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ABSTRACT

COPD 1

COMPARISON OF WORLD HEALTH ORGANIZATION AND
ASIA-PACIFIC BODY MASS INDEX CLASSIFICATIONS IN
COPD PATIENT

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Background and Aims: The Asia-Pacific classification of BMI has a
lower cut-off for overweight and obese categories compared to the World
Health Organization (WHO) classification. The present study assessed the
COPD patients among different BMI categories according to two BMI
classification systems: WHO and Asia-Pacific.

Methods: COPD patients aged 40 years or older from the Korean
COPD Subtype Study cohort were selected for evaluation. Medical history
including age, sex, St George’s Respiratory Questionnaire (SGRQ-C),
and the modified Medical Research Council (mMRC) dyspnea scale, and
post-bronchodilator forced expired volume in 1 second (FEV1) were
evaluated. Patients were categorized into different BMI groups according to
the WHO classification systems.

Results: A total of 1,462 patients were enrolled. FEV1 and the diffusing
capacity of the lung for carbon monoxide (DLCO) percentage revealed
an inverse “U” shaped pattern as the BMI groups changed from under-
weight to obese when WHO cut-offs were applied. When Asia-Pacific cut-
ofs were applied, FEV1 and DLCO (%) exhibited a linearly ascending
relationship as the BMI increased, and the percentage of patients in the
overweight and obese groups linearly decreased with the severity of the
Global Initiative for Chronic Obstructive Lung Disease criteria was
increased. From the underweight to the overweight groups, SGRQ-C and
mMRC had a decreasing relationship in both the WHO and Asia-Pacific
classifications. The prevalence of comorbidities in the different BMI
groups showed similar trends when the two BMI classifications were
applied.

Conclusions: The present study demonstrated that COPD patients
with a high BMI have better pulmonary function and health-related quality
of life and reduced dyspnea symptoms. Furthermore, compared to the
WHO classification, the Asia-Pacific BMI classification more appropriately
reflects the correlation of obesity and disease manifestation in Asian
COPD patients.

Dietary Fibre and Microbial Metabolites Protect
Against Cigarette Smoke-Induced Lung Pathology
in Mice

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Background and Aims: Intake of dietary fibre is associated with a
reduced risk of COPD and improved lung function, although the mecha-
nism remains unclear. Moreover, cigarette smoke exposure is known to
alter the gastrointestinal microbiome and reduce the concentration of the
microbial metabolites, short chain fatty acids (SCFAs). SCFAs are derived
from the fermentation of dietary fibre by the microbiome, and have potent
anti-inflammatory effects both in the gut and in distal organs, including
the lungs. Exploring the protective effects of dietary fibre and the potential
role of SCFAs in mediating this protection may provide novel therapeutic
strategies for COPD.

Methods: Female c57BL/6 mice were exposed to cigarette smoke for
8-12 weeks to develop hallmark features of COPD. Mice were kept on
control chow, or received diets supplemented with readily fermentable
fibre (high amylose maize starch or inulin). In separate experiments, mice
received normal drinking water, or water supplemented with one of three
SCFAs (200mM; acetate, propionate or butyrate as sodium salts). Lung
inflammation and pathology were assessed by bronchoalveolar lavage

Therefore, we attempted to investigate the clinical features of peripheral
atherosclerosis group in non-smokers with airflow limitation.

Methods: We enrolled 9,995 healthy non-smoking volunteers (male =
36.1 %, mean age = 48.0 ± 10.7 years) who underwent spirometry and
brachial-ankle pulse wave velocity (baPWV) for health check-up at Ajou
University Hospital from January 2010 to December 2015. We defined
peripheral atherosclerosis as baPWV>1400 cm/s and airflow limitation as
pre-bronchodilator ratio of FEV1/FVC<70%. Logistic regression analy-
sis was performed to identify predictors independently associated with
peripheral atherosclerosis.

Results: Mean baPWV was higher in airflow limitation group (1472.1
± 316 cm/s, n = 162) than in control group (1341.4 ± 256.2 cm/s, n =
9833, p<0.001). According to the severity of airflow limitation, the value of
baPWV increased significantly (1491.1 ± 268.6 in FEV1<60, 1381.2 ±
271.6 in 60 ≤ FEV1<80, 1339.3 ± 234.3 cm/s in FEV1 ≥80, p<0.001). Peripheral
atherosclerosis group had older age (56.1 ± 10.6 vs. 44.5 ±
8.6 years), higher mean blood pressure (97.6 ± 11.3 vs. 86.1 ± 10.5, mm
Hg), higher low-density lipoprotein (LDL) (122.7 ± 34.1 vs. 115.5 ± 30.6,
mg/dl), and higher serum uric acid count (5.9 ± 1.6 vs. 5.6 ± 1.7, X107/
uL) than control group (p<0.05). Logistic regression analysis showed that
fasting serum glucose, mean blood pressure, serum uric acid count, serum
LDL, and FEV1/FVC were independent predictors associated with
peripheral atherosclerosis (p<0.05).

Conclusion: FEV1/FVC was an independent predictor of peripheral
atherosclerosis in non-smokers with airflow limitation, suggesting airflow
limitation is linked with atherosclerosis irrespective of smoking.
and histological analysis, and caecal SCFA levels quantified by gas chromatography. Cytokine responses were assessed by qPCR.

**Results:** Cigarette smoke exposure reduced caecal SCFA concentration in control mice, which was restored by fibre supplementation. Both fibre supplementation and SCFA administration alleviated cigarette smoke-induced inflammation and alveolar destruction. Acetate was the most effective SCFA at suppressing inflammation and pronate the most effective at suppressing alveolar destruction.

**Conclusions:** Dietary fibre is protective against cigarette smoke-induced lung pathology, mediated in part by facilitating the production of SCFA by the gastrointestinal microbiota.

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**Abstracts**

**VITAMIN E ISOFORM GAMMA-TOCOTRIENOL PROTECTS AGAINST EMPHYSEMA DEVELOPMENT IN CIGARETTE SMOKE-INDUCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

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**Background and Aims:** Inflammation and oxidative stress contribute to emphysema in COPD. Although corticosteroids are the standard of care for COPD, they do not reduce oxidative stress and a majority of COPD patients are steroid-insensitive. Vitamin E isoform γ-tocotrienol possesses both anti-inflammatory and anti-oxidative properties that may protect against emphysema in COPD. We aimed to establish the therapeutic potential of γ-tocotrienol in both acute and chronic cigarette smoke-induced COPD models in comparison with prednisolone.

**Methods:** BALB/c mice were exposed to cigarette smoke daily for 2 weeks or 2 months. γ-Tocotrienol or prednisolone was given orally. Bronchoalveolar lavage (BAL) fluid and lung tissues were assessed for inflammation, oxidative damage, and regulation of transcription factor activities. Emphysema and lung function were also evaluated.

**Results:** γ-Tocotrienol dose-dependently reduced cigarette smoke-induced BAL fluid neutrophil count and levels of cytokines (IL-17, TNF-α, IL-1β), chemokines (CXCL1, CXCL5) and oxidative damage biomarkers (AOPP, 8-OHdG), and pulmonary pro-inflammatory and pro-oxidant gene expression (MUC5B, MMP12), but restored lung endogenous antioxidant activities (SOD, GPx, HO-1). γ-Tocotrienol acted by inhibiting nuclear translocation of STAT3 and NF-κB, and up-regulating Nrf2 activation in lungs. In a chronic 2-month cigarette smoke mouse model, γ-tocotrienol mitigated cigarette smoke-induced bronchial epithelium thickening and destruction of alveolar sacs in lungs, and improved lung function. In comparison with prednisolone, γ-tocotrienol demonstrated better anti-oxidative efficacy, and superior protection against emphysema and lung function in COPD.

**Conclusions:** We revealed for the first time the anti-inflammatory and antioxidant efficiencies of γ-tocotrienol in cigarette smoke-induced COPD models. In addition, γ-tocotrienol was able to attenuate emphysema lesions and improve lung function in COPD. γ-Tocotrienol may have therapeutic potential for the treatment of COPD.

**Acknowledgements:** This work was supported in part by NMRC/CBRG/0027/2012 from the National Medical Research Council of Singapore, NUHS Seed Fund R-184-000-328-112, and National Research Foundation CREATE grant R-184-000-269-592.

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**INVESTIGATION ON THE INDIVIDUAL CHARACTERISTICS OF INFLAMMATORY CYTOKINES IN COPD PATIENTS**

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**Background:** COPD is chronic inflammatory disease and characterized by a progressive and irreversible airflow limitation in which the mechanism is not fully understood yet. In previous studies, C-reactive protein, fibrinogen, IL-6 and TNF-α were identified as potential inflammatory markers. Recently, new markers, IL-8, IL-32 and IL-33 are found to be related with severity of airway disease. We investigated the relations with cytokines and individual susceptibility of virus or bacteria by measuring inflammatory cytokine(IL-6) secreted during viral or bacterial infection like acute exacerbation and tried to explain inflammatory mechanism of COPD.

**Methods:** The blood samples were collected from 75 patients with stable COPD. We measured IL-6, IL-32 and IL-33 in plasma as baseline, lipopolysaccharide (mimics of bacteria infection)-induced IL-6 and poly:IC (mimics of virus infection)-induced IL-6 by ELISA. The peripheral blood mononuclear cells were preincubated with medium containing LPS or POLY:IC, and the cell culture supernatant IL-6 were measured by using ELISA on the next day. We classified the high inflammatory group and low inflammatory group by IL-6. We compared the results with other clinical factors age, sex, smoking history, BMI, pulmonary function, CAT-score and mMRC.

**Results:** The patients with high LPS groups (mean 26mcg/ml, n=35) had lower baseline inflammatory cytokines than the low LPS group, while the patients with high POLY IC had high baseline cytokines in stable stage(p<0.05). We compared other clinical factors of highly responded groups of LPS and Poly:IC. However, no significant difference in the clinical factors is found.

**Conclusion:** The inflammatory response of virus and bacteria in COPD patients was different individually. We investigated how clinical factors are related to high inflammatory response, and we did not find significant relations due to the limited number of patients. We plan to follow up the patients prospectively and compare the FEV1 decline and the frequency of acute exacerbation.

**EOSINOPHILIA IS LESS LIKELY TO OCCUR IN COPD SMOKERS WITH EMPHYSEMA PHENOTYPE**

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**Background and Aim:** Eosinophilia reflects eosinophilic airway inflammation in COPD. Patients with higher blood eosinophil count are more likely to develop exacerbations and respond to inhaled corticosteroid (ICS) treatment. However, we do not know the optimal cut-off point for eosinophilia and the relation between eosinophilia and lung structural
changes. In this study, we aimed to explore the optimal cut-off point for eosinophilia and to investigate the relation between eosinophilia and CT-based phenotypes in COPD.

