0.01), CK-19 1.34 fold lower (p = 0.001) and MMP-2 & 9 activity increased significantly over EMT (MMP-2: 2.66 ± 0.25 units, p = 0.01 for SAEC; 11.56 ± 1.47 units, p = 0.02 for LAEC & MMP-9: 4.31 ± 0.48 units, p = 0.01 for SAEC; 12.71 ± 1.55 units, p = 0.02 for LAEC). MMP activity was greater in SAEC compared to LAEC (MMP-2: 3.4 fold higher, p = 0.02 & MMP-9 2.94 fold higher, p = 0.04).

Conclusions EMT is more rapid and occurs to a greater extent in the SAEC compared to LAEC. This would further support the role for EMT in BOS pathology and may help to explain why BOS is more prevalent in the small airway.

Support The Heart Lung Foundation of WA. Nomination Ann-Woolcock Young Investigator Award. Conflict of Interest No.

Ann Woolcock Young Investigator Award

Journal Compilation © 2010 Asian Pacific Society of Respirology

© 2010 The Author(s)
THE AIRWAY EPITHELIUM IN CYSTIC FIBROSIS IS PRO-INFLAMMATORY TO HUMAN RHINOVIRAL INFECTION COMPARED TO EPITHELIUM FROM HEALTHY CONTROLS

Claire J FDO1,2, Erin A SUTANTO1,2, Anthony KIIC1,2, Stephen M STICK1,2,3

1School of Paediatrics and Child Health, University of Western Australia, Nedlands, Western Australia, Australia, 2Department of Respiratory Medicine, Princess Margaret Hospital for Children, Perth, Western Australia, Australia, and 3Telethon Institute for Child Health Research, Subiaco, Western Australia, Australia.

Human rhinovirus (HRV) infections initiate the release of inflammatory cytokines like interleukin (IL)-8 which have been associated with an exaggerated and sustained inflammatory response, disease progression and respiratory failure in cystic fibrosis (CF) disease. We hypothesise HRV infections act as specific inflammatory triggers in primary airway epithelial cells (pAECs) and investigated this by comparing responses of healthy and CF pAECs following viral infection and non-viral stimulation.

Methods Confluent pAEC cultures established from healthy (HNA) and CF patients were stimulated with non-viral stimuli and infected with HRV serotypes (14, 1b) over time. Inflammatory cytokine responses, cell viability and apoptotic responses were then measured using ELISA/TRFs, MTS assay and an ssDNA apoptosis kit.

Results Non-viral stimulation resulted in similar levels of IL-8 in pAECHNA and pAECCF. Viral infection resulted in five fold of IL-8 (>0.05) in pAECCF compared to pAECHNA. HRV1b serotype induced the greatest production of IL-8 and was more pathogenic. Elevated IL-8 was seen with HRV1b infection over time accompanied by a reduction in cell viability only in pAECCF cells. Furthermore, pAECHNA had a damped up apoptotic response compared to pAECHNA. Gene expression revealed pAECCF to have 1.5-fold greater ICAM-1 receptor expression compared to pAECHNA.

Conclusions Although HRV viral specific responses exist in pAECs, pAECCF are more hyper-inflammatory than pAECHNA and results suggest that this occurs via the ICAM receptor. Also, pAECCF appeared not to initiate the appropriate defensive apoptotic response to viral infection compared to their healthy counterparts.

Support NHMRC and CHRF.

Nomination Ann Woolcock Young Investigator Award.

Conflict of Interest No.

WATER-BASED EXERCISE IMPROVES EXERCISE CAPACITY IN PEOPLE WITH COPD WITH PHYSICAL CO-MORBID CONDITIONS

RJ McNAMARA1,2, JA ALISON1,2, DK MCKENDRICK1, ZZ MCGUINNESS1

1Respiratory Medicine, Prince of Wales Hospital, New South Wales, Australia, 2Discipline of Physiotherapy, The University of Sydney, New South Wales, Australia, and 3Physiotherapy, Royal Prince Alfred Hospital, New South Wales, Australia.

Aim To determine whether a water-based exercise program was effective in improving exercise capacity and quality of life in people with COPD with physical co-morbidities compared to a land-based exercise program or no exercise.

Methods Participants with COPD referred to pulmonary rehabilitation and who had a physical co-morbidity were randomly allocated to one of three groups: land-based exercise, water-based exercise or a control group of no exercise. The two exercise groups trained for eight weeks, three exercise sessions per week. Participants underwent measurements of respiratory function, exercise capacity and quality of life by a blinded investigator at baseline and following intervention.

Results Of 53 participants (mean (SD) age 72 (9) years, mean FEV1 % 62 (19) predicted), 85% completed the study. Compared to control, water-based exercise significantly increased 6 minute walk distance (mean difference 65 m, 95% CI 42 to 88 m), incremental shuttle walk distance (mean difference 49 m, 95% CI 29 to 69 m) and endurance shuttle walk distance (mean difference 371 m, 95% CI 124 to 618 m). There was a significantly greater increase in incremental shuttle walk distance in the water-based exercise group compared to the land-based exercise group (mean difference 40 m, 95% CI 5 to 74 m). Only the water-based exercise group achieved the minimum clinically important difference in quality of life of 4 units change in the St George’s Respiratory Questionnaire. Conclusions Water-based exercise is significantly more effective than no exercise training and as effective as land-based exercise in improving exercise capacity. Water-based training is more effective than land-based training in improving quality of life in people with COPD and physical co-morbidities.

Support Physiotherapy Research Foundation

Nominations Janet Elder International Travel Award

Conflict of Interest No.

BRONCHOSCOPIC APPLICATIONS OF ANATOMICAL OPTICAL COHERENCE TOMOGRAPHY

JP WILLIAMSON1,2, JU PHILLIPS3, PA MCCLAUGHLIN4, WJ NOFFSINGER4, JJ ARMSTRONG5, VB BAKER1, A CURATOL6, PR NOBLE7, AR WEST7, DD SAMPSON8, AL JAMES9,10, DR HILLMAN11,12, PR EASTWOOD13,14

1Departments of Pulmonary Physiology, 2Hesp Medicine, Sir Charles Gairdner Hosp., 3Schools of Anatomy and Human Biology and, 4Physiology, 5Electrical, Electronic and Computer Engineering, University of Western Australia, Australia, and 6Western Australia Sleep Disorders Res Inst, Perth, Western Australia, Australia

Knowledge of airway dimensions is critical for bronchoscopists assessing airway stenoses requiring interventions. It is also important for evaluating phenotypic features of obstructive lung diseases (OLD). However, real-time quantification of airway dimensions during bronchoscopy is lacking. Inserted into the airways via a bronchoscope, anatomical optical coherence tomography (aOCT) is a light-based imaging technique with the unique capability to obtain such measurements. We describe the validation, research and clinical applications of bronchoscopic aOCT.

Methods (Study 1) aOCT was validated in a phantom model, excised porcine airways and in 4 human subjects. (Study 2) Airway compliance curves were constructed and compared from aOCT-based measurements in volunteers with and without OLD during bronchoscopy. (Study 3) Stenosis dimensions (length, calibre) were measured compared to patients with symptomatic airway stenosis using pre-procedure computed tomography (CT) and intra-procedure aOCT (Bland Altman analysis) to determine interventional strategy.

Results In a phantom and porcine airways, aOCT measurements were accurate and reliable. Mean CT-aOCT diameter measurements differed by 0.4 ± 1.3 mm. (2) Airway compliance was increased in COPD (n = 9) relative to control (n = 10) and asthma (16) subjects, which were similar. (3) In 14 patients, the mean difference between CT and aOCT-based stenosis measurements was 0.4 ± 8.6 mm. aOCT provided more reliable when CT image quality was poor or where a delay occurred between CT and bronchoscopy.

Conclusions aOCT provides real-time measurements of airway dimensions which are accurate and reliable and can be used for research and clinical applications.

Nomination Ann Woolcock Young Investigator Award.

Support NHMRC.

Disclosure to declare Yes.
SYNERGISTIC INTERACTIONS BY HUMAN MAST CELLS AND HUMAN AIRWAY SMOOTH MUSCLE CELLS IN INFLAMMATORY PRODUCTION

YC XIA1, T HARRIS1, M POWELL2, PM GOHARTH4, AG STEWART1, GA MACKAY1
1Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia, and 2Lung Institute of Western Australia, 3Ludwig Institute for Cancer Research, 4PathWest Laboratory Medicine, Western Australia, Australia

A notable feature of allergic asthma is the infiltration of mast cells into human airway smooth muscle (hASM) bundles. Thus, mast cells and hASM likely contribute to airway inflammation. It was hypothesized that the interaction of mast cells and hASM via direct cell-cell contact or through released factors would lead to increased inflammatory cytokine production. To examine this possibility, we have used a human mast cell line (HMC-1) to evaluate mast cell modulation of hASM cell function.

Methods HMC-1 cells were transfected with human Fc-RI, Fo-RII, and Fo-RI expressing cells. The functional activity of these cells was examined by measurement of released cytokines via IgE/antigen stimulation. hASM cells were co-cultured with activated mast cells to examine the impact on cytokine release.

Results Our study provides further evidence that the release of soluble mediators from activated mast cells can induce cytokine production from hASM cells. Further work is ongoing to identify the factors responsible for this effect.

Support by: Asthma Queensland and NHMRC.

Conflict of Interest No.

IN Volvement of Specific PI3 Kinase Isoforms in Airway Remodelling

LYN M MOIR1,2, THOMAS TRIAN1,2, Qi GE1, Peter SHEPHERD2, Jane E K BURGESS1,2, Brian GG OLIVER2, Judith L BLACK1,2
1Woolcock Institute of Medical Research, Sydney, New South Wales, Australia, 2Discipline of Pharmacology, University of Sydney, New South Wales, Australia, and 3Monash University, Melbourne, Victoria, Australia

The phosphoinositide 3 kinase (PI3K) signal transduction pathway contributes to the airway remodelling associated with asthma; however, the precise roles of the specific PI3K isoforms are currently unknown. In this study, we investigated the roles of the class IA PI3K isoforms p110α, p110β and p110γ in airway smooth muscle (ASM) cells derived from asthmatic subjects and ASM cells and lung fibroblasts from non-asthmatic subjects.

Methods Cells were stimulated with transforming growth factor β (TGF-β), 1 ng/ml and/or 10% FBS in the presence or absence of specific PI3K inhibitors PIK75 (p110α), TGX221 (p110β) or CI87114 (p110γ) (all 0.01–1 μM) or vehicle control (DMSO). Fibronectin deposition, VEGF and IL-6 secretion were measured using ELISA, mitochondrial activity was assessed by MTT assay and proliferation by Bromodeoxyuridine (BrdU) incorporation assay.

Results In non-asthmatic ASM cells inhibition of p110α and p110γ decreased VEGF and IL-6 secretion and cell proliferation (n = 11; p < 0.05), whereas in asthmatic ASM cells, only inhibition of p110α (n = 4–6, p < 0.05) but not p110β (n = 4–6, p > 0.05) had an effect. Furthermore, we demonstrated isoform specific roles with p110α (n = 4, p < 0.05) but not p110β (n = 3–4) or p110γ (n = 3–5) modulating fibronectin deposition in ASM cells and lung fibroblasts.

Conclusions Specific PI3K isoforms have distinct roles in the regulation of inflammatory cytokines (IL-6), growth factors (VEGF) and extracellular matrix proteins (fibronectin) associated with airway remodelling. Intrinsic differences exist in the roles of the PI3K isoforms in asthma.

Support National Health and Medical Research Council, Australia.

Conflict of Interest No.

SYNERGISTIC INTERACTIONS BY HUMAN MAST CELLS AND HUMAN AIRWAY SMOOTH MUSCLE CELLS IN INFLAMMATORY PRODUCTION

YU M MOOL1,2, THOMAS TRIAN1,2, Qi GE1, Peter SHEPHERD2, Jane E K BURGESS1,2, Brian GG OLIVER2, Judith L BLACK1,2
1Woolcock Institute of Medical Research, Sydney, New South Wales, Australia, 2Discipline of Pharmacology, University of Sydney, New South Wales, Australia, and 3Monash University, Melbourne, Victoria, Australia

The phosphoinositide 3 kinase (PI3K) signal transduction pathway contributes to the airway remodelling associated with asthma; however, the precise roles of the specific PI3K isoforms are currently unknown. In this study, we investigated the roles of the class IA PI3K isoforms p110α, p110β and p110γ in airway smooth muscle (ASM) cells derived from asthmatic subjects and ASM cells and lung fibroblasts from non-asthmatic subjects.

Methods Cells were stimulated with transforming growth factor β (TGF-β), 1 ng/ml and/or 10% FBS in the presence or absence of specific PI3K inhibitors PIK75 (p110α), TGX221 (p110β) or CI87114 (p110γ) (all 0.01–1 μM) or vehicle control (DMSO). Fibronectin deposition, VEGF and IL-6 secretion were measured using ELISA, mitochondrial activity was assessed by MTT assay and proliferation by Bromodeoxyuridine (BrdU) incorporation assay.

Results In non-asthmatic ASM cells inhibition of p110α and p110γ decreased VEGF and IL-6 secretion and cell proliferation (n = 11; p < 0.05), whereas in asthmatic ASM cells, only inhibition of p110α (n = 4–6, p < 0.05) but not p110β (n = 4–6, p > 0.05) had an effect. Furthermore, we demonstrated isoform specific roles with p110α (n = 4, p < 0.05) but not p110β (n = 3–4) or p110γ (n = 3–5) modulating fibronectin deposition in ASM cells and lung fibroblasts.

Conclusions Specific PI3K isoforms have distinct roles in the regulation of inflammatory cytokines (IL-6), growth factors (VEGF) and extracellular matrix proteins (fibronectin) associated with airway remodelling. Intrinsic differences exist in the roles of the PI3K isoforms in asthma.