Methods: Each of 426 smokers (187 without COPD, 239 with COPD) underwent a whole-lung computed tomography and white blood cell count on the same day. COPD patients were classified as emphysema phenotype if their percentage of low attenuation volume at the threshold of -950 Hounsfield units (%LAV) were greater than the upper limit of normal for %LAV, which was derived from the data of smokers without COPD by using quantile regression. Patients had eosinophilia if their blood eosinophils were greater or equal to a chosen cut-off point.

Results: The number of blood eosinophils was significantly higher in smokers with COPD than in smokers without COPD (median 300/mm³ vs 224/mm³, P=0.0119). The proportion of eosinophilia did not differ significantly between smokers with COPD and smokers without COPD at the cut-off point of 2% (74.9% vs 68.5%; P=0.1419), but significantly at the cut-off point of 3% (59.0% vs 48.1%; P=0.0254). In patients with COPD, the cut-off point of 3% showed a good or moderate agreement with the cut-off point of 300/mm³ (Kappa=0.75), 350/mm³ (Kappa=0.67), or 400/mm³ (Kappa=0.52). At the cut-off point of 3%, the proportion of eosinophilia was 30% lower in emphysema phenotype than in non-emphysema phenotype (50.7% vs 72.5%; RR 0.70; 95%CI 0.57 to 0.86; P=0.0007).

Conclusion: Eosinophilia is less likely to occur in COPD patients with emphysema phenotype — the phenotype responds poorly to ICS treatment.

AO007

SPUTUM 6 GENE EXPRESSION SIGNATURE PREDICTS INFLAMMATORY PHENOTYPE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim: We have previously identified a sputum gene expression signature of 6 markers (CLC, CPA3, DNASE1L3, IL1B, ALPL and CXCR2) that can reproducibly differentiate inflammatory phenotypes of asthma as well as predict corticosteroid responsiveness. The aim of this study was to determine the diagnostic ability of the 6 gene expression signature in predicting airway inflammatory phenotype of COPD.

Methods: Induced sputum was collected from 164 participants with COPD, and inflammatory phenotype was determined by sputum differential cell count, where eosinophils >3% and neutrophils >61% were considered high (eosinophilic E-COPD n=37; neutrophilic N-COPD n=56, paucigranulocytic PG-COPD n=52; and mixed granulocytic MG-COPD n=19). RNA was extracted from sputum plugs, reverse-transcribed to cDNA and target gene expression measured by qPCR. The diagnostic performance of the 6-gene signature was evaluated using multiple logistic regression, with receiver operating characteristic curves and area under the curve (AUC) values reported. Reproducibility was assessed using intra class correlation and Bland-Altman plots.

Results: The 6 gene expression signature was able to discriminate patients with E-COPD from those with N-COPD (AUC=95.7%; p=0.0001), PG-COPD (AUC=86.6%; p<0.0001) or MG-COPD (AUC=92.5%; p<0.0001). The 6 gene expression signature also distinguished N-COPD from PG-COPD (AUC=82.6%; p<0.0001) or MG-COPD (AUC=90.2%; p<0.0001), as well as MG-COPD from PG-COPD (AUC=90.6%; p<0.0001). The 6 gene signature was reproducible in the short term (n=24, 1 month apart). Gene expression of CLC, CPA3 and DNASE1L3 were higher with eosinophilic airway inflammation whereas IL1B, ALPL and CXCR2 were higher with neutrophilic airway inflammation. Elevated expression levels of IL1B, ALPL and CXCR2 were associated with lower lung function and higher levels of C-reactive protein.

Conclusion: A sputum gene expression signature of 6 biomarkers reproducibly and significantly discriminates inflammatory phenotypes of COPD. This signature has the potential to become a useful tool to assist in the management of COPD.

RESTORATION OF CORTICOSTEROID SENSITIVITY IN CIGARETTE SMOKE-INDUCED LUNG INJURY MODEL BY ANDROGRAPHOLIDE

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Background and Aim: Corticosteroid resistance poses a major barrier to an effective steroid therapy for chronic obstructive pulmonary disease (COPD). Andrographolide, a bioactive molecule from an herbal plant Andrographis paniculata, has been shown to restore steroid sensitivity in blocking LPS/IFN-γ-induced IL-27 and airway hyperresponsiveness in mice.

Methods: The present study aimed to extend the steroid-resensitization actions of andrographolide to a cigarette smoke (CS)-induced lung injury model.

Results: Upon exposure to 2% CS extract (CSE), mouse macrophage RAW264.7 and human monocyte U937 cells showed decreased sensitivity to dexamethasone against LPS-induced TNF-α and IL-8 production, respectively. Andrographolide restored the suppressive actions of dexamethasone on LPS-stimulated cytokine production. CSE exposure not only reduced the level and activity of histone deacetylase-2 (HDAC2), an essential epigenetic co-repressor responsible for steroid anti-inflammatory action, but increased the level of c-Jun, a component of the pro-inflammatory transcription factor AP-1, attributable to steroid-resistance. Andrographolide restored the level and activity of HDAC2 and decreased c-Jun level, probably via suppression of PI3K/Akt/p70S6K and JNK/SPAK pathways, respectively, and up-regulated of Nrf2 level in vitro. CS exposure (4%) to mice induced steroid-refractory inflammatory cell infiltration into the airway, especially neutrophils. Andrographolide restored dexamethasone actions to inhibit CS-induced neutrophilia in vivo. Andrographolide also facilitated dexamethasone actions to suppress pro-inflammatory cytokine levels including IL-6, IL-1β, KC and IL-17 in the bronchoalveolar lavage of CS-exposed mice. In mouse lung tissues, andrographolide significantly recovered CS-impaired total nuclear HDAC activity. Importantly, in peripheral blood mononuclear cells isolated from COPD patients, treatment of andrographolide significantly restored corticosteroid sensitivity against LPS-induced IL-8 production.

Conclusion: Taken together, our findings reveal a novel steroid resensitizing activity of andrographolide and provide a new option to reversing steroid resistance in COPD.
Asthma 1

REFERENCES BETWEEN THESE DEVICES REMAIN UNCLEAR. USING A CROSS-SECTIONAL AEROCRINE, A PORTABLE ELECTROCHEMICAL ANALYSER. HOWEVER, POTENTIAL DIFFERENCES BETWEEN GE, A STATIONARY, CHEMILUMINESCENCE ANALYSER, AND NIOX VERO

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FeNO IN DIAGNOSIS OF COUGH-VARIANT ASTHMA.

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Fractional exhaled Nitric Oxide (FeNO) is a marker of eosinophilic airway inflammation in asthma thereby predicting steroid-responsiveness. This study was conducted to assess the role of FeNO in diagnosis of cough-variant asthma.

Methods: Retrospective study of newly diagnosed cough variant asthma patients attending out-patient clinic in a tertiary care centre from June to December 2014 were included. Spirometry was also done in all. Statistical analysis was done using SPSS.

Results: 51 patients were included. 41% were male and 59% females. Mean age was 32.2±10.05. FeNO value was more than 25ppb in 88.2%. Spirometry was normal in 82.4%, mild obstruction in 15.7% and moderate obstruction in 2%. Of the patients with normal spirometry values, FeNO was abnormal in 85.7%. This was found to be statistically significant also (p value 0.02). Associated allergic rhinitis was noted in 35.3%. Abnormally high FeNO (>50ppb) was associated with concomitant allergic rhinitis (p value 0.001).

Conclusions: FeNO values are elevated in cough-variant asthma even in patients with normal spirometry. This helps as an add-on test to identify those patients who would have been missed by doing spirometry alone. Indirectly, it may also be possible to identify steroid-responsive subset in patients with cough variant asthma.

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Background and Aim: Fractional exhaled nitric oxide (FeNO) is a biomarker of eosinophilic airway inflammation. Several devices are available to measure FeNO in clinical practice worldwide, including NOA280i (GE), a stationary, chemiluminescence analyser, and NIOX VERO (Aerocrine), a portable electrochemical analyser. However, potential differences between these devices remain unclear. Using a cross-sectional study design, we compared the FeNO values measured using NOA280i and NIOX VERO.

Methods: One hundred seven adult patients with bronchial asthma, who attended outpatient clinics at the Shizuoka General Hospital for routine check-ups between October and December 2015, were enrolled in this study. Patients were excluded from the study if they had any acute viral infections within the last month prior to the study. FeNO was measured using both NOA280i and NIOX VERO following a random order across patients. The correlation between measured values was analysed using Pearson’s correlation coefficient, and the Bland-Altman plot was used to assess the level of agreement between values measured by both devices.

Results: FeNO (NIOX VERO) (mean ± SD: 53.4 ± 38.9 ppb) was significantly higher than FeNO (NOA280i) (41.7 ± 33.2 ppb, p < 0.0001). However, there was a significant correlation between FeNO (NIOX VERO) and FeNO (NOA280i) (r = 0.946, p < 0.0001). The following correction equation was obtained to relate both measures: FeNO (NIOX VERO) = FeNO (NOA280i) × 1.096 + 7.741. A Bland-Altman plot revealed a moderate degree of agreement between the two devices; the mean inter-device difference was 11.7 ppb and the 95% limits of agreement were –13.5 and 37.0 ppb.

Conclusion: The correction equation will enable researchers and clinicians to compare FeNO values measured using the two devices.

David Halpin1, Eckhard HAMELMANN2, Petra MORONI-ZENTGRAF3, Benjamin Van Hecke4, Anna Unseld5, HuiB Kerstjens5

1Royal Devon and Exeter NHS Foundation Trust, Exeter, United Kingdom, 2Evangélico Krankenhaus Bielefeld GmbH, Bielefeld, Germany, 3Boehringer Ingelheim Pty Ltd, New South Wales, Australia, 4Boehringer Ingelheim Pharma GmbH & Co KG, Biberach an der Riss, Germany, and 5University of Groningen, University Medical Centre Groningen, Department of Pulmonary Medicine and Tuberculosis, and Groningen Research Institute for Asthma and COPD, Groningen, The Netherlands

Comparative Responses in Lung Function Measurements in Adolescents and Adults with Moderate Symptomatic Asthma

Background and Aim: Once-daily tiotropium Respimat®️, a long-acting muscarinic antagonist (LAMA), is a well-tolerated and efficacious treatment option for adults and adolescents with moderate symptomatic asthma when added onto at least inhaled corticosteroids (ICS). In this post hoc analysis, we investigated the comparative responses of several lung function measurements in adults and adolescents with moderate symptomatic asthma following treatment with tiotropium Respimat®️️.

Methods: Pooled data from the two replicate Phase III, 24-week MezzoTinA-asthma®️ trials in adults (NCT01172908/NCT01172821) were used for this analysis. RubaTinA-asthma®️ (NCT01252730) was a Phase III, 48-week trial in adolescents (12–17 years of age). Both trials involved patients with moderate symptomatic asthma receiving maintenance treatment with at least ICS. Lung function measurements – forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio and peak expiratory flow (PEF) – were assessed at Week 24 from patients receiving tiotropium 2.5µg or 5µg once daily added onto ICS (400–800µg budesonide equivalent) and compared to placebo.

Results: In adults, significant improvements compared to placebo were observed consistently across peak(0–3h) and trough (pre-dose) FEV1, and FVC, FEV1/FVC and PEF (morning and evening). In adolescent patients, while significant improvements in peak FEV1(p=0.003) were observed for both tiotropium doses, the difference for trough FEV1, FEV1/FVC and morning and evening PEF was only significant for the 5µg dose. Peak FVC(p=0.003) and trough FVC responses were not significant for either tiotropium dose in adolescents in the RubaTinA-asthma®️ trial (Table 1).

Conclusion: The addition of tiotropium Respimat®️ in adults and adolescents with moderate symptomatic asthma improves lung function. Findings in adolescents were numerically smaller than adults, and statistically significant improvements were noted primarily for FEV1 and PEF, and not for FVC. This may indicate larger flow than volume response in adolescents compared to adults.

David Halpin1, Eckhard HAMELMANN2, Petra MORONI-ZENTGRAF3, Benjamin Van Hecke4, Anna Unseld5, HuiB Kerstjens5

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PATIENT-REPORTED ACTIVITY IMPAIRMENT, STRESS, AND Tiredness IMPROVEMENT IN PATIENTS WITH SEVERE, UNCONTROLLED ASTHMA WITH EOSINOPHILIC INFLAMMATION: POOLED RESULTS FROM TWO PHASE III TRIALS OF BENRALIZUMAB

GOKUL GOPALAN1, SEAN O’QUINN1, XIAO XU1, IAN HIRSCH1
1AstraZeneca LP, Gaithersburg, MD, USA

Background and Aims: Patients with severe, uncontrolled asthma may experience symptoms that impair ability to engage in activities and increase perceived feelings of stress and tiredness. We evaluated treatment with the humanized, anti- eosinophil monoclonal antibody benralizumab on asthma-related activity impairment, stress, and tiredness.

Methods: Pooled analyses of two Phase III trials of benralizumab (NCT01928771 and NCT01914757) of adult patients with severe asthma who received high-dosage inhaled corticosteroids/long-acting β2-agonists with baseline blood eosinophil counts ≥300/μL were conducted. Patients received benralizumab 30 mg either every 4 weeks (Q4W, n=515) or every 8 weeks (Q8W, first three doses Q4W, n=501) or placebo Q4W (n=514) to end of treatment (48 or 56 weeks). Patients in these studies completed a daily diary that included items concerning asthma-related activity limitations, the need to pace oneself during activities, activity avoidance, perceived stress, and tiredness. A 5-point categorical response scale was used for each item. Baseline for daily measures was the 10-day period before Week 0 (randomization). Daily assessments were summarized as biweekly means if ≥7 of 14 daily assessments were available. Each outcome measure was compared across treatment arms from baseline to end of treatment for patients in the full pooled data set using repeated-measures analyses, adjusting for baseline value, oral corticosteroid use, and geographic region.

Results: Patients who received the benralizumab Q8W dosing regimen had statistically significant improvements in all 3 aspects of activity impairment, stress, and tiredness compared with placebo recipients at end of treatment. Patients receiving the benralizumab Q4W dosing regimen had statistically significant improvements compared with patients receiving placebo in activity limitations and pacing, but not in activity avoidance, stress, or tiredness (tables).

Conclusions: Benralizumab treatment improves patient-reported activity impairment, stress, and tiredness, consistent with previously published findings that benralizumab treatment reduces exacerbations and asthma symptoms and improves asthma-specific health-related quality of life.

Table 1. Changes in lung function measures in adults and adolescents (12–17 years of age) with moderate symptomatic asthma receiving tiotropium Respimat® at 24 weeks

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MezzoTinA-asthma® Adults</th>
<th>RubaTinA-asthma® Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Adjusted mean difference from placebo (95% CI)</td>
</tr>
<tr>
<td>Peak FEV1_{18,36h}, mL</td>
<td>513</td>
<td>185</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(146, 223)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(185, 262)</td>
</tr>
<tr>
<td>Trough FEV1, mL</td>
<td>513</td>
<td>146</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(105, 188)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(138, 221)</td>
</tr>
<tr>
<td>Peak FVC_{18,36h}, mL</td>
<td>513</td>
<td>95</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(53, 138)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(98, 183)</td>
</tr>
<tr>
<td>Trough FVC, mL</td>
<td>513</td>
<td>80</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(35, 125)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(62, 152)</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>513</td>
<td>2.7</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(1.9, 3.4)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(2.6, 4.0)</td>
</tr>
<tr>
<td>PEF morning, L/min</td>
<td>513</td>
<td>24.3</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(17.9, 30.7)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(19.0, 31.7)</td>
</tr>
<tr>
<td>PEF evening, L/min</td>
<td>513</td>
<td>23.2</td>
</tr>
<tr>
<td>Tiotropium 5μg</td>
<td>515</td>
<td>(16.9, 29.5)</td>
</tr>
<tr>
<td>Tiotropium 2.5μg</td>
<td>515</td>
<td>(22.1</td>
</tr>
</tbody>
</table>

*Within 3 hours post-dosing. Clinical trial primary endpoint in. MezzoTinA-asthma®, RubaTinA-asthma®. Delivered as 2 puffs once daily via the Respimat®. FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow.

AO012

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Table 1. Activity Impairment Assessments: 14-Day Summary Score Change From Baseline to End of Treatment for Two Benralizumab Dosing Regimens vs. Placebo

<table>
<thead>
<tr>
<th>Daily Assessment Measures</th>
<th>Treatment Groups</th>
<th>Benralizumab 30 mg Q4W</th>
<th>Benralizumab 30 mg Q8W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity limitations (LS mean change, 95% CI)</td>
<td>-0.77 (-0.20, 0.35)</td>
<td>-0.83 (-0.26, 0.17)</td>
<td>-0.66 (-0.01, 0.25)</td>
<td></td>
</tr>
<tr>
<td>Activity avoidance (LS mean change, 95% CI)</td>
<td>-0.10 (-0.00, 0.06)</td>
<td>-0.16 (-0.06, 0.04)</td>
<td>-0.68 (-0.26, 0.06)</td>
<td></td>
</tr>
<tr>
<td>Activity pacing (LS mean change, 95% CI)</td>
<td>-0.13 (-0.03, 0.01)</td>
<td>-0.19 (-0.09, 0.01)</td>
<td>-0.68 (-0.26, 0.06)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Daily Stress and Tiredness Assessments: 14-Day Summary Score Change From Baseline to End of Treatment for Two Benralizumab Dosing Regimens vs. Placebo

<table>
<thead>
<tr>
<th>Daily Assessment Measures</th>
<th>Treatment Groups</th>
<th>Benralizumab 30 mg Q4W</th>
<th>Benralizumab 30 mg Q8W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress (LS mean change)</td>
<td>-0.35</td>
<td>-0.41</td>
<td>-0.32</td>
<td></td>
</tr>
<tr>
<td>(Difference (95% CI))</td>
<td>-0.04 (-0.08, 0.01)</td>
<td>-0.09 (-0.14, -0.04)</td>
<td>-0.15 (-0.20, -0.01)</td>
<td></td>
</tr>
<tr>
<td>Feeling tired (LS mean change)</td>
<td>-0.74</td>
<td>-0.82</td>
<td>-0.67</td>
<td></td>
</tr>
<tr>
<td>(Difference (95% CI))</td>
<td>-0.07 (-0.17, 0.03)</td>
<td>-0.14 (-0.25, 0.04)</td>
<td>-0.18 (-0.28, 0.02)</td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval; LS, least squares; Q4W, every 4 weeks; Q8W, every 8 weeks (first three doses Q4W).
without additional controllers, in adults with symptomatic asthma. Although rarely used in clinical practice today, diurnal variability in peak expiratory flow (PEF) could offer insights into asthma control and airway hyperresponsiveness. To investigate diurnal variability in PEF following treatment with tiotropium Respimat® across asthma severities.

**Methods:** A post hoc analysis of PEF diurnal variability from five Phase III trials was conducted: PrimoTinA-asthma® (pooled 2x 48-week trials, tiotropium 5µg or placebo once daily [morning], added onto maintenance ICS ≥800µg budesonide/equivalent + long-acting β₂-agonist ± additional controller medications); MezzoTinA-asthma® (pooled 2x 24-week trials, tiotropium 2.5µg, 5µg or placebo once daily [evening], added onto maintenance ICS 400–800µg budesonide/equivalent); and GraziaTinA-asthma® (12-week trial, tiotropium 2.5µg, 5µg or placebo once daily [evening], added onto maintenance ICS 200–400µg budesonide/equivalent). Pre-dose PEF was self-monitored at home using the asthma monitor AM2+®.

**Results:** Tiotropium improved morning and evening PEF in all studies. Mean baseline PEF variability was 14.14%, 13.51% and 12.08% (all patients) in PrimoTinA-asthma®, MezzoTinA-asthma® and GraziaTinA-asthma®, respectively. Adjusted mean change from baseline in PEF variability at Week 24 for tiotropium 5µg and placebo was −0.33% and −0.87%, respectively, in PrimoTinA-asthma®, and for tiotropium 5µg or 2.5µg and placebo was −0.32% to −1.01%, respectively, in MezzoTinA-asthma®. A similar pattern was observed at Week 12 in GraziaTinA-asthma® (Table 1).