Support National Health and Medical Research Council, Australia.

Conflict of Interest No.

HUMAN PLACENTALLY-DERIVED STEM CELLS ABROGATE FIBROSIS AND AUGMENT LUNG REPAIR BUT DIFFER IN PLASTICITY

YUEN MOODLEY1, Shigami ILANCHERAN2, Christopher SAMUEL2, V Arumugam VAGHIUANI3, Daniel ATienza1, Elizabeth D WILLIAMS3, Graham JENKINS1, Evan M WALLACE1, Richard BOYD3, Allan TROUNSON4, Ursula MANUELPELLA5
1Monash Immunology and Stem Cell Laboratories (MISCL), Monash University, Victoria, Australia, and 2Monash University, Melbourne, Victoria, Australia

Acute Respiratory Distress Syndrome is characterized by inflammation and fibrosis. Cellular therapies potentially restore pneumocytes and reduce inflammation. Aims We evaluated the role of term human umbilical cord mesenchymal stem cells derived from Wharton’s jelly (uMSCs) and Human Amnion Epithelial Cells (HAECS) in treating a Bleomycin-induced model of lung injury. Methods Cells were administered systemically into a mouse model of acute lung injury 24 hours following intra-nasal administered Bleomycin. Results Both HAECS and uMSCs reduced inflammation with decreased TNF-α, IL-1, IL-6 and TGF-β. Collagen in the lung was significantly reduced by both uMSCs and HAECS as a consequence of increased degradation by matrix metalloproteinase-2 (MMP-2) and down-regulation of their endogenous inhibitors the tissue inhibitors of matrix metalloproteinases (TIMPs) -1 and -2. uMSCs were detected in the lung at 2 weeks post-injection, vs. 4 weeks for HAECS. In addition, uMSCs did not demonstrate lung differentiation while HAECS developed an alveolar phenotype.

Conclusions Both uMSCs and HAECS, have anti-inflammatory properties and reduce fibrosis. However, uMSCs do not reduce injury but HAECS adopt a lung phenotype.

Support Small Grant Monash University.

Nomination nil.

Conflict of Interest No.

© 2010 The Author(s)
Cystic Fibrosis SIG Oral Session 2

PREGNANCY OUTCOMES IN THE CURRENT ERA OF CYSTIC FIBROSIS CARE: A 15 YEAR EXPERIENCE

EMERSON MT LAU1, CAROL MORGANTI1, ROBERT OGLE2, RYN DENITCE1, JANE CIVITICO1, ANDREA AVERDA1, DAVID J BARNES1, PAUL J TORZILLO1,2, PETE T BYE1
1 Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia, and 2 Department of Obstetrics and Gynaecology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia

Background With improvement in clinical care and longer survival of patients with cystic fibrosis, pregnancy has become commonplace. However the impact of cystic fibrosis on maternal health and foetal outcomes requires ongoing review.

Methods A retrospective study of 20 pregnancies from 18 women with cystic fibrosis during the period 1995–2009 was performed. Changes in lung function, body mass index, and development of gestational diabetes were recorded. Foetal outcomes and maternal survival were examined and the influence of pre-pregnancy parameters on outcomes were evaluated.

Results Mean age of pregnancy was 29.1 years with a mean pre-pregnancy FEV1 of 69.6% predicted. Eleven out of twenty pregnancies had a pre-pregnancy FEV1 <60% predicted. During pregnancy, FEV1 fell by 7.46% (CI 1.59–7.92), but recovered to baseline within 6 months post-partum. Mothers gained a mean weight of 7.6 kg and gestational diabetes developed in 42.9% of women. All women delivered live births apart from one therapeutic abortion. Five infants were preterm and three had low birthweight for age. Four mothers either died or required lung transplantation after pregnancy on follow up. FEV1 -60% predicted and body mass index <20 kg/m2 were significant predictors of foetal complications.

Conclusion Most women tolerated pregnancy well without major complications despite many having at least moderate lung function impairment. Pre-pregnancy lung function (FEV1) and nutritional status (body mass index) were important predictors of outcomes.

Support Nil
Nomination Nil
Conflict of Interest Nil

ADHERENCE BEHAVIOUR OF ADULT CYSTIC FIBROSIS PATIENTS PRESCRIBED AZITHROMYCIN

S ELMASYRI1, SS MOHI1, M BRAINTHWAITE1, S SOFIANGOPOULOS1, D CLARK1, F FINLAYSON1, E WILLIAMS1, S POOLE1, D MOOLEY1, D LIEW1, J WILSON1
1 Alfred Hospital, Prahran, Victoria, Australia, and 2 Dept of Medicine St. Vincent’s Hospital, Fitzroy, Victoria, Australia

Adherence to medication regimens in patients with cystic fibrosis (CF) vary substantially. Direct measures of adherence using electronic monitors attached to medication bottles enable the precise recording of usage. The macrolide antibiotic, azithromycin has demonstrated clinical benefit when used in CF patients with moderate to severe impairment of lung function.

Aim This study compares the adherence levels of CF patients randomised to two different treatment regimens of azithromycin, measured by electronic monitoring.

Methods Patients were prescribed the medication once (1000 mg) or three times (500 mg) a week. Data were collected over 24 weeks using electronic monitoring devices. Adherence measures were defined as: Total adherence (total amount of medication prescribed and total number of days adhered (number of days where prescribed doses were taken divided by number of days monitored).

Results The study recruited 51 participants (57% male; mean age = 33.7 SD = 8 years, mean FEV1, % = 62.2, SD = 22.8). Total adherence in patients prescribed the weekly regimen (M = 100.19, SD = 6.3%) were significantly different compared to the three times a week regimen (M = 89.4, SD = 17.2%, p < 0.05). No significant difference was observed in total number of days adhered. FEV1 % predicted negatively correlated with adherence to medication (total adherence r2 = 0.28, p<0.05, days adhered r2 = 0.29, p = 0.04) and to BMI (r2 = 0.35, p < 0.01). Positive correlation was observed between age of the participant and adherence to medication (total adherence r2 = 0.31, p<0.01, days adhered r2 = 0.41, p < 0.01).

Conclusion Participants adhered better to a once weekly regimen than a three times a week regimen. Multiple factors including age and FEV1 % predicted play important roles as deterrents to encourage adherence to medication.

Support: ARC Linkage grant, Roche Australia Pty. Ltd
Nomination Nil
Conflict of Interest No.

ATTITUDES TOWARDS POPULATION-BASED CARRIER SCREENING FOR CYSTIC FIBROSIS (CF) BY CF HEALTHCARE PROFESSIONALS

FIONA CUNNINGHAM1, SHAWN LEWIS1, JOSTIN GLAZNER2, JENNA MASSIE1,2
1 Murdoch Children’s Research Institute, Melbourne, Australia, 2 Department of Respiratory Medicine, Royal Children’s Hospital, Victoria, Australia, and 3 University of Melbourne, Victoria, Australia

Background Carrier screening for CF has been available for many years but there is no national program for population-based screening in Australia. Knowledge of Australian CF healthcare professionals’ attitudes towards carrier screening would provide useful information about how a program could be implemented. The aim of this study was to investigate the attitudes of CF respiratory physicians and CF clinic coordinators in Australia towards population-based carrier screening for CF.

Method A purposed designed questionnaire assessing knowledge and attitudes towards CF carrier screening was distributed to respiratory physicians and CF clinic coordinators throughout Australia.

Results There were 111 respiratory physicians registered with the CF special interest group of TSANZ and 30 CF clinic nurses identified through the CF coordinators network. Seventy-five responded, 55 respiratory physicians (49.5%) and 20 coordinators (67%). Forty-two (56%) respondents were in favour of population-based carrier screening for CF. Sixty-four (85%) rated raising a child with CF as difficult/very difficult, 63 (84%) rated the shortened life span as a significant concern and 64 (86%) the daily treatment regimen as a significant concern. Disadvantages of screening were perceived anxiety amongst carriers (n = 65, 87%) and discrimination of carriers (n = 42, 56%). Respondents rated the following barriers as most important: limitations of predicting clinical outcomes (n = 47, 65%) and insufficient time and resources for providers (n = 45, 61%). Fifty-four (76%) of respondents believed they had a role in the development of a CF carrier screening program.

Support Nil
Nomination Nil
Conflict of Interest No.

ADHERENCE BEHAVIOUR OF ADULT CYSTIC FIBROSIS PATIENTS PRESCRIBED AZITHROMYCIN

S ELMASYRI1, SS MOHI1, M BRAINTHWAITE1, S SOFIANGOPOULOS1, D CLARK1, F FINLAYSON1, E WILLIAMS1, S POOLE1, D MOOLEY1, D LIEW1, J WILSON1
1 Alfred Hospital, Prahran, Victoria, Australia, and 2 Dept of Medicine St. Vincent’s Hospital, Fitzroy, Victoria, Australia

Adherence to medication regimens in patients with cystic fibrosis (CF) vary substantially. Direct measures of adherence using electronic monitors attached to medication bottles enable the precise recording of usage. The macrolide antibiotic, azithromycin has demonstrated clinical benefit when used in CF patients with moderate to severe impairment of lung function.

Aim This study compares the adherence levels of CF patients randomised to two different treatment regimens of azithromycin, measured by electronic monitoring.

Methods Patients were prescribed the medication once (1000 mg) or three times (500 mg) a week. Data were collected over 24 weeks using electronic monitoring devices. Adherence measures were defined as: Total adherence (total amount of medication prescribed and total number of days adhered (number of days where prescribed doses were taken divided by number of days monitored).

Results The study recruited 51 participants (57% male; mean age = 33.7 SD = 8 years, mean FEV1, % = 62.2, SD = 22.8). Total adherence in patients prescribed the weekly regimen (M = 100.19, SD = 6.3%) were significantly different compared to the three times a week regimen (M = 89.4, SD = 17.2%, p < 0.05). No significant difference was observed in total number of days adhered. FEV1 % predicted negatively correlated with adherence to medication (total adherence r2 = 0.28, p<0.05, days adhered r2 = 0.29, p = 0.04) and to BMI (r2 = 0.35, p < 0.01). Positive correlation was observed between age of the participant and adherence to medication (total adherence r2 = 0.31, p<0.01, days adhered r2 = 0.41, p < 0.01).

Conclusion Participants adhered better to a once weekly regimen than a three times a week regimen. Multiple factors including age and FEV1 % predicted play important roles as deterrents to encourage adherence to medication.

Support: ARC Linkage grant, Roche Australia Pty. Ltd
Nomination Nil
Conflict of Interest No.

LENTIVIRAL GENE TRANSFER INTO MARMOSET AIRWAY

David PARSONS1,2,4, Richard BRIGHT2, Darren MILLER2, Donald ANSON3,4
1 Respiratory & Sleep Medicine, 2Women’s & Children’s Health Research Institute, 3University of Melbourne, Victoria, Australia and 4Centre for Stem Cell Research, University of Adelaide, South Australia

Preclinical studies in non-human primates (NHP) are essential to estimate effectiveness and safety in developing gene transfer protocols to treat cystic fibrosis (CF) airway disease prior to clinical trials. Lentiviral (LV) vectors can provide in vivo gene expression and persistence suited to long lasting CF airway correction in mice. We have begun examination of LV gene transfer in lungs of marmosets (Callithrix jacchus), a small non-human primate with lung anatomy and physiology similar to humans.

Methods Lysophosphatidylcholine (LPC, 0.1%) pre-treatment was followed by a LV vector encoding the lacZ (LV-lacZ) reporter gene, pseudotyped with the VSV-G surface protein. Doses were delivered into the trachea of four intubated marmosets. Trachea and lungs in two animals were examined after 1 week; blood taken daily was tested for presence of vector particles.

Results Epithelial cell lacZ gene expression was present primarily in conducting airways in a patchy distribution. A transient O2 desaturation was noted in some animals after LPC administration; behavioural and physiological indices were normal postoperatively. Limited patches of haemorrhage and neutrophil / mononuclear cell infiltration were deemed unremarkable by a veterinary pathologist. Serum p24 LV capsid protein levels that appeared after dosing were absent after day two.

Conclusions These first studies indicate LPC/LV dosing procedures are well tolerated and can induce target-cell gene expression. Further histological and immunological analyses are in progress. The remaining two animals will undergo longer-term assessment of the success of lentiviral lung gene transfer.

Reference 1 Stocker et al. Journal of Gene Medicine. 2009

Acknowledgements NHMRC, CureCF Foundation SA.

Conflict of Interest No.
CT-DETECTED EARLY STRUCTURAL LUNG DAMAGE IS PROGRESSIVE IN INFANTS AND PRESCHOOL CHILDREN WITH CYSTIC FIBROSIS

L MOTT1,2, C MURRAY, N DE KLERK, C GANGELL, S RANGANATHAN4,5, P ROBINSON4,5, P SLY1,2, Sir Charles Gairdner Hospital, Perth, Western Australia, Australia, 2School of Physiotherapy and Exercise Science, Griffith University, Queensland, Australia, 4Alfred Health, Melbourne Victoria, Australia, 5Department of Respiratory Medicine, Royal Children’s Hospital, Melbourne, Australia

Background Bronchiectasis and air trapping are important features of cystic fibrosis (CF) structural lung damage, however data on disease progression in young children are lacking.

AIM To assess longitudinal changes in CT-detected early structural lung damage in the CF-affected airways of infants and young children.

METHODS Subjects included 117 children (age range 0.2 to 6.9 years) who underwent 327 annual CT scans, with 210 paired scans. Each CT scan consisted of three slices at end-inspiration and three slices at end-expiration. The left and right upper, middle and lower zones were assessed for the presence and extent (none, less than 50%, more than 50%) of bronchiectasis and air trapping using previously described methods. Infection and inflammation were assessed using bronchoalveolar lavage at the time of CT scan.