**Conclusion:** The differences between tiotropium Respimat® and placebo were generally small and variable (even though the trials showed significant improvements in peak [0–3 hours post-dose] forced expiratory volume in 1 second [FEV₁], trough FEV₁ and PEF am/pm versus placebo). In these trials where tiotropium was added onto other maintenance asthma therapy, PEF diurnal variability was not a sensitive measure of bronchodilation.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Treatment duration, weeks</th>
<th>N</th>
<th>Lung function analyses</th>
<th>Adjusted mean difference from placebo (5µg* dose)</th>
<th>Adjusted mean difference from placebo (2.5µg* dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrimoTinA-asthma®</td>
<td>48</td>
<td>907</td>
<td>Peak FEV₁, Week 24, mL (95% CI)</td>
<td>110 (63, 158);</td>
<td>–</td>
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<tr>
<td>Severe symptomatic asthma (pooled)</td>
<td></td>
<td></td>
<td>Trough FEV₁, Week 24, mL (95% CI)</td>
<td>93 (50, 137);</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peak FVC, Week 24, mL (95% CI)</td>
<td>87 (26, 148);</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trough FVC, Week 24, mL (95% CI)</td>
<td>118 (62, 175);</td>
<td>–</td>
</tr>
<tr>
<td>MezzoTinA-asthma®</td>
<td>24</td>
<td>2081</td>
<td>Peak FEV₁, Week 24, mL (95% CI)</td>
<td>185 (146, 223);</td>
<td>223 (185, 262);</td>
</tr>
<tr>
<td>Moderate symptomatic asthma (pooled)</td>
<td></td>
<td></td>
<td>Trough FEV₁, Week 24, mL (95% CI)</td>
<td>146 (105, 188);</td>
<td>180 (138, 221);</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peak FVC, Week 24, mL (95% CI)</td>
<td>95 (53, 138);</td>
<td>141 (98, 183);</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trough FVC, Week 24, mL (95% CI)</td>
<td>80 (35, 125);</td>
<td>107 (62, 152);</td>
</tr>
<tr>
<td>GraziaTinA-asthma®</td>
<td>12</td>
<td>464</td>
<td>Peak FEV₁, Week 12, mL (95% CI)</td>
<td>128 (57, 199);</td>
<td>159 (88, 230);</td>
</tr>
<tr>
<td>Mild symptomatic asthma</td>
<td></td>
<td></td>
<td>Trough FEV₁, Week 12, mL (95% CI)</td>
<td>122 (49, 194);</td>
<td>110 (38, 182);</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Peak FVC, Week 12, mL (95% CI)</td>
<td>57 (–26, 140);</td>
<td>106 (23, 188);</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trough FVC, Week 12, mL (95% CI)</td>
<td>66 (–19, 151);</td>
<td>98 (13, 183);</td>
</tr>
</tbody>
</table>

*Delivered as 2 puffs once daily via the Respimat®. *Clinical trial primary endpoint. CI, confidence interval; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FEV₁(10–3h), forced expiratory volume in 1 second 3 hours post dose; trough FEV₁, forced expiratory volume in 1 second 24 hours post dose.

Background and Aim: Tiotropium Respimat® is a well-tolerated and efficacious once-daily long-acting muscarinic antagonist (LAMA) that can be added to inhaled corticosteroids (ICS) with or without additional controllers in adults with symptomatic asthma. Here we investigate the impact of treatment on different measures of lung function across asthma severities. We compared forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) response in patients with persistent asthma across different severities.

**Methods:** Lung function data from five Phase III clinical trials involving adult patients with severe, moderate or mild symptomatic asthma were compared in this post hoc analysis. Data were from pooled PrimoTinA-asthma® (severe symptomatic asthma: 2x 48-week trials, tiotropium 5µg or placebo, once daily, added onto ICS ≥800µg budesonide/equivalent + long-acting β₂-agonists ± additional controller controllers in adults with symptomatic asthma. Here we investigate the impact of treatment on different measures of lung function across asthma severities. We compared forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) response in patients with persistent asthma across different severities.

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FEVIPIPRANT REDUCES AIRWAY SMOOTH MUSCLE MASS IN ASTHMATICS VIA PGD2 RECEPTOR ANTAGONISM

RUTH M SAUNDERS1, ALESSANDRA SANDRINI2, HAIMANSHU KAUL1, RACHID BERAIR1, AMISHA SINGAPURI1, IGOR CHERNYAVSKY2, LATIFA CHACHI2, MICHAEL BIDDE1, AMANDA SUTCLIFFE1, MARIE LAURENCIN1, GERALD BACHER2, MICHELLE BOURNE1, IAN D PAVORD3, ANDREW J WARDLAW1, SALMAN H SIDDIQUI1, RICHARD KAY4, BINDI S BROOK2, ROD SMALLWOOD1, CHRISTOPHER E BRIGHTLING1

1University of Leicester, Leicester, United Kingdom, 2Novartis Pharmaceuticals Australia Pty Limited, Macquarie Park, Australia, 3University of Manchester, Manchester, United Kingdom, 4Novartis Pharma AG, Basel, Switzerland, 5Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 6University of Oxford, Oxford, United Kingdom, 7University of Nottingham, Nottingham, United Kingdom, and 8University of Sheffield, Sheffield, United Kingdom

Background and Aims: In asthma, increased airway smooth muscle (ASM) mass is associated with disease severity and impaired lung function. The prostaglandin D2 (PGD2) receptor 2 (DP2) antagonist, fevipiprant, reduces airway eosinophilia and improves epithelial integrity, lung function, Asthma Control Questionnaire (ACQ) score and Asthma Quality of Life Questionnaire (AQLQ) score. We investigated whether fevipiprant reduces ASM mass in asthma and potential mechanistic role of DP2 in airway remodelling using in vitro and computational modelling approaches.

Methods: ASM mass was assessed in bronchial biopsies from 12 patients with moderate-to-severe asthma in 12 weeks randomised, placebo-controlled study of fevipiprant 225 mg twice daily orally. In primary ASM cells in vitro, we assessed DP2 expression by flow cytometry, gene expression of PGD synthase, PGD2 release by ELISA, migration in a wound healing assay, and proliferation using the MTS assay.

Results: ASM mass was significantly reduced following 12 weeks treatment with fevipiprant (n = 14) versus placebo (n = 13) (mean ± SE change in % ASM area, −13 ± 5% versus 4 ± 5%, P = 0.034). Computational modelling predicted that reduction in eosinophilic inflammation and direct effect on ASM cell recruitment was required to explain reduction in ASM mass. ASM cells secreted more PGD2 following wounding (129 ± 19 versus 181 ± 25 pg/mL/105 cells, P = 0.020, n = 10). Inhibition of DP2 activation by endogenous PGD2 resulted in reduced ASM migration (median [interquartile range] difference after 24 h in presence of CAY10471 100 nM versus control, −11.0 [17.5] %; P = 0.008), but did not affect ASM proliferation over 72 h.

Conclusion: Fevipiprant reduced airway smooth muscle mass in moderate-to-severe asthma patients. This might reflect both reduced eosinophilic airway inflammation and a direct effect on airway smooth muscle cells.

Tuberculosis 1

RISK FACTORS FOR DELAYED DIAGNOSIS OF PULMONARY TUBERCULOSIS IN INTERMEDIATE TB BURDEN COUNTRY

GYUNG EUI LEE1, JAE CHOL CHOI1, HO JONG KIM2, BYOUNG WHUI CHOI1, JONG WOOK SHIN2, JAE YEOL KIM2, IN WON PARK2, TAE YUN PARK1

1Division of Pulmonary Medicine, Department of Internal Medicine, Chung-Ang University, School of Medicine, Seoul, South Korea

Background and Aims: Delayed diagnosis of active pulmonary tuberculosis (PTB) is significant with regard to not only the disease progression at the individual level but also transmission within the community. Therefore, it is important to know the risk factors of delayed diagnosis of PTB.
Methods: We performed a retrospective study between January 2011 and December 2016 in the Chung-Ang university hospital. We included all culture positive PTB patients who were older than 15 years old. We checked demographic parameters, laboratory parameters, initial impression, initial visiting date and treatment starting date.

Results: During these periods, 627 patients were diagnosed as culture proven PTB. The median hospital delays were 4 days (IQR 2-10), and 70 (11.2%) experienced hospital delay more than 4 weeks. In univariate analysis, the risk factors for hospital delays more than 4 weeks were female (p=0.03), age over 65 years old (p=0.02), absence of cavity (p<0.01), history of COPD (p=0.03), history of malignancy (p=0.02), negative sputum smear (p<0.01), unchecking sputum TB-PCR (p<0.01), initial impression of non-TB (p<0.01), and use of antibiotics (p<0.01). In multivariate analysis, absence of cough (p=0.008), female (p=0.045), over 65 years old (p=0.022), smear negative (p=0.002), unchecking sputum TB-PCR (p=0.001), and initial impression of non-TB (p=0.001) were risk factors for hospital delays more than 4 weeks. Initial impression of these 627 patients was PTB (n=411), pneumonia (n=134), TB scar (n=26), malignancy (n=23), non-tuberculous mycobacterium lung disease (n=9) and others (n=24). Among 411 patients those who suspected as PTB, only 2 patients experienced hospital delay more than 4 weeks. However, 134 patients those who suspected as pneumonia, 30 (22.4%) experienced hospital delay more than 4 weeks.

Conclusions: In intermediate TB burden country, 11.2% experienced hospital delay more than 4 weeks and the most important risk factor was initial impression of non-TB.
was 6.65 (2.47-17.92) and 5.79 (2.11-15.84) when adjusted with other variables to have bacterial load as 1+, 2+ and 3+ other than negative-scanty.

Conclusion: Subjects with new case of pulmonary TB in primary health center who had malnutrition risk tend to have higher bacterial load.

TO ASSESS RISK FACTORS FOR “LOST TO FOLLOW-UP” IN THE TREATMENT FOR TUBERCULOSIS – ANALYSIS OF JAPAN TB SURVEILLANCE DATA

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Background: Minimizing lost to follow-up (LTFU) from tuberculosis (TB) treatment is important, not only in terms of improving treatment outcome of patient but also of preventing development of drug-resistance.

Aims: To describe the characteristics of, and analyze the risk factors for the LTFU among pulmonary TB patients aged 64 and below in Japan.

Method: Cohort data from the Japan TB Surveillance of pulmonary TB patients newly notified between 2007 and 2014 was analyzed. Multiple-regression analysis was conducted with LTFU as independent variable, and the following as dependent variables – sex, job, homelessness, cavity, sputum smear, welfare status, multi-drug resistance, country of birth, diabetes mellitus (DM) and whether or not the patient was initially hospitalized.

Results: Between 2007 and 2014, a total of 58,524 pulmonary TB patients aged 65 and below were newly notified, and among them, 7.7% (n=4,513) were LTFU. Characteristics of those LTFU are summarized in Table 1 and Figure 1. Among males, positive sputum smear (aOR 0.69, 95% CI 0.54-0.88), cavity disease (aOR 0.76, 95% CI 0.63-0.92) and DM (aOR 0.71, 95% CI 0.55-0.93) were identified as protective factors, while not requiring hospitalization (aOR 1.58, 95% CI 1.24-2.02) as risk factor. However, among females, not being hospitalized (aOR 1.91, 95% CI 1.47-2.48) and being a medical doctor (aOR 2.95 95% CI 1.20-7.28) were risk factors for LTFU.

Conclusion: In Japan, smear positive patients are hospitalized for two months, during which the risk LTFU is minimal, and patients’ motivation towards treatment is also probably high. Hospitalization may thus play a critical role not only in containing the infection, but also in ensuring adherence. Female medical doctors were at a higher risk of becoming LTFU – reasons may be explored by further qualitative investigation.

Acknowledgement: This research was supported by the Research Program on Emerging and Re-emerging Infectious Diseases from Japan Agency for Medical Research and Development.