RESULTS Bronchiectasis was present in 37% of initial scans, persisting in 75% of subsequent scans. Median extent increased from initial to subsequent scan (p = 0.000). Preceding PISA infection and neutrophilic inflammation was associated with increased prevalence of bronchiectasis at subsequent scan (OR = 2.9). Air trapping was present in 67% of initial scans, persisting in 86% of subsequent scans. Median extent increased from initial to subsequent scan (p = 0.0005). Infection and inflammation did not increase risk of air trapping, but air trapping was more common in girls (OR = 2.0). Bronchiectasis and air trapping commonly occurred together.

CONCLUSION Early CF structural lung disease persists and is progressive. Risk factors for bronchiectasis and air trapping are not the same, suggesting separate pathophysiological processes.

Nomination: Nil.
Support: CFIT, Inc (USA); NHMRC, ACFRT, MCR and PMH Foundation (Australia).
Conflict of Interest: Nil.
Abbreviation: OR = odds ratio.

OLIV SIG – Physiotherapy SIG Combined Oral Session

DOES THE ISWT ELICIT MORE MAXIMAL CARDIORESPIRATORY RESPONSES IN NON-CYSTIC FIBROSIS (CF) BRONCHIECTASIS?

N CEGINS1,2,3, A LEE5,7, AE HOLLAND5,6, C HILL2, L RAUTELA7, P J THOMPSON2,3, RG STIRLING5, CF MCDONALD7, S JENKINS2,3,4,5

1St Charles Gairdner Hospital, Perth, Western Australia, Australia, 2Curtin University of Technology, Perth, Western Australia, Australia, 3Lung Institute of Western Australia, Perth, Western Australia, Australia, 4Alfred Health, Melbourne Victoria, Australia, 5The University of Melbourne, Victoria, Australia, 6La Trobe University, Melbourne Victoria, Australia, and 7Institute for Breathing and Sleep, Austin Health, Melbourne, Victoria, Australia

The 6 minute walk test (6MWT) and incremental shuttle walk test (ISWT) are commonly used to assess functional exercise capacity, prescribe the training intensity and measure the efficacy of pulmonary rehabilitation. No studies have compared these tests in patients with non-CF bronchiectasis.

Aims To compare peak dyspnea and heart rate (HR), and nadir oxygen saturation (SpO2) during the 6MWT and ISWT in subjects with non-CF bronchiectasis.

METHODS Twenty-seven participants (aged 64 ± 13 years, FEV1 70 ± 17% predicted, FVC 82 ± 16% predicted) with non-CF bronchiectasis enrolled in a trial of pulmonary rehabilitation, completed two 6MWTs and two ISWTs in random order.

RESULTS The 6 minute walk distance (6MWD) and the incremental shuttle walk distance (ISWD) were significantly greater on the 2nd test (both p < 0.02). The mean (95% CI) increase in the 6MWD was 22 m (9 to 35 m); 4% (2 to 7%) and in the ISWD was 22 m (4 to 39 m); 6% (2 to 10%). The greatest 6MWD and ISWD was 560 ± 86 m and 448 ± 151 m respectively. There was a strong relationship between the 6MWD and ISWD (r = 0.89, p < 0.001). Peak dyspnea was higher for the ISWT (4.2 ± 1.2 vs. 3.6 ± 1.2, p = 0.02) but there was no difference in peak HR (78 ± 11 vs. 75 ± 10% age pred maximal HR, p = 0.67) or nadir SpO2 (93.5 ± 0.6% vs. 93.3%, p = 0.65).

CONCLUSION Although peak HR was similar, the externally paced, incremental nature of the ISWT may account for the higher dyspnea scores in these subjects with non-CF bronchiectasis. Further research will determine the responsiveness of the ISWT and 6MWT following pulmonary rehabilitation in this population.

Support Sir Charles Gairdner Research Fund, The Alfred Research Trust, Institute for Breathing and Sleep.
Conflict of Interest: No.

UTILITY OF HBA1C IN DIAGNOSIS OF IMPAIRED GLUCOSE TOLERANCE AND DIABETES IN ADULT CYSTIC FIBROSIS PATIENTS

SHYAMALA PRADEEPAN, SALLY CHAPMAN, HUGH GREVILLE

Adult Cystic Fibrosis Service Royal Adelaide Hospital, Adelaide, Australia

OGTT is considered the gold standard test in the diagnosis of CFD. However, this test is tedious and time consuming. Instead HbA1c is an easily performed test. There are many studies comparing these two tests, overall the conclusions are contradictory. There is a need for a sensitive and specific tool in diagnosing CF related impaired glucose tolerance and diabetes.

METHODS We identified patients who had a OGTT and HbA1C done with ≤ 3 months of each other. HbA1C results were categorised into two groups (<6 and > = 6.5). Correlation between OGTT and HbA1C was calculated using linear regression.

RESULTS Thirty patients had HbA1C and OGTT with in 3 months HbA1C was able to diagnose IGT (27.3 ± 7.1 kg, p = 0.03). 6MWD improvement at 2 weeks was related to change in step test (28.6 ± 12.1 steps p = 0.02) with continued improvement at 26 weeks (35.6 ± 11.9 steps p < 0.01). 6MWD improved from baseline of 405 m in 158% at 2 weeks (55 m (p = 0.02) and 26 weeks (151 m (p < 0.01)). ISWT did not significantly improve from baseline (24.5 ± 10.7 steps) until 6 weeks (31.4 ± 10.5 steps p = 0.02) with continued improvement at 26 weeks (35.6 ± 11.9 steps p < 0.01). QSO recovery from baseline (19.6 ± 4.8 kg) did not change significantly until 26 weeks (27.3 ± 7.1 kg, p = 0.03). 6MWD improvement at 2 weeks was related to change in test (r = 0.64 p = 0.02) but not FEV1% (r = 0.09 p = 0.64) and QSO (r = 0.55 p = 0.16). By 3 months, improvement in 6MWD were related to QSO (r = 0.84 p < 0.01) but not FEV1% (r = 0.01 p = 0.98).

CONCLUSION Our data show a temporal association in improvement between lung function and 6MWD. In contrast, ambulatory muscle strength recovery is delayed with QSO taking greater than 3 months to improve. This may account for self reports of exercise limitation in the months post transplant.

Support Nil.
Nomination: Nil.
Conflict of Interest: No.

AMPUTATORY MUSCLE STRENGTH RECOVERY IS DELAYED WHEN COMPARED TO LUNG FUNCTION AND SIX MINUTE WALK DISTANCE AFTER LUNG TRANSPLANTATION

J WALSH1, D CHAMBERS1, R DAVIS2, H SEALE3, N MORRIS3, F KERMEEN1, PH POMPSON1

1Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Queensland, Australia, and 2School of Physiotherapy and Exercise Science, Griffith University, Queensland, Australia

Lung transplant patients commonly report reduced exercise capacity despite satisfactory graft function. Improvements in lung function relative to indicators of exercise capacity are not well described. Our aim was to analyse the trajectory of improvement in exercise tolerance as assessed by six minute walk distance (6MWD), step test and quadriceps muscle strength (QS) compared to lung function in the first six months post transplant.

METHODS We prospectively evaluated all lung transplant recipients at a single institution between Dec 2006 and Feb 2009. Lung function (FEV1%, 6MWD, QS (Lafayette Manual Muscle Test System) and number of steps completed in one minute were recorded pre-transplant, 2, 6, 13 and 26 wks post-operatively. Data were analysed using descriptive statistics, ANOVA and bivariate correlations.

RESULTS Thirty patients (28 bilateral and 2 single; mean age 40 ± 13 years; 17 female) were studied. FEV1% improved from pre-transplant of 26.5% ± 11.3% to 61.2% ± 15.7% at 2 weeks (p = 0.01) and 85.8% ± 26.2% at 26 weeks (p < 0.01). 6MWD improved from baseline of 405 m in 158% at 2 weeks (55 m (p = 0.02) and 26 weeks (151 m (p < 0.01)). Step test did not significantly improve from baseline (24.5 ± 10.7 steps) until 6 weeks (31.4 ± 10.5 steps p = 0.02) with continued improvement at 26 weeks (35.6 ± 11.9 steps p < 0.01). QSO recovery from baseline (19.6 ± 4.8 kg) did not change significantly until 26 weeks (27.3 ± 7.1 kg, p = 0.03). 6MWD improvement at 2 weeks was related to change in test (r = 0.64 p = 0.02) but not FEV1% (r = 0.09 p = 0.64) and QSO (r = 0.55 p = 0.16). By 3 months, improvement in 6MWD were related to QSO (r = 0.84 p < 0.01) but not FEV1% (r = 0.01 p = 0.98).

CONCLUSION Our data show a temporal association in improvement between lung function and 6MWD. In contrast, ambulatory muscle strength recovery is delayed with QSO taking greater than 3 months to improve. This may account for self reports of exercise limitation in the months post transplant.

Support Nil.
Nomination: Nil.
Conflict of Interest: No.
RELATIONSHIP BETWEEN SIX MINUTE WALK TEST, CYCLE TESTING, QUALITY OF LIFE AND ACTIVITY IN DUST-RELATED LUNG DISEASE

M DALE1, J ALISON1,2, Z MCELDOUGH1, P MUNOZ3, P BYE3, P CORTE1
1Discipline of Physiotherapy, The University of Sydney, New South Wales, Australia, and 2Department of Respiratory Medicine, Royal Prince Alfred Hospital, Camperdown New South Wales, Australia

The six minute walk test (6MWT) is extensively used in clinical practice. However, the role of this test in people with dust-related lung disease remains unclear.

Aim The aims of the study were to investigate the relationships between exercise capacity measured by the 6MWT and the incremental peak and endurance cycle tests, the 6MWT and health-related quality of life, and the 6MWT and activity levels in people with dust-related lung disease.

Methods Thirty male participants with asbestos related pleural disease, asbestosis or silicosis performed two 6MWTs separated by 30 minutes with the better of the tests used for analysis. During the rest period, participants completed the St George’s Respiratory Questionnaire (SGRQ). On a separate day, participants performed spirometry, lung volumes, DLco and a peak and endurance cycle test. Participants were an activity monitor (SenseWear Pro3) for a period of seven days.

Results Mean (SD) age of participants was 71 (6) years. As a percentage of predicted lung function, TLC was 89 (20)%, FRC 83 (25)%, RV 85 (34)%, FVC 82 (18)%, FEV1/FVC 68 (10)%, and DLco 64 (15)%. There was a significant increase of 11 m between the first and second 6MWT (p = 0.002). The mean of the better 6MWT was 461 m (79). There was a significant correlation between 6MWT distance and peak watts (r = 0.67, p < 0.001) but not with endurance cycle time. There were significant correlations between the 6MWT and all components of the SGRQ, the strongest correlation being with the ‘Activity’ domain (r = -0.61, p = 0.001) and significant correlations between 6MWT and average daily steps (r = 0.57, p = 0.002) and average METs (r = 0.59, p < 0.001).

Conclusion Findings suggest the 6MWT may be a useful measure of exercise capacity and may reflect daily activity in people with dust-related lung disease.

Support Workers’ Compensation (Dust Diseases) Board of NSW.

Nomination Nil.

Conflict of Interest Nil.

SEVERE HYPOXIA IN EISENMENGER SYNDROME DOES NOT PRECLUDE SAFE PERFORMANCE OF THE SIX MINUTE WALK TEST

R DAVIS1, K HALL1, J WALSHE1, H SEALE1, J HARRIS1, D RADFORD2, F KERMEEN1
1Queensland Centre for Pulmonary Transplantation and Vascular Disease, The Prince Charles Hospital, Brisbane, Queensland, Australia, and 2Adult Congenital Heart Disease Unit, The Prince Charles Hospital, Brisbane, Queensland, Australia

Guidelines for the performance of the six minute walk test (6MWT) list oxygen saturations (SpO2) <88% as a contraindication. Patients with Eisenmenger Syndrome (ES) experience significant hypoxia at rest and are considered high risk for assessment of exercise capacity. The aim of this study was to report the safety and outcome of 6MWT in an ES cohort prescribed specific pulmonary arterial hypertension (PAH) therapies.

Methods Retrospective review of all 6MWT performed by ES patients at a tertiary PAH referral centre from January 2003 to July 2009. 6MWTs were supervised by experienced physiotherapists on a 30 m circuit with continuous oximetry and heart rate (HR) monitoring. Adverse events were identified as defined by American Thoracic Society guidelines. Outcome measures of six minute walk distance (6MWD), resting SpO2, nadir exercise induced desaturation (EID) and HR response to 6MWT were analysed using descriptive statistics and non-parametric tests

Results Fifty-three patients with ES (33 females; 14 Trisomy 21) of mean age 34 ± 12 years and mean duration of PAH therapy 15 ± 13 months had completed 6MWTs performed. Prior to beginning PAH therapy, three patients were NYHA-Functional Class II, n = 40

PEER REVIEW

6MWD was 345 ± 131 m, Baseline SpO2 was 85 ± 8% with EID decreasing to 66 ± 15%. Thirteen minor adverse events (8 cardiac in origin) were identified as defined by American Thoracic Society guidelines. Thirteen (24%) participants had EID < 85% with EID decreasing to 66 ± 15%. The 6MWD was 345 ± 131 m. Peak SpO2 measured during the 6MWT was lower than during CPET (15.1 ± 3.5 vs 17.5 ± 2.6 mL/min; p = 0.03). Oxygen consumption during 6MWT reached a mean of 87% of VO2peak achieved on CPET (95% confidence interval 76–98%VO2peak). Peak ventilation, carbon dioxide production and peak heart rate were significantly lower during 6MWT, but there was no difference in nadir SpO2 (90.4% vs. 91.3%) on 6MWT and CPET respectively, p = 0.14. A higher 6MWD was associated with a higher peak work rate (r = 0.93, p < 0.001) but there were no relationships between 6MWD and peak cardiopulmonary responses on CPET.