Table 1. Characteristics of those lost to follow-up (2007-2014)

<table>
<thead>
<tr>
<th>Age groups</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>4,513</td>
<td>100.0</td>
</tr>
<tr>
<td>Male</td>
<td>2,736</td>
<td>60.6</td>
</tr>
<tr>
<td>Female</td>
<td>1,777</td>
<td>39.4</td>
</tr>
</tbody>
</table>

RECURRENT PYOPNEUMOTHORAX IN MULTI DRUG RESISTANT TUBERCULOSIS PATIENT: A CASE REPORT

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Background and Aims: One of the complications of Multi Drug Resistant Tuberculosis (MDR-TB) is pyopneumothorax which is quite difficult to treat since there is differential penetration of anti-tuberculosis drug (ATD) through the pleura and recurrence cases might be difficult to treat. Untreated pyopneumothorax could also cause drug resistance since the ATD could be under dosage.

Results: We report a case of 29 years old female with chronic productive cough and worsening dyspnea. She had been treated previously with ATD 2 times but without smear evaluation neither drug susceptibility test (DST). Chest x-ray showed hydropneumothorax. Thoracal CT-Scan showed cavity, bronchiectasis, left lung atelectasis and left hydropneumothorax. Bronchoscopy showed narrowing and hyperemic of distal part of the left main bronchus, half compression stenosis of left upper lobe and hyperemic in left lower lobe. We managed the patient with large bore chest tube placement of 24-Fr on her left chest. The sputum Xpert®Mtbc/Rf resulted in Rifampicin resistant Mtbc thus she was diagnosed as MDR-TB. The patient was given standard MDR-TB drug regimen which was consist of Kanamycin, Levofloxacin, Ethionamide, Cycloserine, Pyrazinamide and Ethambutol. The chest tube was placed for 41 days. The spirometry resulted in severe restriction and moderate obstruction. The final chest x-ray showed markedly fluid reduction thus the chest tube was removed and the patient was discharged. During two months of follow up the patient experienced another episode of worsening dyspnea and the chest x-ray showed recurrence of hydropneumothorax. The patient might receive benefit from decortication surgery but the sputum smear AFB reverse to positive and the contralateral lung is still compromised thus the patient was treated conservatively.

Conclusions: Pyopneumothorax can be a compromise complication of MDR-TB since it presence can cause poor penetration of ATD and reducing ATD effectiveness. Evacuation of pyopneumothorax might be beneficial for MDR-TB patients.
LATENT TUBERCULOSIS INFECTION INCREASES IN PATIENTS RECEIVING KIDNEY TRANSPLANTATION

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Background and Aims: Patients with renal failure or kidney transplantation are risky for tuberculosis. There is lacking of investigation for latent tuberculosis infection (LTBI) before and after renal transplantation, an important data for TB prevention strategy.

Methods: Patients with renal failure or kidney transplantation were screened for LTBI from January 2014 to October 2016 under approval of institutional review board. QuantiFERON-TB Gold In-tube (QFT-GIT) was used to define the status of LTBI.

Results: Among the 273 recruited patients, 124, 109 and 40 participated were classified as waiting kidney transplantation (WKT group), dialysis controls (DC group) and after kidney transplantation (AKT) group, respectively. In comparing WKT group, DNT group was older and had more proportion of diabetes mellitus, and hemodialysis whereas AKT group had more prior TB history and chronic respiratory symptoms. Notably, there were 44 subjects with positive QFT-GIT, 11 (8.9%) in WKT group, 22 (20.2%) in DC group, and the remaining 11(27.5%) in AKT group. The positive rate of QFT-GIT is statistically significant lower in WKT group than DC or AKT group. Ten patients of WKT group had 20% positive QFT-GIT rate, measured within 2 months after transplant. In multivariable logistic regression analysis, AKT group was significantly associated with LTBI status.

Conclusions: Positive LTBI was around 8.9% in patients waiting for kidney transplantation, which was lower than those after kidney transplantation (27.5%). In addition, the positive rate of LTBI is high after kidney transplant. Because kidney transplantation is high risk for getting LTBI, a bundle of protecting TB transmission is as important as LTBI therapy for preventing reactivation.

Key words: latent tuberculosis infection, kidney transplantation, renal failure, dialysis

PULMONARY TUBERCULOSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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Background and Aim: It is difficult to diagnose pulmonary tuberculosis (PTB) associated with interstitial lung disease (ILD) because of the shadow of fibrosis on a chest X-ray. In addition, patients of ILD take immunosuppression agent which makes symptoms of PTB uncommon. Some previous reports showed that patients of PTB associated with ILD have poor prognosis because of immunosuppression agent for ILD. However, characteristics and prognosis of PTB associated with ILD has not been well-known today.

Methods: We researched 118 patients diagnosed as PTB since January 2009 to August 2015 in our hospital, about characteristics of PTB with ILD and risk factors of delay in diagnosis.

Results: PTB with ILD group (21) vs PTB without ILD (97); Male were 19 vs 57. Mean age was 75 years old vs 67. Current or former smokers were 19 vs 45. Oral corticosteroids were prescribed for 6 patients vs 13. Immunosuppressants were prescribed for 4 vs 10. Ziehl-Neelsen stains of sputum were positive in 12 cases vs 32. About delay in diagnosis, patient’s delay was 10.5 days vs 30. Doctor’s delay was 27 vs 8. Risk factors of delay in diagnosis were high C-reactive protein and negative Ziehl-Neelsen stains of sputum.

Conclusion: It took longer to diagnose PTB with ILD. These patients might have nosocomial infection. During following ILD patients, we need to take care of complication of PTB.
Background and Aims: Zinc finger E-box binding homeobox-1 (ZEB1) played important role in the maintenance of cancer stem cells (CSCs) that are involved in the cancer progression and recurrence. Microenvironment condition such as hypoxia is a preferred niche for CSCs. One of the established markers for lung CSC is CD133. The purposes of this study were to address the role of ZEB1 in the hypoxia-induced CD133 upregulation in NSCLC and to determine whether silencing of ZEB1 might reverse hypoxia-induced CD133 expression as well as self-renewal capacity.

Methods: NSCLC cell lines PC9, HCC827, HCC2935, and A549, were exposed to hypoxia to investigate the expression of CD133 and ZEB1 by quantitative real-time PCR (qPCR). Transient ZEB1 knockdown was performed by small-interfering RNA, and stable silencing of ZEB1 was done by lentivirus transduction-mediated plasmid transfection in PC9 and HCC827 cells. Self-renewal property was studied by sphere formation assay, and protein expressions of spheres were analyzed by immunofluorescence.

Results: Hypoxia increased expression of CD133 and ZEB1 mRNA in NSCLC cell lines. In particular, ZEB1- and CD133-coexpressing PC9 cell population were increased under hypoxic condition. Hypoxia inducible factors 1α (HIF1α) was accumulated in hypoxic cells and knockdown of HIF1α reduced ZEB1 expressions. Furthermore, transient silencing of ZEB1 reduced CD133 expression induced in hypoxic conditions. Hypoxic ZEB1-silenced PC9 and HCC827 cells showed reduced sphere numbers as well as CD133 expressions in spheres.

Conclusions: Collectively, our findings indicated that hypoxia induced CD133 expression in NSCLC cells through the activation of ZEB1, and that ZEB1 inhibition reversed CD133 expression and self-renewal capacity of hypoxic cells. These results suggest a potential role for targeting ZEB1 in the prevention of hypoxia-induced cancer progression mediated by CSCs.
GLUTATHIONE S-TRANSFERASE M1 AND T1 POLYMORPHISMS PREVALENCE IN LUNG CANCER PATIENTS IN MALANG, INDONESIA

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Background and Aims: Detoxification has known to have a role in lung carcinogenesis. Glutathione S-transferase is one of the enzymes that have roles in detoxification. Its role is influenced by GSTM1 (Glutathione S-transferase M1) and GSTT1 (Glutathione S-transferase T1) polymorphisms. However, relation between GSTM1 and GSTT1 polymorphisms with lung cancer susceptibility remains unclear. In this study, we aimed to determine the influence of GSTM1 and GSTT1 polymorphisms on susceptibility of lung cancer in Indonesian people.

Methods: Case control study design. 46 lung cancer patients and 46 patients non-lung cancer patients. Research was conducted in Dr. Saiful Anwar Hospital, Malang, Indonesia. Lung cancer diagnosis based on the results of histopathologic finding. Examination GSTM1 and GSTT1 polymorphisms using multiplex electrophoresis. Polymorphisms were observed and statistical analysis was performed.

Results: The prevalence of each positive GSTM1 gene and GSTT1 gene in the lung cancer group and the non-lung cancer group did not differ significantly with p = 0.293 and p = 0.778, respectively.

Conclusions: There are no significant differences between the prevalence of each GSTM1 and GSTT1 polymorphisms in the lung cancer group and non-lung cancer group. GSTM1 and GSTT1 gene polymorphisms do not affect susceptibility to lung cancer in Indonesia.

Keywords: GSTM1, GSTT1, lung cancer, multiplex electrophoresis, polymorphism

Cell and Molecular Biology

MESENCHYMAL STEM CELL-CONDITIONED MEDIUM INDUCES NEUTROPHILS APOPTOSIS VIA INHIBITION OF NF-κB PATHWAY IN ENDOTOXIN-INDUCED ACUTE LUNG INJURY

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Background and Aims: Mesenchymal stem cells (MSCs) have immunomodulatory effects, but the exact role of MSCs within neutrophil activities in acute lung injury (ALI) is still not well known. We investigated the effect of mesenchymal stem cell-conditioned medium (MSC-CM) in moderating neutrophils apoptosis of endotoxin-induced ALI.

Methods: Male C57BL/6 8-12 week-old mice were studied. Mouse MSC-CM was delivered through the tail veins of mice after intratracheal instillation of endotoxin-induced ALI. Lung histopathological findings, levels of interleukin-6 (IL-6), macrophage inflammatory protein-2 (MIP-2), myeloperoxidase (MPO), expression of NF-κB p65 and phospho-NF-κB p65, neutrophil counts in the lungs, the apoptosis and the expression of anti-apoptotic factor, and Bcl-2 & Mcl-1 in pulmonary neutrophils were analyzed. In vitro study, NF-κB and matrix metalloproteinase-9 (MMP-9) activities in neutrophils isolated from human ARDS patients were also investigated.

Results: MSC-CM significantly diminished the histopathological changes and the lung injury score in comparison with ALI mice. There was also a significant reduction in the numbers and activity of neutrophils in the lung of MSC-CM-treated ALI mice, confirmed by immunostaining with Ly6G and MPO activity. MSC-CM therapy decreased the levels of IL-6, MIP-2, and the expression of NF-κB p65 and phospho-NF-κB p65. MSC-CM mediated the neutrophil apoptosis by reducing Bcl-2 & Mcl-1 expression in mice neutrophils of BAL. Moreover, human MSC-CM effects were also confirmed with reduced NF-κB & MMP-9 activities isolated from peripheral-blood neutrophils in ARDS patients.