Conclusions The 6MWT elicits a high but submaximal oxygen uptake in people with ILD. Given the poor relationship between 6MWD and peak cardiopulmonary responses elicited by CPET, the prognostic value of the 6MWT may be related to the degree of oxygen desaturation elicited by this test.

Conflict of Interest Nil.

THE 6-MINUTE WALK TEST ELICITS HIGH BUT SUBMAXIMAL CARDIORESPIRATORY RESPONSES IN INTERSTITIAL LUNG DISEASE

ANNE E HOLLAND1,2, LEONA KNAPMAN1,2, DARRY BRAZZALE1,6, MATTHEW CONRON1,2, IRIS GLASPLOE3, NICOLE GÖHL1,2, CATHERINE HILL1,6, CHRISTINE F MCDONALD1,6
1School of Physiotherapy, La Trobe University, Victoria, Australia, 2Departments of Physiotherapy, Departments of Allergy, Immunology and Respiratory Medicine, Alfred Hospital, Victoria, Australia, 3Institute for Breathing and Sleep, Victoria, Australia, 4Departments of Respiratory and Sleep Medicine, 5Physiotherapy, Austin Health, Victoria, Australia, and 6Department of Respiratory Medicine, St Vincent’s Hospital, Victoria, Australia

The 6minute walk test (6MWT) is used to assess prognosis and evaluate exercise capacity in interstitial lung disease (ILD), however the physiological load imposed by the 6MWT is unknown. This study compared cardiorespiratory responses to 6MWT and cardiopulmonary exercise testing (CPET) in ILD.

Methods Fifteen participants with ILD (nine IPF), mean age 70 (standard deviation 12) years and TLCO 57 (17)%predicted undertook 6MWT and CPET on the same day in random order. Pulmonary oxygen uptake (VO2), ventilation (V̇E), carbon dioxide production (VCO2), oxhaemoglobin saturation (SpO2) and heart rate were compared between the tests using a portable metabolic cart. Relationships between 6 minute walk distance (6MWD) and peak cardiorespiratory responses on CPET were evaluated using correlations.

Results Peak VO2 measured during the 6MWT was lower than during CPET (15.1(3.5) vs 17.5(2.6) mL/min; p = 0.03). Oxygen consumption during 6MWT reached a mean of 87% of VO2peak achieved on CPET (95% confidence interval 76–98%VO2peak). Peak ventilation, carbon dioxide production and peak heart rate were significantly lower during 6MWT, but there was no difference in nadir SpO2 (90.4% vs. 91.3%) on 6MWT and CPET respectively, p = 0.14. A higher 6MWD was associated with a higher peak work rate (r = 0.93, p < 0.001) but there were no relationships between 6MWD and peak cardiorespiratory responses on CPET.

Conclusions The 6MWT elicits a high but submaximal oxygen uptake in people with ILD. Given the poor relationship between 6MWD and peak cardiorespiratory responses elicited by CPET, the prognostic value of the 6MWT may be related to the degree of oxygen desaturation elicited by this test.

Conflict of Interest Nil.

THE LONG TERM EFFECT OF INHALED HYPERTONIC SALINE (6%) IN NON-CYSTIC FIBROSIS BRONCHIECTASIA

C NICOLSON1,2, R STIRLING1,3, B BORG1, R GOURLAY1, B BUTTON1,2, J WILSON1,2, A HOLLAND1,4
1The Alfred Hospital, Melbourne, Victoria, Australia, 2The University of Melbourne, Melbourne, Victoria, Australia, 3Monash University, Melbourne, Victoria, Australia, and 4La Trobe University, Melbourne, Victoria, Australia

Patients with bronchiectasis have chronic cough and sputum production, frequent exacerbations and progressive decline in lung function. The aim of this double-blind randomized controlled trial was to determine if the long term inhalation of hypertonic saline (6%) improved lung function and quality of life in patients with non-cystic fibrosis bronchiectasia.

Methods Forty subjects (mean [SD] age 57 [15] years, FEV1 82.6 [20.7] %predicted) with demonstrated bronchiectasis were randomized to inhale either hypertonic saline (6%) or isotonic saline (0.9%) through an AeronebGo nebulizer twice a day for 12 months while performing the active cycle of breathing technique. Participants and assessors were blinded to the treatment allocation. Spirometry and quality of life questionnaires (St George respiratory questionnaire [SGRQ] and Leicester cough questionnaire [LCQ]) were performed at baseline, three, six and twelve months.

Results There were no differences between groups at baseline for age, gender, body mass index or respiratory function. After twelve months both groups had similar improvements in FEF25–75% (mean 0.181 L/sec, 95% confidence interval 0.059 – 0.303 L/sec).

Conclusions The inhalation of both isotonic (0.9%) and hypertonic (6%) saline improved small airways function and improved quality of life over 12 months, however both treatments were equally effective.

Support The Alfred Hospital Research Trust, Physiotherapy Research Foundation, The Alfred Physiotherapy Department Research Foundation.

Conflict of Interest Nil.

© 2010 The Author(s)
Journal Compilation © 2010 Asian Pacific Society of Respirology
IMPLEMENTATION OF A CLINICAL PREDICTION TOOL FOR PULMONARY EMBOLISM DIAGNOSIS IN A TEACHING HOSPITAL

CHONG WENG ONG1, PAUL COUGHLIN2, DEBORAH LEACH2, FRANKS THIEN1
1Departments of Respiratory and Sleep Medicine, 2Haematology and Emergency, and 3Medicine Box Hill Hospital and Monash University, Box Hill, Victoria, Australia

Investigation of pulmonary embolism with CTPA is often performed despite low clinical risk and results in unnecessary exposure to radiation and radiocontrast as well as inefficient use of medical resources. Risk stratification with a validated prediction tool (Wells score) complements clinical decision making and rationalises the use of CTPA to appropriate patient groups.

Methods Prospective assignment of Wells score by requesting clinicians on a formal algorithm form was instituted in 2009. All patients being investigated for pulmonary embolism were required to have the form filled prior to performance of CTPA. Patients stratified low clinical risk (Wells < 2) did not proceed to CTPA unless a senior physician override was applied. Intermediate risk patients (Wells 2-6) proceeded to D-dimer measurement and if above the laboratory cutoff (0.3) proceeded to imaging. All high risk patients (Wells > 6) proceeded to CTPA directly. CTPA outcomes, D-dimer levels, request locations and dates were collected. Data were collected from February to August 2009.

Results A total of 333 patients were investigated with CTPA in this period. 65 patients (19%) did not have the Wells score assigned but 268 patients (81%) had complete data. 215 (64%) request originated from the emergency department, 107 (32%) from inpatient wards and 8 (2%) and 3 (1%) from ICU and outpatients respectively. The prevalence of pulmonary embolism in our study population was 13% similar to data from Wells and others. 57 (21%) patients were stratified to low risk, 169 (63%) to intermediate risk and 42 (16%) to high risk. The prevalences of pulmonary embolism were 9%, 12% and 24% respectively in these risk groups, comparable with published data. When evaluated against the same period in 2008, there was an absolute reduction of 136 (30%) CTPAs performed.

Conclusion Institutional implementation of a formal clinical prediction tool into the decision making process is feasible and yields significant reduction in CTPAs performed, with substantial cost savings and patient benefits.

Support Nil

Conflict of Interest No

ADHERENCE WITH INHALED CORTICOSTEROIDS IN ASTHMA IS PREDICTED BY BELIEFS, BEHAVIOURS AND SIDE EFFECTS

JIM FOSTER1, L SMITH1, SZ BOSZTA-ANTICEVICH1, T USHERWOOD2, SM SAWYER2, CS RANK3, HK REESE1
1University of Sydney, Australia, 2Royal Childrens Hospital Melbourne, Melbourne, Australia, and 3Johns Hopkins University, Baltimore, USA

Aim To identify beliefs and behaviours associated with poor adherence which could be used to guide tailored interventions in primary care.

Methods Patients aged >14 years with doctor-diagnosed asthma and a current ICS/LABA prescription completed questionnaires on beliefs and behaviours, side-effects, asthma control (ACQ), and underwent spirometry. Adherence with ICS/LABA was measured over the previous month using a 7-day diary card. Univariate and multivariate analyses of 61 questionnaire items identified predictors of adherence.

Results Ninety-nine of 100 patients completed the study (57 female; mean ± SD FEV1 % predicted 83 ± 23; ACQ 0.76 ± 0.76). Mean adherence was 75% ± 25 (n = 85). Thirty-one beliefs or behaviours were significantly associated with poor adherence (p < 0.05). Factor analysis of these 31 items identified 7 themes: F1. Perceived Necessity; F2. Safety Concerns; F3. Acceptance of asthma chronicity and ICS/LABA effectiveness; F4. Advice from family/friends; F5. Motivation/routine; F6. Ease of Use; and F7. Satisfaction with asthma management. Regression analysis demonstrated that 10 items in 5 themes independently predicted poor adherence (model Adj. R sq = 0.67; p < 0.001) including ‘My preventer is necessary to keep my asthma under control’ (F1), ‘I get side effects from my steroid inhaler’ (F2), ‘I will have asthma for a long time’ (F3), ‘My family/friends tell me I should use my preventer inhaler more often’ (F4), ‘I have a fixed daily routine for taking my asthma medications’ (F5). Adherence was lower for patients who attributed dental deterioration or dry eyes to their ICS, but not for hoarseness.

Conclusions This study identified 10 key beliefs or behaviours associated with poor adherence which may be amenable to change in patient-specific primary care interventions.

Support Asthma Foundation NSW, GlaxoSmithKline (medications).
PAEDIATRIC ASTHMA EDUCATION AND COMMUNICATION IN GENERAL PRACTICE: WHAT DO DOCTORS AND PARENTS SAY?

JK ROYDHOUSE1, S SHAH1, BG TOELE1,2, SM SAWYER2, JK PEAT1, CR JENKING1,3 FOR PACE AUSTRALIA
1University of Sydney, Sydney, New South Wales, Australia, 2Woolcock Institute, Glebe New South Wales, Australia, 3Royal Children’s Hospital, Melbourne, Victoria, Australia, and 4Research Consultant, Tomerong New South Wales, Australia

We aimed to compare GP and parent reports of asthma management styles from an RCT of Practitioner Asthma Communication and Education (PACE). Methods GPs recruited through local networks identified patients aged 2–14 with diagnosed asthma. Intervention GPs participated in two 3-hour workshops of patient education and counselling) provided by TEJ since 1995 and 5-yearly surveys are conducted to assess benefits and ongoing need.

Results At 12 months, 106 GPs (57 intervention, 49 control) and 213 parents (106 intervention, 107 control) provided data. More intervention GPs (50.0%) reported checking device use (vs. 39.1%; diff = 10.9%, p = 0.03). Intervention parents (83.9%) reported providing educational messages (vs. 72.3%; diff = 10.9%, p = 0.33). More control GPs (50.0%) reported checking device use (vs. 39.1%; diff = 10.9%, p = 0.33). More control GPs (50.0%) reported checking device use (vs. 39.1%; diff = 10.9%, p = 0.33). More control GPs (50.0%) reported checking device use (vs. 39.1%; diff = 10.9%, p = 0.33).

Conclusions GP and parental reports of device use checking were consistent. Reports of educational messages and communication were less consistent, though these may have been provided or used but not recognised by parents. These findings highlight that parents and their GPs can have very different perceptions of some aspects of a child’s asthma management. Care should be taken when selecting outcome measures for clinical trials.

Support Australian Government Department of Health and Ageing. Nomination Nil. Conflict of Interest Nil.
NON T CELL- DERIVED IL-17A REGULATES CIGARETTE SMOKE-INDUCED LUNG INFLAMMATION

R VLAHOVIĆ, HJ SEOW1, S BOZINOVSKI1, JS CHAN1, B JENKINS2, GP ANDERSON
1 Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia, and
2 Woolcock Institute of Medical Research, Sydney, New South Wales, Australia, and
3 University of Sydney, Sydney, New South Wales, Australia

Introduction Interleukin-17A is a cytokine released from T helper 17 (Th17) cells which induces and mediates various pro-inflammatory responses. As a result, IL-17A has been linked to many immune/autoimmune related diseases but its role in COPD has not been explored. In the present study we investigated whether IL-17A regulates cigarette smoke (CS)-induced lung inflammation.

Methods Wild-type (WT) or mice deficient in IL-17A (IL-17A−/−) were placed in a perspex chamber and exposed to CS generated from nine cigs per day for 4 days. In separate experiments, CS-exposed WT mice were treated with anti-IL-17A antibody. On the fifth day, mice were killed, the lungs lavaged with PBS and then harvested for genomic analysis.

Results WT mice exposed to CS for 4 days had significantly more BALF macrophages (4.3 ± 0.3(SEM) × 10^5) and neutrophils (3.8 ± 0.3 × 10^5) than sham-exposed mice (1.0 ± 0.2 × 10^5 and 0, respectively) (n = 5–26, p < 0.05). However, CS-exposed IL-17A−/− mice had significantly fewer macrophages (2.1 ± 0.1 × 10^5) and neutrophils (0.6 ± 0.1 × 10^5) than CS-exposed WT mice (n = 5–26, p < 0.05). Macrophage and neutrophil numbers in sham-exposed IL-17A−/− mice (1.2 ± 0.1 × 10^5 and 0 ± 0.2 × 10^5) were similar to those of sham-exposed WT mice. Gene expression analysis by qPCR showed that CS-exposed IL-17A−/− mice had markedly reduced MCP-1, TNFα, IL-17A, IL-23 and MIP-12 expression compared to CS-exposed WT mice. Treatment of CS-exposed mice with anti-IL-17A antibody significantly reduced CS-exposed BALF macrophages and neutrophils (n = 8, p < 0.05). In addition, we found that lungs of NOD-SCID mice deficient in T & B lymphocytes exposed IL-17A in response to CS.