Conclusions: MSC-CM provides a beneficial effect to regulate the neutrophils apoptosis and reduce the chemokines secretion in endotoxin-induced ALI, which is in part mediated by suppression in NF-κB pathway.
Abstracts

AO030
ENHANCED CD147 EXPRESSION AFTER H1N1 INFECTION: A POTENTIAL MECHANISM FOR AIRWAY EPITHELIUM IMPAIRMENT IN ASTHMA
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Background and Aims: Airway epithelium of asthmatics is characterised by structural and functional abnormalities. Epithelial cells are the target of H1N1 virus. The H1N1 may further impair epithelium integrity. CD147 is a transmembrane protein which induces the production of matrix metalloproteinases; e.g. MMP-9. MMP-9 causes airway remodelling and inflammation. The miR-22/Sp1/c-Myc network has reported to regulate CD147 transcription. We hypothesised that H1N1 infection induces CD147 leading to increased MMP9 in epithelium and these responses are elevated in asthma. Our aims were to determine the level of CD147 and MMP-9 in primary bronchial epithelial cells (pBEC) of asthmatics and non-asthmatics following H1N1 infection.

Methods: pBEC from asthmatics and non-asthmatics were obtained from bronchial brushings and cultured under ALI. Cells were incubated with H1N1 (MOI5) for 6h. miRNAs/mRNAs were isolated and assessed at 6, 8 and 24h post infection.

Results: CD147 expressed at the similar level in pBEC of asthmatics and non-asthmatics at baseline. After H1N1 infection, CD147 increased in pBEC of asthmatics whereas its expression was reduced in non-asthmatics. While miR-22 expression remained unchanged in asthmatics, it increased in non-asthmatics after infection. Conversely, H1N1 infection induced SP-1 and c-Myc in asthmatics whereas had no effect on non-asthmatics. The MMP-9 expression was very low in pBEC. Pro-MMP-9 was also detected at the same level from pBEC of both groups.

Conclusions: CD147 expression increased in pBEC of asthmatics after H1N1 infection. While miR-22 expression remained unchanged, increased SP1 and c-Myc expressions may potentiate elevation of CD147 after H1N1 infection in asthmatics. While no difference in pro-MMP-9 in epithelial cells of two cohorts was detected, increased expression of CD147 after H1N1 infection may induce expression of MMP-9 from neighbouring cells leading to tissue remodelling in asthmatics.

AO031
DIETARY OMEGA-6, BUT NOT OMEGA-3 POLYUNSATURATED OR SATURATED FATTY ACIDS INCREASE INFLAMMATION IN HUMAN PULMONARY FIBROBLASTS
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Background and Aim: Obesity is an important risk factor for developing severe asthma. Dietary fatty acids, increased in sera of obese individuals and after high fat meals, activate the innate immune system, induce inflammation and impair responses to treatment in the airways. The aim of this study was to investigate whether dietary fatty acids directly cause inflammation and/or synergise with obesity-induced cytokines in human pulmonary fibroblasts in vitro and the underlying mechanisms.

Methods: Primary human pulmonary fibroblasts were challenged with BSA-conjugated fatty acids (ω-6 PUFAs, ω-3 PUFAs or SFAs) with or without TNFα. Release of the pro-inflammatory cytokines, ω-6 and CXCL8, was measured using ELISA. Underlying signaling pathways were examined using specific inhibitors for COX, p38 MAPK, MEK1, JNK, PI3K and NF-κB. Activation of p38 MAP kinase and NF-κB was also assessed by western blotting.

Results: We found that the ω-6 PUFAs might promote airway inflammation via multiple pathways, including COX dependent- and independent pathways, and in an obese person may lead to more severe airway inflammation.
Conclusion: PM2.5 downregulates miR-194-3p resulting in aggravating DAPK1 and caspase-dependent apoptosis in cigarette-smoke inflamed pulmonary epithelium.

**AO033**

**INVESTIGATION OF THE CD1b LIPID ANTIGEN PRESENTATION PATHWAY IN COPD**

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**Background and Aim:** Oxidised self-lipid production and reduced apoptotic bronchial cell clearance by alveolar macrophages has been described in COPD. We investigated whether CD1b, a saposin C-dependent lipid T cell presenting immune protein, is altered in macrophages from COPD subjects or in response to cigarette smoke, and assessed oxidation of human bronchial epithelial cell-derived lipids by cigarette smoke.

**Methods:** CD1b expression by primary bronchoalveolar-lavage derived alveolar macrophages from never-smoker, ex-smoker and current-smoker controls, and current- and ex-smoker COPD patients was measured by flow cytometry. CD1b, saposin C and their intracellular distribution was measured in primary and smoke-exposed alveolar macrophages and smoke-exposed MDM using immunofluorescence; flow cytometry or western blot. Oxidation states of lipid films produced from mechanically detached 16HBE bronchial epithelial cells were measured by spectrophotometry.

**Results:** Alveolar macrophages from COPD patients and smokers showed higher expression of CD1b than healthy controls (7.25 compared to 1.5). There was a significant correlation between CD1b expression and FEV1. Immunofluorescence demonstrated upregulation and changed intracellular distribution of CD1b and saposin C in primary COPD and smoke-exposed alveolar macrophages. 16HBE cellular lipids were successfully oxidised by cigarette smoke (average increase of 272% compared to controls).

**Conclusion:** CD1b upregulation is associated with changed intracellular distribution in alveolar macrophages from COPD patients and in response to cigarette smoke exposure. Oxidised lipids from uncleared apoptotic airway cells in COPD or in response to cigarette smoke may be presented by CD1b, potentially identifying an autoimmune component of COPD which could be exploited in future treatment strategies.

**Grant Support:** This work is not currently funded. No authors have any conflicts of Interest to declare.

**AO034**

**RAGE-SPECIFIC ANTAGONIST ALLEVIATES ELASTASE-INDUCED EMPHYSEMA DEVELOPMENT BY PREVENTING RAGE-DAMP SIGNALING**

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**Background and Aims:** The receptor for advanced glycan end products (RAGE) among a multifigand receptor of the immunoglobulin superfamily of cell surface receptor has been identified as a susceptibility gene for chronic obstructive pulmonary disease (COPD) in genome-wide data analysis. However, less is known about how RAGE involves in the pathogenesis of COPD. Therefore, we aimed to determine the molecular mechanism by which RAGE influences COPD in experimental COPD models.

**Methods:** We investigated the effect of the RAGE-specific antagonist FPS-ZM1 administration in vivo and in vitro COPD models. We injected elastase intratracheally and the RAGE antagonist FPS-ZM1 in mice, and the infiltrated inflammatory cells and cytokines were assessed by ELISA. The expression of RAGE was determined in lung tissue, serum, and bronchoalveolar lavage fluid (BALF) of mice and lung tissue and serum of human donors and patients with COPD. Moreover, downstream damage-associated molecular pattern (DAMP) pathway including MAPK, NF-κB and Nrf2 was assessed immunofluorescence staining, western blotting, or ELISA. Downstream damage-associated molecular pattern (DAMP) pathway including MAPK, NF-κB and Nrf2 was assessed immunofluorescence staining, western blotting, or ELISA.

**Results:** The expression of membrane RAGE in initiating the inflammatory response and of soluble RAGE acting as a decoy were associated with up-regulation of the DAMP-related signaling pathway via Nrf2. FPS-ZM1 administration remarkably reversed emphysematous lung in mice. Additionally, FPS-ZM1 significantly reduced lung inflammation in Nrf2−/− mice, but not in Nrf2+/- mice.

**Conclusions:** Thus, our data indicate for the first time that RAGE inhibition has an essential protective role in COPD. Our observation of RAGE inhibition provided novel insight into its potential as a therapeutic target in emphysema/COPD.

**Acknowledgment:** This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (NRF-2017R1A2B4006197).

**AO035**

**ROLE OF QUIESCENCE CANCER STEM CELLS IN THE GEFITINIB RESISTANCE IN EGFR MUTATION-POSITIVE NON-SMALL CELL LUNG CANCER**

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**Background and Aim:** Several recent evidence have shown that cancer stem cells (CSCs) have the ability in increasing intrinsic resistance to gefitinib in non-small cell lung cancer (NSCLC). We previously addressed that putative CSC marker CD133 was highly expressed on gefitinib-resistant persisters (GRPs) and showed distinctive features of the CSCs phenotype. FBXW7 is a type of F-box protein, which has the ability to regulate quiescence by reducing the level of c-Myc through ubiquitination. The goal of this study is to investigate the role of FBXW7 in the resistance to gefitinib in NSCLC with EGFR mutation.

**Methods:** NSCLC cell lines, PC9 and HCC827, harbouring sensitive-gefitinib mutation were exposed to high concentration of gefitinib in order to develop GRPs. We tried to knockdown FBXW7 gene expression, and evaluated their sensitivity to gefitinib and CD133-positive stem cell population in GRPs. We also introduced Fucci plasmid via lentiviral infection in the cells and then investigated the cell cycle and G0/phase cells in GRPs. Furthermore, we established gefitinib-resistant tumor (GRT) model by injecting PC9 cells into NOG-mice followed by gefitinib administration
after tumor growth, and evaluated mRNA and protein expression of quiescence-related markers including FBXW7 in vivo.

Results: In vitro, GRPs showed high expression of stem cell marker CD133 and quiescence-related markers including FBXW7 and low expression of c-Myc at protein level. Cell cycle analysis revealed that majority of GRPs existed in G0/G1 phase. Silencing of FBXW7 gene reduced CD133-positive cell population in GRPs. Knockdown of FBXW7 also increased susceptibility of cells to gefitinib, reversed population of G0/G1-arrested cells to G2/S/M cells, and decreased cell number of GRPs. In vivo, GRTs after gefitinib treatment revealed high expression of FBXW7 and low expression of c-Myc.

Conclusion: These findings suggest that FBXW7 plays a crucial role in the maintenance of quiescent CSCs resistant to gefitinib in EGFR mutation-positive NSCLC.

Respiratory Infections (non-tuberculosis) 1

AETIOLOGY OF COMMUNITY ACQUIRED PNEUMONIA WITH FEVER AND THE PRESENTATION AND PROGNOSIS OF VIRAL INFECTION: A PROSPECTIVE OBSERVATIONAL STUDY

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Background and Aim: Patients with community acquired pneumonia (CAP) caused by viruses can develop severe complications, which result in hospitalization and death. The purpose of this study was to analyze the aetiology, incidence, clinical characteristics, and outcomes of CAP patients with fever during non-pandemics in one pulmonary hospital.

Methods: A management system was established for monitoring the CAP patients with fever. Multiplex polymerase chain reaction (mPCR) kits were used to detect 10 viruses (influenza A and B, adenovirus, respiratory syncytial virus A and B, picornavirus, parainfluenza virus, coronavirus, human metapneumovirus, and bocavirus). Data on age, gender, underlying diseases, complications, laboratory indexes, and outcomes were collected by physicians.