Conclusions These data show that IL-17A regulates CS-induced lung inflammation and that targeting IL-17A may have therapeutic utility in inflammatory lung diseases where CS plays a role.

Conflict of Interest No.

THE EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE AND LUNG FUNCTION AT AGE 8 YEARS

E BELOUSOVA1, B TOELE1, S LEEDER1, G MARKS1,2
1 Woolcock Institute of Medical Research, Sydney, New South Wales, Australia, and
2 University of Sydney, Sydney, New South Wales, Australia

Introduction There are few birth cohort studies in which frequent, contemporary measures of tobacco smoke exposure have been related to lung function and airway responsiveness in later childhood.

AIM To examine the effects of in utero and postnatal exposure to ETS on lung function and airway responsiveness at age 8 years.

Methods Children with a family history of asthma were recruited antenatally into a randomised trial of house dust mite avoidance and dietary modification. At age 8 years we measured spirometric lung function, performed a methacholine challenge test to measure airway responsiveness (expressed as dose response ratio, DRR) and assessed sputum by skin prick tests. Smoking status during pregnancy was recorded soon after the birth of the child. Cumulative exposure to ETS was assessed at 3–6 monthly intervals to 7.5 years. Current exposure at age 8 years was assessed during the clinical visit at that age.

Results There was no significant effect of in utero or postnatal exposure on spirometric lung function at 8 years. Current exposure to ETS at age 8 years was associated with 0.24 fold lower DRR (less airway responsiveness) at 8 years in atopic children (95% CI: 0.1–0.64 fold, p = 0.004, adjusted for potential confounders). This effect was not seen in non-atopic children and was not significant for exposures at earlier ages.

Conclusion In this cohort at risk for asthma, ETS exposure did not significantly influence lung function at 8 years. If parents had avoided smoking around children with asthma at age 8 years, this might explain the apparent paradoxical effect of current ETS exposure on DRR at this age.

Reference 1. Marks GB et al. J Allergy Clin Immunol. 2006;118:53–61.

Support NHMRC, Australia and Asthma CRC.

Conflict of Interest Nil.

QUALITY OF LIFE ASSESSMENT – VALIDATING IN A REMOTE INDIGENOUS AUSTRALIAN AND INDONESIAN SETTING

GIANRE MAGUIRE1, NICHOLAS ANSTEY1, PAUL KELLY1, BARBARA MOLANUS2, MARIAN TCHAN1, BURT CURRIE1
1 School of Medicine & Dentistry, James Cook University, Queensland, Australia, 2 Menzies School of Health Research, Darwin, Northern Territory, Australia, and 3 National Centre for Epidemiology and Population Health, ANU Canberra, ACT, Australia

Introduction Quality of life (QoL) measurement is important in assessing the impact of lung disease on individuals and evaluating interventions. Whilst respiratory-related QoL measures are well validated in high income populations their utility in middle-low income countries, such as Indonesia, and for Indigenous Australians is less well understood.

Methods The St George’s Respiratory Questionnaire (SGRQ) was adapted for Indigenous Australian and Indonesian use utilising local health care staff. These were validated using a clinical trial involving Aboriginal Australians with COPD and a cohort study of Indigenous Australians with pulmonary tuberculosis (PTB). Scores were correlated with lung function, acute exacerbations of COPD, exercise tolerance and, in PTB patients, with the extent of CXR involvement and over time with treatment.

Results A total of 220 subjects were enrolled (105 Indigenous Australians, 115 Indonesians). In the Indigenous Australian setting the SGRQ total score was independently associated with exacerbation frequency and lung function (% predicted FEV1) whilst the symptom score was associated more strongly with AE frequency and activity score with lung function. In Indonesians with PTB the total SGRQ score correlated with treatment response over time as well as lung function (% predicted FVC), exercise tolerance (6MWT) and the extent of involvement on CXR.

Conclusions In an Indigenous Australian and Indonesia, setting respiratory-related QoL measures are important in assessing the impact of lung disease. The SGRQ correlates with lung function, exercise performance, disease activity and treatment. These tools should be a useful addition to evaluating interventions in this setting.

Support NHMRC, CRC for Aboriginal Health, Australian Respiratory Council, Welcome Trust, Tudor Foundation.

Nominations Nil.

Conflict of Interest No.
SMOKING HAS POTENTIAL TO INITIATE EPITHELIAL MESENCHYMA TRANSITION (EMT) IN THE AIRWAY MUCOSA

Respirology (2010) 15 (Suppl. 1), A11–A40

INTERLEUKIN-6 (IL-6) CYTOKINE FAMILY IN THE PATHOGENESIS OF EMPHYSEMA

SABELLA RUWANPURA1, JESSICA JONES2, LOUISE MCLEOD1, AUSTIN MILLER1, PHILIP BARDIN3, GARY ANDERSON1 and BRENDAN JENKINS1
1Monash Institute of Medical Research, Victoria, Australia, and 2The University of Melbourne; Melbourne, Victoria, Australia

Pulmonary emphysema is a major component of the Chronic Obstructive Pulmonary Disease (COPD), and also predisposes affected individuals to lung cancer. Emphysema can be a familial or acquired disease, with the great variation in development of disease in at-risk populations reflecting the influence of other susceptibility determinants. In this regard, the IL-6 cytokine family has been linked with emphysema pathogenesis. However, studies into the definitive mechanisms by which these cytokines cause emphysema have been hampered by the absence of informative animal disease models. To address this issue, we have utilized a sophisticated animal model (gp130F/F mice) with a subtle mutation in gp130 signalling by IL-6 cause’s alveolar cells to undergo apoptosis, which coincide with increased GSH would increase gal-3 levels and improve efferocytosis. We investigated

Conflict of Interest Nil.

Supported by The NHMRC project grant 490023.
BASEMENT MEMBRANE REMODELLING IN COPD RESPONDS TO INHALED CORTICOSTEROIDS

AMIR SOLTANI, SUMNAMINI S SOHAL, DAVID REID, STEVE WESTON, HK MULLER, RICHARD WOOD-BAKER, EH WALTERS
Menzies Research Institute, University of Tasmania, Tasmania, Australia

Introduction Our knowledge about the effects of inhaled corticosteroids (ICS) on airway remodelling in chronic obstructive pulmonary disease (COPD) is limited. We have previously reported that in bronchial biopsies (BB) from COPD subjects the reticular basement membrane (Rbm) is fragmented and hypervascular. In this study we have examined the effects of ICS on these airway remodelling changes in COPD.

Methods In a double blind and randomised study we compared the effects of 6 months of fluticasone propionate (FP, 0.5 mg/twice daily) with placebo. BB were stained with collagen IV antibody to mark vessel endothelial basement membrane. The length of Rbm splits and the number and area of vessels in the Rbm were compared before and after treatment.

Results COPD subjects were randomized 2:1 to receive either FP (n = 15) or placebo (n = 7). There were no differences between the groups before the treatment. The length of Rbm splitting, as an index of Rbm fragmentation, was significantly decreased by FP (median [range] 19.1 (0.2–42.8) before vs. 2.6 (0–88.6) µm/µm Rbm × 100 after, p < 0.003) but not by placebo [24 (6.6–109) before vs. 26.9 (2.5–48.5) µm/µm Rbm × 100 after, p = 0.7]. The number and area of vessels within the Rbm did not change following either FP or placebo.

Conclusion We have proposed that Rbm fragmentation is the result of local proteolytic activity involved in active epithelial-mesenchymal transition (EMT). The results are likely to represent a suppression of this process by ICS, but this needs confirmation by further investigation of specific EMT markers.

Supported by NHMRC and the Royal Hobart Hospital Research Foundation.

Conflict of Interest No. GSK has provided untied funding to our research group.

THE RELATIONSHIP BETWEEN SYSTEMIC INFLAMMATION, AIRWAY INFLAMMATION AND AIRWAY OBSTRUCTION IN COPD

Jocie L SIMPSON1,2, VENEDA M MCDONALD1,2, PETRON G GIBSON1,2
1Centre for Asthma and Respiratory Disease, The University of Newcastle, New South Wales, Australia, and 2Department of Respiratory and Sleep Medicine, Hunter Medical Research Institute, New South Wales, Australia

Introduction COPD is a complex disease characterised by fixed airflow obstruction and neutrophilic airway inflammation. Markers of systemic inflammation such as serum amyloid A (SAA) are elevated in COPD. However, little is known about the relationship between airway and systemic inflammation. This study tested the hypothesis that systemic inflammation is associated with airway neutrophils in COPD.

Methods Participants with COPD (n = 65, >55 years, with FEV1/FVC <70 and FEV1% predicted <50) underwent clinical assessment, sputum blood, and CRP and sputum induction. Sputum was processed for differential cell count and mediators.

Results Airway proportions of neutrophils and eosinophils, levels of IL-8, total MMP-9 and gene expression of IL-4 were increased in participants with COPD. Serum IL-6 (median q1–q3: 2.9 (1.7–4.9)) vs. 1.7 (1.1–2.5) pg/mL, p = 0.006), CRP (15.5 (2.0–12.2) vs. 2.4 (1.1–7.0) mg/L, p = 0.01) and SAA (4184 (2289–8873) vs. 2532 (1568–4325) ng/mL, p = 0.006) were significantly elevated in COPD compared to HC. All markers of systemic inflammation were associated with the BOODE index while IL-6 and CRP were associated with FEV1% and CRP with BMI. SAA and CRP were only weakly associated with sputum neutrophils (r = 0.24 p = 0.04 and r = 0.29 p = 0.02 respectively). No marker of systemic inflammation was correlated to sputum eosinophils.

Conclusion Systemic inflammation is increased in COPD and relates to clinical outcomes but is distinct from airway inflammation. This suggests that systemic inflammation is not a surrogate marker for airway inflammation in COPD, may have a different pathogenesis, and may respond to specific therapy.

Supported by NHMRC.

Conflict of Interest No.
TRANSFORMING GROWTH FACTOR ETA SIGNALING IN MALIGNANT MESOTHELIOMA GROWTH AND COLLAGEN PRODUCTION

B BADRIAN1, S MUTSAERS2, G LEE2
1PathWest Laboratory Medicine, Lung Institute of Western Australia, QEII Medical Centre, and 2Medicine & Physiopathology, Lung Institute of Western Australia, University of Western Australia, Perth, Western Australia, Australia

Introduction Malignant Mesothelioma (MM) is an aggressive cancer with a very poor prognosis. Interactions of the components of the extracellular matrix (ECM) are now known to be important for the growth and regulation of cancer cells. TGF-β is an important regulator of the ECM and in particular collagen. Previous data in our laboratory has shown that blocking TGF-β signaling by using TGF-β antibodies inhibits collagen production and MM growth.

Aim To determine the signaling pathways downstream of TGF-β that are important in the regulation of collagen expression in MM.

Methods Components of the TGF-β pathway were inhibited by use of chemical inhibitors and overexpression of the endogenous inhibitor Smad7 in control and MM cell lines. Collagen levels were measured by real-time PCR.

Results Collagen regulation is thought to occur through the classic Smad2/3 signaling pathway. Our data show that Smad7 overexpression inhibits TGF-β-induced collagen production in normal mesothelial cells and the mesothelial cell line MET-5A but not in the MM cell lines investigated. Therefore, the Smad2/3 pathway for collagen regulation appears to be altered in malignant mesothelioma. It was shown that Smad2/3 are expressed, phosphorylated and activated by TGF-β in the MM cell lines. Our results indicate that nuclear import of Smad4, which is responsible for the nuclear import of Smad2/3, is altered in MM.

Conclusions Collagen is not regulated by the Smad2/3 signaling pathway in MM, and this may be due to the altered function of Smad4. These results are important for understanding the growth and regulation of MM.

Conflict of Interest No.

Funding NHMRC.

Nomination Nil.

Mesothelioma in Western Australia and Bristol (UK)

FRASER JH BRIMS1, ROHAN S FINN1, AKKAR GANDHI1, NASSIF IBRAHIM1, NOEL OLSEN1, AW MUSK1, NICK MASKELL2, YC GARY LEE1
1University of Western Australia/Sir Charles Gairdner Hospital, Perth, Western Australia, Australia, and 2North Bristol Lung Centre, Southmead Hospital, Bristol, UK

Background Malignant pleural mesothelioma (MPM) is an incurable malignancy caused by asbestos exposure. We sought to study the disease distribution and cause of death in two cohorts exposed to predominantly crocidolite (WA) or chrysotile (UK) asbestos.

Methods We interrogated the Western Australia (WA) mesothelioma registry and Bristol (UK) Coroner’s reports for post-mortem (PM) records of confirmed MPM cases.

Results Despite different asbestos exposures, the two cohorts were very similar in demographics, rates of histological subtype and extent of disease. A total of 318 complete PM records were identified (WA 169, UK 149). 300 (94.3%) were male, with a mean (SD) age of 68.4 (11.5) years, and predominantly (56%) right sided tumour. Distant metastases were very common, affecting 59.7% of patients. An anatomical cause of death was established in only 92 (28.9%) cases. Pulmonary embolus (PE) contributed to death in 13 (4.1%) cases. In the Western Australia cohort, median survival from diagnosis was significantly shorter in the sarcomatoid group despite no significant difference in rates of distant metastases (Table 1).

Table 1. Histological Subtype, Distant Metastases and Survival in MPM.

| Subtype          | Metastases | Survival (months) |
|------------------|------------|-------------------|
| Epithelioid      | 61 (67.0%) | 262 days          |
| Biphasic         | 53 (70.7%) | 214 days          |
| Sarcomatoid      | 34 (55.7%) | 127 days          |

Conclusion To our knowledge, this is the largest post-mortem series of metastases in MPM in English literature. We found that distant metastases were common and sarcomatoid MPM has a significantly poorer prognosis. Rates of PE were relatively low in this combined cohort.

Conflict of Interest No.

OCCUPATIONAL EXPOSURES AND ADULT ONSET ASTHMA IN A POPULATION BASED COHORT

RF HOY1, G BENKE1, MR MATHESON2, EH WALTERS1,2,3, SC DHARMAGE2, MJ ABRAMS1
1Department of Epidemiology & Preventive Medicine, Monash University, 2Centre for MEGA Epidemiology, The University of Melbourne, Victoria, and 3Menzies Research Institute, University of Tasmania, Hobart, Tasmania, Australia

Introduction Specific jobs and exposures are known to be risk factors for the development of occupational asthma. We examined the associations between adult onset asthma and occupational exposures in a population-based cohort.

Methods Participants in the Tasmanian Longitudinal Health Study (TAHS) have been followed from 7 (n = 8583) to 44 years of age. Occupational histories were obtained from 1592 subjects at the age of 44. Occupations were linked to an asthma-specific Job Exposure Matrix with additional expert judgment of exposure to 18 high-risk substances. Adult onset asthma was defined by a positive response to asthma specific questions at ages 7 or 14. Odds Ratios (OR and 95% confidence intervals) were estimated in SPSS.

Results There were 290 subjects with adult onset asthma, which was significantly associated with occupational exposure to latex (OR 1.78, 95% CI 1.16–2.75) and reactive cleaning or disinfecting products (1.52, 1.03–2.24). Negative associations were seen for exposure to combustion products or exhaust fumes (0.58, 0.39–0.86) and high probability of accidental peak exposures to irritants (0.51, 0.27–0.97). No associations were identified for other well-described causes of occupational asthma such as isocyanates, agricultural antigens or wood dust.

Conclusions There was no increased risk of adult onset asthma associated with occupational exposures to latex and cleaning or disinfecting products. Apparent protective associations may be as a result of selection bias.

Support NHMRC; Victorian & Tasmanian Asthma Foundations, Clifford Craig Medical Research Trust, Royal Hobart Hospital Research Foundation.

Conflict of Interest No.

MORTALITY OF CHILDREN EXPOSED TO CROCIDOLITE AT WITTONOOK, WESTERN AUSTRALIA

AW MUSK1, R MINA1, J SLEITH1, NOEL OLSEN, N KLERK1, A REID1,4
1School of Population Health, University of Western Australia, Crawley, Australia, 2Sir Charles Gairdner Hospital, Nedlands, Australia, 3Institute for Child Health Research, Subiaco, Australia, and 4Centre for Medical Research, University of Western Australia, Crawley, Australia

Introduction Blue asbestos (crocidolite) was mined and milled at Wittenoom between 1943 and 1966. Tailings from the mine were distributed and used extensively throughout the town. Exposure to children also occurred from the laundering of workers clothes at home. Earlier work has shown a lower risk of malignant mesothelioma (MM) in children from Wittenoom than in those exposed to blue asbestos as adults.

Aim To examine the health outcomes of 2,483 children first exposed to blue asbestos at Wittenoom when they were less than 16 years of age.

Methods Standardised Mortality Ratios (SMRs) were calculated to compare Wittenoom children’s mortality with the Western Australian population.

Results About 1,204 females and 1,279 males were children at Wittenoom, mean age of arrival 4 years (SD 4 years); 419 (17%) were born there or moved there soon after birth. Median duration of residence was 19 months (Q3 7–41 months). There were 228 deaths (75 females and 153 males) between 1950 and end of 2006. 40 deaths were from malignant mesothelioma (17% of all deaths – 12 females, 28 males, - 39 pleural, 1 peritoneal). Among males, there was excess mortality from all causes (SMR = 1.89), all cancers (SMR = 3.70), MM (SMR = 73), accidents, injuries and poisonings (SMR = 1.54) and circulatory disease (SMR = 2.21). Mortality from suicide and transport accidents were also in excess but not statistically significantly increased. Among females there was excess but not statistically significantly increased. Among females there was excess but not statistically significantly increased. Among females there was excess but not statistically significantly increased.

Conclusion Former children of Wittenoom experience high cancer mortality.

Support NHMRC.

Nomination Nil.

Conflict of Interest Nil.

© 2010 The Author(s)
VARIABILITY OF RESPIRATORY SYSTEM IMPEDANCE IN SCHOOL-AGED CHILDREN WITH ASTHMA

P ROBINSON1,2,3, M TURNER1,2,3, G KING1,2,4, N BROWN1,2,4, L MORAWSKA1,2,4, G MARKS1,2,3, THE UPTECH INVESTIGATORS1
1Woolcock Institute of Medical Research, 2University of Sydney, Sydney, Australia, 3Children’s Hospital at Westmead, Sydney, 4Children’s Medical Research Institute, Royal Children’s Hospital, Sydney, Australia

Introduction The role of FOT variability in disease monitoring is unclear.

 Aim To characterise impedance variability at 6 Hz in asthma and its relationship to asthma severity.

Methods A school-based cohort of 38 non-asthmatic children, aged (mean (SD)) 9.5 (1.8) years (UPTECH feasibility study) were tested on two occasions 2 weeks apart. An asthma camp cohort of 22 asthmatics, aged 10.5 (1.2) years, were tested daily for 5 days. Mean Resistance (Rrs6) and reactance (Xrs6) of at least three technically acceptable one minute recordings were reported. Medications were not withheld. Variability was assessed by Intraclass Correlation Coefficient (ICC) and within-subject Standard Deviation (SDw) using first and last testing day data, and all 5 days of data for SDw severity comparison amongst asthmatics.

Results Repeat FOT measures at 6 Hz were obtained in 34/38 non-asthmatic children. Mean (SD) Rrs6 and Xrs6 was 6.89 (1.1) and -1.57 (0.52) cmH2O/l/s in the asthma camp cohort respectively. Rrs6 variability tended to be higher in persistent vs. intermittent asthmatics but did not reach statistical significance (p > 0.07).

Conclusions Rrs6 variability is increased in children with asthma and tends to be higher with increased severity.

Support NHMRC PhD scholarship. Allen & Hanbury Paediatric Grant in aid award. Nomination Nil. Conflict of Interest Nil.  

DUAL-CENTRE RANDOMISED TRIAL ON TAILORED ASTHMA THERAPY BASED ON EXHALED NITRIC OXIDE (FENO) VS. ROUTINE CLINICAL CARE

HL PETSKY1,2, AM LI1, JA KYNASTON1, C TURNER2, AB CHANG1
1Queensland Children’s Respiratory Centre, Royal Children’s Hospital, Brisbane, Australia, 2School of Nursing and Midwifery, The University of Queensland, Brisbane, Australia, 3Prince of Wales Hospital, Chinese University of Hong Kong, and 4General Paediatrics, Royal Children’s Hospital, Brisbane, Australia

Introduction Our Cochrane review examining the efficacy of using FeNO to tailor the dose of inhaled corticosteroid showed that FeNO cannot be routinely recommended for clinical practice at this stage and remains uncertain. However all the 6 studies used a single FeNO cut-off. In this RCT we determined if asthma monitoring using FeNO (using two different cut-offs dependent on atopy) is better than control (symptoms and FEV1) in preventing asthma exacerbations in children on inhaled corticosteroids.

Methods Over 12-months, children underwent spirometry, FeNO, QOL and asthma cough diary during every visit. Treatment for asthma was adjusted according to pre-determined criteria taking into account atopy status and dependent on allocation group (FeNO or control).

Results About 63 children were randomised: FeNO group (N = 31, median age 10.2, IQR 5.75), or control group (N = 32, median age 10.1, IQR 5.69). Significantly fewer children in the FeNO group had asthma exacerbations compared to the control group (6 vs. 15; p = 0.021) over 12-months. Number needed to treat (NNT) to prevent one child from having any exacerbation in 12 months = 4 (95%CI 3, 24). Parental QOL improved in FeNO group at final visit in comparison to the QOL in control group (p = 0.042). FEV1 increased in both groups over the duration of the study but there was no difference between the groups when measured at baseline (p = 0.661) and at final (p = 0.385).

Conclusion Tailoring of asthma medications in accordance to FeNO levels (compared to usual management), taking into account atopy status, reduces asthma exacerbations and improves asthma QOL. However both strategies equally improved FEV1.

Conflict of Interest Nil. Supported by Asthma Foundation of Queensland.

FUNHALER® IMPROVES SPACER TECHNIQUE BUT NOT CLINICAL OUTCOME IN PRECHOOL CHILDREN WITH ASTHMA

André SCHULTZ1,2,4, PETER SLY2, GUGCHEN ZHANG1, PETER LE SOUEF1,2,4, SCHAADEN DEVADASON1,2
1School of Paediatric and Child Health, University of Western Australia, Perth, Western Australia, Australia, 2Department of Respiratory Medicine, Princess Margaret Hospital for Children, Perth, Western Australia, Australia, 3Telethon Institute for Child Health Research and Centre for Child Health Research, Australia, 4University of Western Australia, Perth, Western Australia, Australia, and 5Division of Clinical Research, Princess Margaret Hospital for Children, Perth, Western Australia, Australia

Background Inhaled corticosteroids have a modest effect on improving symptom control in preschool asthmatic children. Delivery of inhaled steroids with pMDI-scarpers are influenced by the children’s proficiency in spacer technique, and adherence to prescribed medication.

Aim To investigate the influence of an incentive spacer (Funhaler), on spacer technique, adherence to treatment, and asthma control in preschool asthmatic children.

Methods About 132 children aged 2–6 years, and being prescribed regular inhaled steroids in the community were randomised to receive regular inhaled fluticasone through either an Aerolacher Plus1,2 of a Funhaler1. Subjects were followed up three times a year for a month. In competency in spacer technique was measured at each visit by measuring the amount of salbutamol inhaled from spacer onto a filter interposed between subject and spacer. Adherence was monitored by Smartinha1 electronic devices. Symptoms were recorded on diary cards for a week before each study visit.

Results There was no difference between the Funhaler group and the Aerolacher group in terms of adherence to medication or measures of asthma control (p > 0.05). Spacer technique was significantly better in the Funhaler group in subjects younger than 4 years of age at time of randomisation (p < 0.00). There was large inter subject variation in drug dose inhaled on filter, ranging from 0–100% (drug dose recovered from filter as a percentage of total dose recovered), and mean adherence over each 3 month period ranging from 0–100%.

Discussion The Funhaler1 does not improve clinical outcome, but improves spacer technique in children younger than 4 years of age. The large variability in adherence and drug delivery should encourage both efforts to improve adherence, and efforts to standardise inhaled drug delivery in preschool children.

Supported by The NIH. Conflict of Interest No.

Respiratory Infectious Disease SIG Oral Session 2

TUBERCULOSIS IN CHILDREN IN QUEENSLAND AUSTRALIA 1990–2007: EPIDEMIOLOGICAL AND CLINICAL FEATURES

H WALKER1, V VASKA2, M STICKLEY1, K GRIMWOOD1, A KONSTANTINOS2
1Queensland Tuberculosis Control Centre, Brisbane, Australia, and 2Queensland Children’s Medical Research Institute, Royal Children’s Hospital, Brisbane, Australia

Introduction Queensland has a low incidence of tuberculosis (TB) (<4/105/year), with most cases occurring in high risk group migrants (HRGM) from countries with a high TB incidence (>50/105/year). Many children with TB diagnosed in Far North Queensland are visitors from Papua New Guinea (PNG). We describe the epidemiology and clinical characteristics of TB cases aged <15 years in Queensland residents from 1990–2007, and briefly describe characteristics of the PNG childhood TB cases from 2002–2007.

Methods Retrospective review of case records at Queensland TB Control Centre. Results There were 85 notified cases of TB in Queensland resident children from 1990–2007. About 41 were female and 42 were <5 years old. 44 were overseas-born (OB), with 42 HRGM. 28 were non-indigenous and 13 indigenous Australians. Annual incidence rates have declined from 1.2/105/year to 0.2/105/year between periods 1990–1994 and 2005–2007. About 75% of OB cases were notified within 1 year of arrival. 30 of the Australian-born cases were close household contacts of an adult TB case. About 18 cases had culture confirmed disease (15 fully sensitive to first line drugs, one multidrug resistant), 70% had pulmonary and 23% had lymph node TB. About 82 cases completed the treatment, two were lost to follow-up and one died. Compared to adult TB cases, children were more likely to be refugees (OR 2.1 (CI 1.1–3.7)), diagnosed on contact screening (OR 14.4 (7.9–25.8)), have lymphatic TB (OR 2.54 (CI 1.5–4.3)), and less likely to be culture confirmed (OR 0.7 (CI 0.4–1.2)). The PNG child visitors’ cases diagnosed in Queensland had a higher level of severe and culture-confirmed disease.

Conclusion Queensland has a very low burden of childhood TB, indicating low levels of TB transmission in the community. HRGM children, especially refugees, will remain at risk due to infection acquired overseas. Contact screening is an important method of diagnosing early TB, and refugee screening and preventive treatment may play a role in protecting this group.

Funding Support Nil. Conflicts of Interest Nil.

© 2010 The Author(s)
Journal Compilation © 2010 Asian Pacific Society of Respirology
THE USE OF PROCALCITONIN REDUCED HOSPITAL ADMISSION AND LENGTH OF STAY IN COMMUNITY-ACQUIRED PNEUMONIA

Erich WONG, Steven Lindstrom
Department of Respiratory Medicine, St George Hospital, New South Wales, Australia

Introduction Community-acquired pneumonia (CAP) is a leading cause of mortality, morbidity and hospital admission places strain on our healthcare system. Procalcitonin (PCT) is a biomarker of bacterial infection which may help gauge the severity and prognosis of patients with CAP.