Results: This prospective study included 320 patients with fever, 23.4% were viral-positive by mPCR, with influenza virus most prominent followed by picornavirus. Strong variation in seasonal distribution was shown in viral infections, with peak months from December to February. Patients with influenza infection were likely to be taken to emergency rooms and have respiratory failure with higher creatinine kinase levels and lower white blood cell counts. Streptococcus pneumoniae followed by Haemophilus influenzae were the most common bacteria in viral coinfections, which accounted for one third of virus-positive patients. Co-infection can independently act as a risk factor for the CURB65 severity score, but not for death in hospitalization.

Conclusion: Viruses play an important role in CAP patients with fever, a systematic clinical, radiological and biological analysis of these patients can contribute to effective therapy that may prevent the development of CAP and improve the outcomes. The present work showed the first and an elaborate analysis evidence of viral infection among fever CAP inpatients.

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CLINICAL, LABORATORY FEATURES AND OUTCOME OF COMMUNITY-ACQUIRED PNEUMONIA IN ALCOHOLIC PATIENTS IN RESPIRATORY CENTER, BACH MAI HOSPITAL

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Background: Community-acquired pneumonia (CAP) is one of the most common infectious diseases and is an important cause of mortality and morbidity worldwide. Alcoholism has been identified to be a risk factor for CAP, especially severe CAP.

Aims: To describe clinical, laboratory features and outcomes of CAP in alcoholic patients hospitalized in a respiratory center.

Methods: Retrospective descriptive study of CAP hospitalized in Respiratory Center of Bach Mai hospital in Ha Noi, Vietnam, from January 2015 to December 2015. Our study included 419 patients divided into 2 groups: 1st group including 73 alcoholic patients and 2nd group including 346 non-alcoholic patients.

Results: There was a higher rate of male gender in alcoholic group – 100% vs 48.6% in non-alcoholic group (p<0.01). The average age of alcoholic patients was 55.3 ± 9.1 (years), younger than non-alcoholic patients with 61.0 ± 19.6 (years). 31.5% alcoholic patients suffered from alcohol withdrawal syndromes within 24 hour of admission, with the most common symptom of tremulousness (95.7%). The most common symptoms of alcoholic patients were fever, productive cough, dyspnea and crackles, which accounted for 75.3%, 71.2%, 60.3% and 75.3% respectively. Some laboratory data of alcoholic patients was worse than non-alcoholic patients, for detail, higher percentage of anemia, thrombocytopenia, and hypoalbuminemia in alcoholic patients: 80.8% vs 49.7%, 35.6% vs 14.1%, 66.7% vs 45.0% respectively (p<0.05). Pathogens were found in only 5.4% of alcoholic patients, 2/3 of them were Gram negative bacteria. Mortality rate was 30.1% in alcoholic group vs 14.7% in non-alcoholic group. Nearly a half of alcoholic patients had complications (45.2%) with the most common one of pleural effusion, respiratory failure and abscess.

Conclusions: In our study, alcoholic patients suffered from CAP at the younger age, with worse laboratory test results and higher mortality rate, compared to non-alcoholic patients.

RISK STRATIFICATION FOR THE DEVELOPMENT OF CHRONIC PULMONARY ASPERGILLOSIS IN PATIENTS WITH MYCOBACTERIUM AVIUM COMPLEX LUNG DISEASE

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Background and Aim: The number of patients with pulmonary non-tuberculous mycobacterial disease complicated by chronic pulmonary aspergillosis (CPA) has been increasing recently. Moreover, CPA is reportedly associated with mortality in patients with Mycobacterium avium complex lung disease (MAC-LD). In the present study, we aimed to identify the risk factors for developing CPA and to stratify the risk for CPA development in patients with MAC-LD.

Methods: We retrospectively examined 361 patients who were newly diagnosed with MAC-LD. The risk factors for CPA development were examined using multivariate Cox proportional hazards regression analyses. A risk stratification system was established using the risk factors and receiver operating characteristic curve analyses.

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ASSOCIATION BETWEEN IMPLEMENTATION OF “BUNDLES OF CARE” AND POSSIBLE VENTILATOR ASSOCIATED PNEUMONIA (VAP) AMONG MECHANICALLY VENTILATED PATIENTS IN THE INTENSIVE CARE UNIT: A QUASI-EXPERIMENTAL STUDY

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Background and Aims: Ventilator Associated Pneumonia (VAP) is a serious medical condition causing significant morbidity and mortality among mechanically ventilated patients. “VAP Bundles of Care” is a process improvement program that lessens the incidence of VAP. This study aims to determine the impact of “VAP Bundles of Care” program in reducing the episodes of Possible Ventilator Associated Pneumonia (pVAP) in The Medical City Adult Intensive Care Unit (TMC-ICU). It also aims to determine the association between the implementation of “Bundles of Care” with secondary outcomes namely ventilator days, length of ICU stay, length of hospital stay and mortality among intubated adult patients in TMC-ICU from January 2008-December 2015.

Methods: A Quasi-experimental study design was used to compare pVAP rates pre and post intervention period. A total of 235 patients were included in the study. 124 patients did not receive “VAP Bundles of Care” while 111 patients received “VAP Bundles of Care”.

Results: Majority of the patients who developed pVAP occurred prior to implementation of the “Bundles of Care”. Those with VAP bundle had lower odds of acquiring pVAP. However, there was no significant difference between the secondary outcomes between the two groups. Moreover, mortality rate increased from 11% (n=14) to 19% (n=21) after its implementation. This may have been influenced by other baseline characteristics and complications that developed during the patients’ admission.

Conclusions: Continued implementation and improvement of VAP bundles of care are still recommended.

MODIFICATION OF CURB-65 SCORE AS MORTALITY PREDICTOR OF HOSPITALIZED PNEUMONIA PATIENTS WITH COMORBIDITY: CAR SCORE

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Background: CURB-65 is a simple and prominent scoring system to stratify the severity of community acquired pneumonia. Several studies indicated CURB-65 performance is not superior in some groups of patients which open possibility to modify the scoring system. Albumin is a potential prognostic factor for infection patients as reported in some studies. The purpose of this study was to search for alternative scoring system based on established CURB-65 variables and albumin level as mortality predictor in hospitalized pneumonia patients with comorbidity.

Methods: This is a retrospective cohort study of CAP and HCAP patients with comorbidity who admitted to Cipto Mangunkusumo Hospital Jakarta. There were 250 patients taken by consecutive sampling. A new scoring system was developed based on CURB-65 variables and albumin. The performance of severity scores to predict mortality was compared, then the performance of the new score was internally validated by bootstrapping-based method.

Results: There were 250 CAP and HCAP patients with comorbidity included in this study. In-hospital mortality rate was 42.4 %. Confusion (p<0.01 OR 3.4 [95% CI 1.9-6.1]), respiratory rate ≥ 30/min (p<0.01 OR 2.8 [95% CI 1.6-4.8]) and albumin level ≤ 3.125 (p<0.01 OR 2.3 [95% CI 1.2-4.4]) were independently associated with in-hospital mortality. Using those three variables we developed modification of CURB-65 named as CAR. The AUCs in the prediction of in-hospital mortality were 0.725 (95% CI 0.659-0.79), 0.677 (95% CI 0.608-0.746), 0.723 (95% CI 0.657-0.789) for the CAR, CURB-65 and CURB-65+albumin respectively.

Conclusion: Performance of CURB-65 score is relatively low in pneumonia with comorbidity patients. The performance of CAR score is superior than CURB-65 and CURB-65+albumin. CAR score may be useful to predict mortality in pneumonia patients with comorbidity.

Key Words: pneumonia, mortality, CURB-65 score, albumin, comorbidity

CAR score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Criteria</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Confusion</td>
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<td>2</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>≥ 30x/min</td>
<td>1</td>
</tr>
<tr>
<td>Albumin</td>
<td>≤ 3.125</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;3.125</td>
<td>0</td>
</tr>
</tbody>
</table>

Total Score Classification

0-1 Low risk of mortality
2 Intermediate risk of mortality
3-4 High risk of mortality
A NEW CRITERION IN PREDICTING 30-DAY MORTALITY IN HOSPITALIZED ADULT PATIENTS WITH INFECTIOUS DISEASES: A RETROSPECTIVE SINGLE CENTER STUDY

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Background and Aim: The qSOFA score is a tool for assessing the probability of sepsis in outside the ICU, however, few reports have been described that the qSOFA score can predict the mortality in elderly infectious patients. To develop a new clinical model for predicting 30-day mortality, and compared the score with that of qSOFA (≥2points) in patients with infectious diseases.

Methods: We retrospectively performed a chart review of hospitalized patients via emergency room due to infectious diseases for eight months. Relationship between 30-day mortality and new factors such as heart rate=100/min, body temperature (BT) and SpO2=90% was independently investigated. Additionally, we examined the hazard ratio (HR) of 30-day mortality in each 3 components of qSOFA (altered mental status, respiratory rates ≥ 22 breaths/min, s-blood pressure ≤100mmHg). The diagnostic accuracy for 30-day mortality between the qSOFA and a new criteria was compared.

Results: Of 585 patients, 41 (7%) died within 30 days. On single logistic analysis, hazard ratio of 30-mortality in four factors were as follows. Impaired consciousness (HR 3.03, 95%CI: 1.60-5.75, p<0.01), BT <37.0°C(HR 4.45, 95%CI: 2.41-8.23 p<0.01), BP ≤100mmHg(HR 3.66, 95%CI: 1.98-6.77, p<0.01) and SpO2<90%(HR 2.75, 95%CI: 1.49-5.10, p<0.01). A new criteria using those four components showed that the sensitivity or specificity for 30-day mortality was 78.0% and 79.4% if the total score was 2 points or more (each point is 1), which was superior than in qSOFA (sensitivity 65.9%, specificity 77.2%). Thereafter, the new criteria was applied to three divided groups (16-64, 65-84, 85+years), and the superiority was seen in the latter two groups with a statistical significance.

Conclusion: A new criteria might be a more powerful tool for predicting the 30-day mortality in ER, especially in the elderly patients with infection.

PRESENCE OF PNEUMONIA IN PATIENT WITH HIV IN DEVELOPED COUNTRIES: A SYSTEMIC REVIEW AND META-ANALYSIS

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Background and Aims: Pneumonia is one of the most common opportunistic infections in patients with HIV and various studies have assessed the presence of pneumonia in HIV patients. Here, we conducted a systematic review and meta-analysis on these studies according to the PRISMA abstract guidelines. The aim of this systematic review and meta-analysis was to assess the presence of pneumonia in HIV positive patients in compared to HIV negative controls from developed countries.

Methods: Studies were searched through PubMed, Web of Science, Scopus, ScienceDirect and Google Scholar electronic databases without restricting language and year (up to 12th August 2017) and eligible studies were selected based on the inclusion criteria. The meta-analysis was conducted using a random-effects model to calculate the odds ratio (OR) and 95% confidence interval (CI). Quality assessment was carried out by using a nine-scale modified Newcastle-Ottawa Scale (NOS). Publication bias was evaluated via visualization of funnel plot, Begg’s and Egger’s tests. All analyses were carried out by using the software RevMan (Ver 5.3) and using metafor package (Ver 2.0-0) in RStudio (Ver 1.0.153).