Aim To examine the role of PCT measurement in reducing hospital admissions, length of stay (LOS), and antibiotic (AB) usage in patients with CAP.

Methods Prospective, single-blinded, externally controlled study of consenting adult patients admitted with CAP. PCT levels were obtained on day 1 and day 9 (if indicated). The investigator evaluated clinical parameters and the PCT values to determine the timing of oral AB switch and discharge. This process was used to compare with standard practice but was not actually implemented for the purpose of this study.

Results Sixty patients were included in the study. The mean age was 66.5±21.2y and 56.3% were male. The average PSI was 91 ± 40 (Class IV) and the median CURB-65 was 2. The mean LOS for this cohort was 5.32±7.46 d and the calculated LOS using PCT guidance pathway was 3.68±2.81 d. (p = 0.00006) A multivariate analysis will be presented.

Conclusions Our study supports the hypothesis that the incorporation of PCT levels can reduce the requirement for hospital admission and LOS in patients with CAP. A randomised prospective clinical trial is planned to help clarify these findings.

Support Nil.

Nomination Nil.

Conflict of Interest No.

RESPIRATORY VIRUSES, PARTICULARLY RHINOVIRUSES, ARE COMMONLY DETECTED IN PAPUA NEW GUINEAN CHILDREN WITH LOWER RESPIRATORY INFECTION AND WHEN HEALTHY

INGRID A LAING1, GLENNY CHIDLOW2, AUDREY MICHAEL3, CELESTINE AHO3, MILDERE LAPI3, ANDREW GREENHILL2, DAVID SMITH4, PETER SIBA1, GERRY HARNETT2, DEBORAH LEHMANN1

1Telethon Institute for Child Health Research, Western Australia, Australia, 2Pathwest Laboratory Medicine, Western Australia, Australia, and 3Papua New Guinea Institute for Medical Research, EHP, Papua New Guinea

Introduction Children in the highlands of Papua New Guinea (PNG) suffer on average 4.3 acute lower respiratory infections (ALRIs) before age 18 months, 1/3 of which are moderate or severe. While Streptococcus pneumoniae and Haemophilus influenzae are the primary bacterial cause of ALRI in PNG, the role of viruses in the aetiology of ALRI is uncertain.

Aim Determine identification rates of respiratory viruses in nasal samples collected from children with moderate/severe ALRI and healthy children aged <18 months in PNG.

Methods As part of a neonatal pneumococcal conjugate vaccine trial in the PNG highlands, we collected pernasal swabs from children with moderate/severe ALRI (n = 49) and at routine follow-up (n = 48). RT-PCR methods were used to identify a broad range of respiratory viruses. The frequency of viral detection was compared between groups of samples collected during an ALRI and routinely using Chi-square analysis.

Results Several viruses were detected more frequently in ALRI than routine samples: adenoviruses 33.3/12.5% (of ALRI samples positive%/of routine samples positive) p = 0.032, influenza viruses 22.5/7.9% p = 0.023 and respiratory syncytial virus (RSV) 8.2/ 0.0 p = 0.043. Human metapneumovirus and parainfluenza viruses were detected in four and three samples, with no difference between groups. Human coronaviruses and human rhinoviruses (HRV) were less commonly detected in ALRI than in routine samples (4.2/9.3 p = 0.042 and 57.1/72.3 p = 0.178, respectively). A total of 62 different HRV strains were identified.

Conclusion in young children in PNG, viral identification rates are high, with RSV, adenoviruses and influenza viruses associated with moderate/severe ALRI and a large amount of genetic diversity of rhinoviruses in both sick and healthy children.

Support Wellcome/NHMRC/Australian Respiratory Council.

Nomination Janet Eldon International Travel Award.

Conflict of Interest No.
Asthma and Allergy SIG Oral Session

DYSREGULATED REPAIR IS AN INTRINSIC ABNORMALITY OF ASTHMATIC EPITHELIUM INDEPENDENT OF ATOPY

KIM LINCH1,2, EN SUTANTO1,3, SM STICK1,2,3, A KICIO1,2,3 1THCHR, Subiaco Western Australia, Australia, 2Department of Respiratory Medicine, Princess Margaret Hospital, Perth, Western Australia, Australia, and 3School of Paediatrics and Child Health, University of Western Australia, Nedlands, Western Australia, Australia

Introduction In response to injury, normal and efficient epithelial repair is essential in order to maintain barrier integrity and immune function. However, aberrant repair has been suggested as a contributor to disease progression in asthma. Many studies have only included subjects with atopic asthma and thus any intrinsic epithelial abnormality common to all asthmatic phenotypes is difficult to isolate. This study aimed to assess whether epithelial repair is dysregulated in asthmatic subjects and if this is common to the disease or is phenotype specific. The regulatory mechanisms promoting the cellular proliferation and migratory aspects of the repair process were also assessed.

Methods Paediatric airway epithelial cells (pAEC) of atopic and non-atopic healthy and asthmatic subjects were isolated by non-bronchoscopic bronchial brushings. Culture monolayers were wounded using an in-house wounding device, and the percentage of wound closure determined daily. Proliferation and migration were also assessed over the course of repair using Western Blot.

Results pAECs from healthy non-atopic (pAECA) and healthy atopic (pAECA) subjects successfully achieved full wound closure between 8–10 days. In contrast, atopic asthmatic (pAECAA) and non atopic asthmatic (pAECAAA) subjects failed to fully repair and only achieved 40% wound closure by 10 days. Protein analysis showed a 4-fold increase in proliferation and 2-fold increase in migratory markers during repair in pAECAAA. However, reduced proliferation and no migration activity were seen in pAECAAA.

Conclusion Atopic and non-atopic asthmatic epithelial cells possess dysfunctional repair profiles in response to mechanical wounding. Results suggest dysregulated repair is an intrinsic epithelial abnormality in asthma and this appears to be independent of phenotypic criteria or atopy.

Supported by The NHMRC, RAINER, CHRF.

Conflict of Interest No.

COUGH REFLLEX SENSITIVITY IMPROVES WITH SPEECH LANGUAGE PATHOLOGY MANAGEMENT OF REFRACTORY CHRONIC COUGH

NICOLE RYAN1,2, ANNE VERTIGAN1,3, SARAH BONE, PETER GIBSON1,2 1Centre for Asthma and Respiratory Diseases, School of Medicine and Public Health, The University of Newcastle, New South Wales, Australia, 2Department of Respiratory and Sleep Medicine, Hunter Medical Research Institute, John Hunter Hospital, New South Wales, Australia, and 3Department of Speech Pathology, John Hunter Hospital, New South Wales, Australia

Introduction Refractory chronic cough is associated with increased cough sensitivity. Speech pathology intervention has been shown to be an effective intervention for refractory cough but the mechanism behind the improvement is not known. This study provides objective measures of the mechanism and the number of treatments required to effect a response.

Methods Adults with chronic cough (n = 17) were assessed before, during and after speech pathology intervention. The primary outcome measures were capsaicin cough reflex sensitivity, automated cough frequency detection and cough-related quality of life.

Results Participants responded to the treatment with a significant improvement in cough-related quality of life, p = 0.002, cough reflex sensitivity, C5: Mean ± SD 13.2 ± 15.8 vs. CS:174.9 ± 227.3 μmol/L, p = 0.013, cough frequency CF: 72.5 ± 55.8 vs. 26 ± 27.9 coughs/h, p = 0.009, cough threshold CT: 4.21 ± 3.65 vs. 46.9 ± 69.1 μmol/L, p = 0.009, and urge-to-cough UTC: Median (IQR), 5(1) vs. 14(3), p = 0.01.

Conclusion Speech pathology management is an effective treatment for refractory chronic cough. The mechanism behind the improvement is due to reduced laryngeal irritation which results in decreased cough sensitivity, improvement in cough symptoms, laryngeal symptoms, and cough quality of life.

Supported by NHMRC CRE in Respiratory and Sleep Medicine, and Hunter Medical Research Institute RHD Support Grant.

Nomination Janet Elder International Travel Award, and TSANZ travel grant to the 2010 TSANZ ASM.

Conflict of Interest No.

THE PREDICTORS OF AIRWAY HYPERRESPONSIVENESS ARE DIFFERENT IN YOUNGER AND OLDER ASTHMATICS

KATE HARDAKER1,2,3, SUB DOWNE1,3, JESSICA KERMODE1,2,3, CLAIRE FARAH1,2,3, NORBERT BEREND1,2,3, GREGORY KING1,2,4, CHERYL SALOME1,2,3 1Woolcock Institute of Medical Research, New South Wales, Australia, 2University of Sydney, New South Wales, Australia, 3Department of Respiratory Medicine, Royal North Shore Hospital, New South Wales, Australia

Introduction Airway hyperresponsiveness (AHR) is a characteristic feature of asthma. In young asthmatics, severity of AHR is related to exhaled nitric oxide (eNO), a marker of eosinophilic airway inflammation, and ventilation heterogeneity in the conducting airways (Scond). With increasing age, eosinophilic inflammation decreases and ventilation heterogeneity in the very peripheral, acinar, airways worsens.

 Aim To determine if the predictors of AHR differ in young and older asthmatics.

Methods About 61 young (18–46) and 41 older (50–80) asthmatic subjects underwent baseline spirometry, body plethysmography, eNO, multiple breath nitrogen washout (MBNW), and methacholine (MCh) challenge. AHR was expressed as dose response slope (DRS = %fall FEV1/μmol MCh). Ventilation heterogeneity of the conducting (Scond) and acinar (SACIN) airways were calculated from the MBNW. Predictors of AHR in each group were determined by multiple linear regression.

Results Compared to younger asthmatics, older asthmatics had lower values of eNO, less severe AHR, worse acinar heterogeneity; however there were no differences in Scond values. In younger asthmatics, AHR was predicted by FEV1/FVC (partial r2 = 0.29), eNO (partial r2 = 0.13) and Scond (partial r2 = 0.06) (overall r2 = 0.48, p < 0.0001). In older asthmatics, AHR was predicted by RV % predicted (partial r2 = 0.29), SACIN (partial r2 = 0.17) and FEV1 % predicted (partial r2 = 0.05) (overall r2 = 0.51, p < 0.0001).

Conclusions The predictors of AHR are different in young and old asthmatics. In older asthmatics, eNO is not a significant predictor of AHR, which may reflect the changing inflammatory profile associated with aging. The association between AHR and both RV and SACIN suggests that AHR in older asthmatics is determined by abnormalities in very peripheral airways.

Supported by NHMRC & Asthma NSW.

Nomination Nil.

Conflict of Interest No.

A META-ANALYSIS OF ADVERSE PERINATAL OUTCOMES IN ASTHMATIC WOMEN: EFFECT OF ASTHMA ON SIZE AT BIRTH AND TIMING OF BIRTH

VANESSA E MURPHY1, JENNIFER NAMAZY2, HEATHER POWELL1, MICHAEL SCHATZ2, CHRISTINA CHAMBERS2, JOHN ATTILLA1, and PETER G GIBSON1 1University of Newcastle and HMRI, Newcastle New South Wales, Australia, 2Scripps Clinic San Diego, USA, 3Kaiser Permanente Medical Center, San Diego, USA, and 4University of California, San Diego, USA

Introduction In this systematic review and meta-analysis, we sought to establish if maternal asthma is associated with an increased risk of adverse perinatal outcomes associated with size at birth and timing of birth.

Methods Electronic databases were searched for the following terms: (asthma or wheeze) and (pregnan* or perinat* or obstet*). Cohort studies published between 1975 and March 2009 were considered for inclusion. 103 articles were identified, and 40 publications involving 1,637,180 subjects met the inclusion criteria, by reporting at least one perinatal outcome in pregnant women with and without asthma. Meta-analysis was conducted with subgroup analyses by study design and active asthma management.

Results (Maternal asthma was associated with an increased risk of low birth weight (relative risk [RR] 1.46, 95% confidence interval [CI] 1.22, 1.75), small for gestational age (SGA), RR 1.22, CI 1.14, 1.31), very SGA (RR 1.27, CI 1.18, 1.37), significantly reduced mean birth weight (weighted mean difference –93 g, CI 169, –25 g), and reduced risk of high birth weight (RR 0.84, CI 0.74, 0.95). Maternal asthma was associated with an increased risk of preterm labor (RR 1.71, CI 1.14, 2.57), early preterm labor (RR 1.93, CI 1.58, 2.34) and preterm delivery (RR 1.41, CI 1.22, 1.61). The risk for preterm labor and delivery was reduced to a non-significant level in those studies reporting active management of asthma during pregnancy (RR 0.95, CI 0.73, 1.26; RR 1.07, CI 0.991, 1.26).

Conclusion Pregnant women with asthma are at increased risk of perinatal complications which affect the baby’s size and timing at birth. Active asthma management may reduce the risk of preterm labor and delivery.

Conflict of Interest No.
IMPROVING ASTHMA CARE FOR CHILDREN: THE DEVELOPMENT OF AN ELECTRONIC ASTHMA ACTION PLAN

TRACEY MARSHALL1, FENTON O'LEARY2, PETER VAN ASPEREN1, MARGARET ALLEN1, AYAN BENDITT1
1Department of Respiratory Medicine, The Children's Hospital at Westmead (CHW), New South Wales, Australia, and 2Clinical Applications Support Unit, CHW, New South Wales, Australia

Introduction

To increase the documentation and provided electronic asthma care, a new asthma action plan (eAAP) was introduced. This plan allows for continuous and more effective asthma care.

Methods

An electronic AAP (eAAP) was introduced in 2008 by a multidisciplinary team comprising representatives of CHW. This team was responsible for the eAAP's design and implementation.

Results

The total number of new AAPs (n = 122) was recorded, with 81% of patients having a new AAP at discharge. There was a significant increase in the use of AAPs over time (p < 0.001).

Conclusion

The eAAP significantly increased the number of recorded AAPs and patients discharged with a recorded AAP.

Support: NHMRC project grant.

Nomination: Asthma/Allergy.

Conflict of Interest: No.

DIETARY FAT ENHANCES AIRWAY INFLAMMATION IN ASTHMA

LISA WOOD1,2, MANOHAR GARG1, AMBER WOOD3,4, PETER GIBSON1,2,3,4
1Centre for Asthma and Respiratory Diseases, University of Newcastle, New South Wales, Australia, and 2Nutracaceutics Research Group, University of Newcastle, Newcastle, New South Wales, Australia

Introduction

Dietary fat activates innate immune responses, leading to an increase in systemic inflammation. However, the effect of dietary fat on airway inflammation has not been investigated.

Methods

Subjects were assigned to low fat (LF) or high fat (HF) challenges. Subjects on the LF challenge consumed a meal containing 13% of energy from fat. At baseline, subjects on the HF challenge consumed a meal containing 52% of energy from fat.

Results

At 4 hours after the food challenge, subjects on the HF challenge had a significant increase in airway inflammation compared to the LF challenge (1.0 (2.0–6.8) % vs. 4.5 (2.7–6.8) %, p = 0.001). There were no differences in the responses of obese vs. non-obese asthmatics.

Conclusion

The eAAP significantly increased the number of recorded AAPs and patients discharged with a recorded AAP.

Support: NHMRC project grant.

Nomination: Asthma/Allergy.

Conflict of Interest: No.

LONGITUDINAL GROWTH AND LUNG FUNCTION IN PEDIATRIC NON-CF BRONCHIECTASIS—WHAT INFLUENCES LUNG FUNCTION STABILITY?

Nikhil KAPUR1,2, Ian B MASTERS1,2, Anne B CHANG1,2
1Queensland Children’s Respiratory Centre, Royal Children’s Hospital, Herston, Queensland, Australia, and 2Child Health Division, Menzies School of Health Research, Darwin, Northern Territory, Australia

Introduction

Longitudinal FEV1 data in children with non-cystic fibrosis (non-CF) bronchiectasis is contradictory and there is no multi-factor data on the evolution of lung function and growth in this group. We longitudinally reviewed lung function and growth in children with non-CF bronchiectasis and explored biologically plausible factors associated with changes in these parameters over time.

Methods

Fifty-two children with >3 years of lung function data were retrospectively reviewed. Changes in annual anthropometry and spirometry at year-3 and year-5 from baseline were analysed. The impact of gender, age, aetiology, baseline FEV1, exacerbation frequency, radiological extent and period of diagnosis was evaluated.

Results

Over 3 years, the group mean FEV1% predicted and BMI z-score improved by 3.01 (p = 0.04, 95% CI 0.14–5.86) and 0.089 (p = 0.01, 95% CI 0.02–0.15) per annum, respectively. FEV1% predicted, FVC% predicted and height z-score all showed non-significant improvement. Over 5 years, there was improvement in FVC %predicted (slope 1.74, p = 0.001) annually but only minor improvement in other parameters. Children with immunodeficiencies or those with low baseline FEV1 had significantly lower BMI at diagnosis. Frequency of hospitalized exacerbation and low baseline FEV1 were the only significant predictors of change in FEV1 over 3 years. Decline in FEV1 %predicted was large (but non-significant) for each additional year in age of diagnosis.

Conclusions

Spirometric and anthropometric parameters in children with non-CF bronchiectasis remain stable over 3–5 year follow-up period once appropriate therapy is instituted. Severe exacerbations result in accelerated lung function decline. Increased medical cognizance of children with chronic moist cough is needed for early diagnosis, better management and improving overall outcome in bronchiectasis.

Conflict of Interest: Nil.
HIGH RESOLUTION CT CHEST FINDINGS IN YOUNG ADULTS WITH A HISTORY OF BRONCHOPULMONARY DYSPLASIA

ANDREW WILSON1,2, DANIEL CHAMBERS3, PATRICK WONG4, JEANNE LOUW4, KEVIN GAIN5, CONNOR MURRAY1,4
1Princess Margaret Hospital, Perth, Western Australia, Australia, 2School of Paediatrics and Child Health, University of Western Australia, Perth, Western Australia, Australia, 3Queensland Centre for Pulmonary Transplantation and Vascular Disease, Perth, Western Australia, Australia, and 4Royal Perth Hospital, Perth, Western Australia, Australia

Introduction Bronchopulmonary dysplasia (BPD) is a common complication of preterm birth. Although there is evidence that individuals with a history of BPD have respiratory abnormalities in childhood, there remains a paucity of evidence regarding the outcome of the disease in adulthood. In a pilot study we recently described high resolution computed tomography (HRCT) appearances of emphysema in young adults with a history of BPD.

Aims To describe the structural pulmonary sequelae of bronchopulmonary dysplasia in adulthood and to evaluate a scoring system originally designed for paediatric subjects.

Methods About 91 adult survivors of BPD underwent HRCT of the chest, along with lung function testing (spirometry, lung volumes and diffusing capacity) and a respiratory health survey. The CT studies were scored by two thoracic radiologists blinded to the patient’s clinical details, using a previously described system developed for children and adolescents who were born prematurely using 14 parameters.

Results Abnormal findings were seen in all scans, the most common findings were subpleural triangular opacities (94%), linear opacities (90%), air trapping (85%) and emphysema (47%). Agreement between the two observers for total score and common abnormalities varied with a linear weighted kappa value of 0.18 for linear opacities, 0.71 for triangular opacities, 0.76 for air trapping, and 0.66 for emphysema.

Conclusions Linear and sub-triangular opacities on HRCT chest are almost universal in young adults with a history of BPD. Findings of emphysema and gas trapping are common and there is good interobserver agreement for these abnormalities.

Support Raine Medical Research Foundation.

Conflict of Interest No.

INTRAUTERINE GROWTH RESTRICTION DELAYS SURFACTANT PROTEIN MATURATION IN THE SHEEP FETUS

SANDRA ORGEIG1, TAMARA A CRITTENDEN1, CELIDH MARCHANT1, IC MCMILLEN2, JANNA L MORRISON2
1School of Pharmacy & Medical Sciences, Adelaide, South Australia, Australia, and 2Early Origins of Adult Health Research Group, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, Australia

Introduction Pulmonary surfactant (PS) is synthesised by alveolar type II epithelial cells to regulate the surface tension at the air-liquid interface of the air breathing lung. Developmental maturation of PS is controlled by many factors including oxygen, glucose, catecholamines and cortisol. The intrauterine growth restricted (IUGR) fetus is hypoxicemic and hyperglycaemic, with elevated plasma catecholamines and cortisol.

Aim To determine the impact of IUGR induced by chronic placental restriction via the carunclectomy model on PS maturation.

Methods We investigated the expression of surfactant protein (SP) –A, –B and –C and their genes in lung tissue of fetal sheep at 133 days and 141 days gestation (term, 150 ± 3 days) from control and carunclectomised Merino ewes.

Results Placentally restricted (PR) fetuses had a body weight <2 SD from the mean of control fetuses and a mean gestational PaO2 <17 mmHg. PR fetuses had a reduced absolute, but not relative lung weight, decreased plasma glucose and increased plasma cortisol concentration. Lung SP–A, –B and –C protein and mRNA expression were reduced in PR compared with control fetuses at both ages. SP–B and –C, but not SP–A mRNA expression and SP–A, but not SP–B or –C protein expression increased with gestational age. Mean gestational PaO2 was positively correlated with SP–A, –B and –C protein and –A mRNA expression. SP–A and –B gene expression were inversely related to plasma cortisol concentration.

Conclusion Chronic placental restriction and hypoxemia results in an inhibition of PS maturation and thus IUGR fetuses are at risk of lung complications, especially if born prematurely.

Support by The ARC & NHMRC.

Nomination Nil.

Conflict of Interest Nil.

MORPHINE ALLEVIATES LABORATORY DYSPNEA IN PROPORTION TO THE DEGREE OF RESPIRATORY DEPRESSION

L ADAMS1, R S CHATTERTON2, R SCHWARTZSTEIN2, R LANGING3, S GILMAN, R BANZET2
1Physio & Ex Sci, Griffith University, Gold Coast, Queensland, Australia, and 2Pulm, Crit Care & Sleep Med, Beth Israel Deaconess Med Center, Boston, MA, USA

Introduction There is weak support for use of opiates in palliation of refractory dyspnea; respiratory depression is perceived as a major risk. We evaluated the effect of i.v. morphine on dyspnea in controlled conditions and related this to concomitant respiratory depression.

Methods With ethical approval, 6 healthy subjects received 0.07 mg/kg morphine sulphate or saline on separate days in a randomised controlled design. Before and for 2 hours after administration, subjects performed (i) dyspnea responses (measured with a Visual Analog Scale) to increasing PETCO2 with ventilation () constrained at resting levels (ii) Unconstrained responses to increasing PETCO2 to assess respiratory drive.

Results Pre morphine with constrained , all subjects tolerated an elevated PETCO2 of 50–55 mmHg; mean dyspnea rating was 56% (7(SEM)). Post morphine, at the same PETCO2, mean dyspnea rating fell to 29 % (5, p < 0.05, paired t). All subjects reported reduced dyspnea at 20 minutes and this was sustained for 2 hours. No changes in dyspnea scores were seen following saline. With unconstrained, at equivalent levels of PETCO2, morphine, but not saline, was associated with a lower in each subject for up to 2 hours; mean fell from 30 (3) to 22 (2) l/min (p < 0.05). To assess if respiratory depression could account for reduced dyspnea, scores were compared at the different PETCO2 levels that induced equivalent unconstrained levels with and without morphine; mean dyspnea scores were not different (S4 (10) vs. S2 (10) %).

Conclusion A clinically moderate dose of morphine results in substantial and sustained relief of laboratory dyspnea in a small group of healthy subjects consistent with the associated degree of respiratory depression.

Support Breathlessness Research Charitable Trust UK; NIH, USA.

Nomination Nil.

Conflict of Interest Nil.
WHAT PREVENTS PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE FROM ATTENDING PULMONARY REHABILITATION?

Andrew Keating1, Bernadette Lee2, Anni Holland1,2
1School of Physiotherapy, La Trobe University, Melbourne, Victoria, Australia, 2Discipline of Physiotherapy, The University of Sydney, New South Wales, Australia.

Introduction Pulmonary rehabilitation (PR) is a cornerstone of management for patients with chronic obstructive pulmonary disease (COPD) and its efficacy is supported with Level 1 evidence. Despite the known benefits of PR, up to one third of those people with COPD who are referred to PR choose not to participate. There is little information regarding perceived barriers to attendance in an Australian health care context.

Methods Nineteen people with COPD (10 women and nine men, GOLD stage I–IV, age range 53–86 years) who had declined to take part in an outpatient PR program at a metropolitan teaching hospital participated in a qualitative study. Semi-structured interviews were used to establish reasons for failing to attend the PR program. These interviews were transcribed verbatim and analysed using the principles of grounded theory.

Results Three major themes were identified regarding barriers to attendance at PR. The first related to difficulties with getting there, including a lack of available transport and poor mobility. The second theme related to a lack of perceived benefit, including perceptions that PR would not improve their health or that they were currently doing enough exercise. The third major theme involved restrictions imposed by underlying medical conditions and included the influence of comorbidities and pain. Minor themes that arose included competing demands, age, fatigue and program timing.

Conclusions In Australia many patients with COPD who are invited to attend PR do not perceive the program would be beneficial, feel they are too unwell to attend or have difficulty with access. Further support should be offered to PR candidates and alternative methods of delivering PR to enhance uptake should be considered.

Conflict of Interest: No.

PULMONARY REHABILITATION FAILS TO INCREASE THE LEVEL OF PHYSICAL ACTIVITY IN COPD

Norman Morris1, Helen Seale2, Nicolle Stroud3, James Walsh3
1School of Physiotherapy and Exercise Science, Griffith University, Gold Coast, Australia, and 2Physiotherapy Department, The Prince Charles Hospital, Chermside, Queensland, Australia.

Introduction For Chronic Obstructive Pulmonary Disease (COPD) patients, physical inactivity is a major health management concern. Recent studies have shown that individuals with higher levels of physical activity (PAL) have increased hospital admissions and prolonged survival. In Australia, the implementation of effective exercise-based pulmonary rehabilitation (PR) has translated into improved quality of life and decreased direct and indirect costs for health care; however the impact of PR in Australia on PAL remains unknown. Therefore the aim of this study was to examine the impact of a standard, 8-week exercise-based PR program on PAL.

Methods About 19 subjects (65 (9) years) with COPD (FEV1% predicted 58 (22)) completed PR in a study where they undertook twice weekly exercise classes consisting of one hour of upper and lower limb strengthening and aerobic exercise. PAL was estimated using a multi-sensor device (SenseWear, HealthCare Bodymedia) worn for a 7-day period. An index of PAL was derived by dividing daily total energy expenditure in metabolic equivalents (METS) by whole night sleeping energy expenditure (average of 3 nights sleeping). PAL was measured in the week immediately prior and in the immediately following PR.

Results Despite a significant increase in exercise capacity (6MWD), PR resulted in a mean increase in PAL (PAL pre: 1.50 (0.22), post 1.51 (0.18), p = 0.79). Moreover there was no significant change in the daily number of steps (Steps pre: 6461 (3521), post: 6332 (3152), p = 0.74). All results are presented as mean, (SD).

Conclusions While the current study demonstrated improvements in standard outcome measures, COPD patients failed to increase their PAL. While changes in PAL may take longer to elicit i.e. the change in PAL may be delayed following PR, it is possible that the current focus of PR on increasing outcomes such as 6MWD may be too narrow to elicit changes in PAL.

Grant support: NIL.

Conflict of Interest: No.