Results: The database searches produced 6,101 articles, 10 of which were selected (42,363 HIV positive cases and 413,908 HIV negative controls). A significant presence of pneumonia (OR: 2.44, 95% CI: 1.27 - 4.67, p < 0.00001; I² = 96%, p = 0.007) was observed in HIV positive patients. Based on the study quality assessment using modified NOS for case-control studies, eight of ten studies were of high methodological quality scoring 7 (median value) and no significant publication bias was observed from Begg’s (p = 0.055) and Egger’s tests (p = 1.00).

Conclusions: Although antiretroviral therapies have been successfully used to substantially decrease HIV infection, we observed that the presence of pneumonia is significantly higher in HIV positive patients compared to HIV negative controls which can be a risk factor for increased mortality.

<table>
<thead>
<tr>
<th>Study ID*</th>
<th>Country</th>
<th>HIV positive</th>
<th>HIV negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male/Female</td>
<td>Mean age ± SD (years)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cillóniz</td>
<td>Spain</td>
<td>35/15</td>
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<tr>
<td>2017</td>
<td></td>
<td></td>
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<tr>
<td>Wiezel</td>
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<td>49.6±12</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Barakat</td>
<td>USA</td>
<td>36922/0</td>
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</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Louis</td>
<td>France</td>
<td>146/54</td>
<td>50±12</td>
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<tr>
<td>2015</td>
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<td></td>
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<tr>
<td>Sogaard</td>
<td>Denmark</td>
<td>2719</td>
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</tr>
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<tr>
<td>Johnson</td>
<td>Canada</td>
<td>0/176</td>
<td>38.5±0/704</td>
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<td>Mientjes</td>
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<tr>
<td>Touchen</td>
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<td>Hirschrick</td>
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<tr>
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<td>Australia</td>
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</tr>
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*All studies represent community acquired pneumonia patients
NIA = No information available
Background and Aims: It has been claimed that the introduction of tobacco plain packaging together with tobacco excise increases would lead to increases in illicit tobacco sales and this has formed a considerable part of the tobacco industry arguments against these policies. Questionnaire surveys and the collection of discarded cigarette packs have been used to estimate illicit sales. Neither is perfect. Surveys rely on comprehension and honesty of respondents and discarded packs sourced from overseas may have been legitimately imported for personal use. We therefore sought not to estimate the illicit sales fraction itself but to detect trends developing after 2013.

Methods: An initial survey was conducted between December 2013 and February 2014. This marked 12 months are plain packaging introduced by which time discarded packs could be regarded as recently sold. Packs were collected from public spaces in 17 Sydney LGAs covering the sociodemographic spectrum. The survey was repeated at the same time of year, with the same number of packs from each locality, in the three subsequent years. A non-conforming pack (NCP) was one not complying with plain packaging requirement. Country of origin, brand and status duty free or not was determined. For complying packs, brand, variant and whether it was in the premium, moderate or value market segment.

Results: The number of packs collected was 1604 in year 1, and 1665, 1659 and 1673 years 2-4. Adjusting for pack size, 13.1% in year 1 were NCP with 11.5%, 10.2% and 10.9% in years 2-4. Between surveys, there were substantial differences in country of origin and brand on NCPs. Over the 4 surveys, premium cigarettes fell from 30.6% to 14.6% with value segment cigarettes increasing from 33.3% to 51.1%.

Conclusions: There is significant non-conforming tobacco use in parts of Sydney but this has decreased not increased over 4 surveys. Instead of purchasing illicit tobacco, smokers are switching to cheaper cigarettes. Mandatory plain packaging and tobacco excise increases have not produced a flood of illicit tobacco on the Sydney market. In association with declining smoking prevalence, this confirms the success of these policies.

Clinical Respiratory Medicine 1

HEALTH IMPACT OF E-CIGARETTES: A PROSPECTIVE 3.5-YEAR STUDY OF REGULAR USERS WHO HAVE NEVER SMOKED

RICCARDO POLOSA 1,2,3, FABIO CIBELLA 4, PASQUALE CAPONNETTO 1,2, MARILENA MAGLIA 1,3, DONALD TASHKIN 5

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Table

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<tr>
<th></th>
<th>Baseline</th>
<th>F/up 1</th>
<th>F/up 2</th>
<th>F/up 3</th>
<th>Between effect p value</th>
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<td>FEV1 (l, mean±SD)</td>
<td>EC users</td>
<td>3.82±0.78</td>
<td>3.81±0.78</td>
<td>3.78±0.71</td>
<td>3.87±0.76</td>
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<td></td>
<td>Control subjects</td>
<td>4.08±0.30</td>
<td>4.06±0.28</td>
<td>4.03±0.26</td>
<td>4.11±0.30</td>
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<tr>
<td>FVC (l, mean±SD)</td>
<td>EC users</td>
<td>4.93±0.95</td>
<td>4.80±0.82</td>
<td>4.82±0.91</td>
<td>4.87±0.83</td>
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<td>5.03±0.48</td>
<td>4.97±0.42</td>
<td>5.01±0.45</td>
<td>5.02±0.42</td>
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<tr>
<td>FEV1/FVC (%)</td>
<td>EC users</td>
<td>81.45±5.03</td>
<td>82.02±4.67</td>
<td>80.86±6.18</td>
<td>82.06±4.25</td>
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<td></td>
<td>Control subjects</td>
<td>79.01±3.63</td>
<td>78.46±2.34</td>
<td>79.08±2.93</td>
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<td>FEF25-75% (l/min, mean±SD)</td>
<td>EC users</td>
<td>3.29±0.70</td>
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<td>Control subjects</td>
<td>3.43±0.64</td>
<td>3.49±0.61</td>
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<td>Weight (kg, mean±SD)</td>
<td>EC users</td>
<td>71.3±11.2</td>
<td>72.9±11.5</td>
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<td>Control subjects</td>
<td>72.9±11.8</td>
<td>74.0±12.1</td>
<td>73.2±12.3</td>
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<td>Systolic blood pressure (mmHg, mean±SD)</td>
<td>EC users</td>
<td>115±9</td>
<td>116±5</td>
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<tr>
<td></td>
<td>Control subjects</td>
<td>117±9</td>
<td>117±10</td>
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<tr>
<td>Diastolic blood pressure (mmHg, mean±SD)</td>
<td>EC users</td>
<td>79±6</td>
<td>78±4</td>
<td>73±9</td>
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<td>74±9</td>
<td>76±6</td>
<td>75±9</td>
<td>73±9</td>
</tr>
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</table>
Background and Aim: There is concern as to whether long-term ECs use may cause risks to human health. When investigating these health effects, it is important to consider that it is difficult (if not impossible) to disentangle responses driven by chronic exposure EC aerosol emissions from those related to previous smoking history, unless conducting long-term studies on regular vapers who have never smoked.

Methods: Here we report health outcomes (blood pressure, heart rate, body weight, lung function, respiratory symptoms, exhaled breath nitric oxide [eNO], carbon monoxide [eCO], and high-resolution computed tomography [HRCT] of the lungs) from a prospective 3.5-year observational study of a cohort of daily EC users (mean age 29.7 years) who have never smoked and a reference group of sex-age-matched never smokers.

Results: All EC users were exposed daily to EC aerosol emissions for >4 yrs with an average consumption of 4 ml e-liquid/day. No significant changes could be detected over the observation period from baseline and between EC users and control subjects in any of the health outcomes investigated (Table). Moreover, no pathological findings could be identified on HRCT of the lungs and no respiratory symptoms were consistently reported in the EC user group.

Conclusion: Although it cannot be excluded that some harm may occur at later stages, this study did not demonstrate any health concerns associated with long-term use of EC in relatively young users.

THE STAGES OF CHANGE (SOC) AND THE LONG-TERM OUTCOME OF AN OUTPATIENT SMOKING-CESSATION PROGRAMME WITH MEDICALLY ILL SMOKERS
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Background and Aim: The stages-of-change (SOC) model has been validated in the area of smoking, predominately for non-medically ill smokers. The present study aimed to investigate whether the SOC model is applicable among medically ill smokers.

Methods: The participants were patients (n = 306, Msex = 52 years, 93.1% male) who attended a smoking-cessation programme in a respiratory medical setting of a tertiary hospital in Singapore from January 2008 to December 2012. The data were collected via a database (to serve as a baseline) and a telephone interview at a follow-up (M = 4 years). These data were analysed with descriptive statistics, chi-square, one-way ANOVA, and Tukey post-hoc procedure by the SPSS 23.0 version.

Results: There were more smokers in contemplation stage (77.5%) than in pre-contemplation stage (11.1%), action stage (7.8%) or preparation stage (3.6%). Among those who participated in the follow-up (n = 73), 42.5% of participants advanced to the maintenance stage (quit smoking for more than 6 months). Furthermore, smokers at the maintenance stage were less tempted to smoke (p < .0001) and had fewer barriers to cessation compared with smokers in other stages (i.e., pre-contemplation, contemplation, preparation or action; p < .001). No significant relationship was found between the stages of change and the reasons for quitting.

Conclusion: The predicted relationships between the stages of change and the temptation to smoke and the barriers to cessation were supported. These results have demonstrated the applicability of the SOC model for medically ill smokers who received smoking cessation service. Thus, healthcare providers should consider including the stages of change in smoking-cessation interventions. For medically ill smokers, the challenge remains to move the majority of them from the early stages of change (pre-contemplation, contemplation and preparation) to the later stages (action and maintenance).

A RETROSPECTIVE STUDY ON AMIODARONE PULMONARY TOXICITY IN CHINESE PATIENTS IN HONG KONG
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Background and Aim: Amiodarone is one of the most commonly used anti-arrhythmic agents in atrial and ventricular arrhythmias. Amiodarone pulmonary toxicity is a potentially fatal adverse effect associated with amiodarone use. Previous studies on the epidemiology and risk factors for amiodarone pulmonary toxicity showed diverse results. The objective of this study is to identify clinico-epidemiologic markers associated with amiodarone pulmonary toxicity in a cohort with defined amiodarone exposure.

Methods: List of patients taking amiodarone who were managed in Queen Mary Hospital and Grantham Hospital from 2005 to 2015 was retrieved. Those who fulfilled the inclusion criteria were obtained and analyzed on the risk factors associated with amiodarone pulmonary toxicity.

Results: A total of 25 cases with amiodarone pulmonary toxicity were identified among 1113 patients taking amiodarone for at least 90 days from 2005 to 2015. The incidence of amiodarone pulmonary toxicity was estimated to be 2.2% The risk factors for amiodarone pulmonary toxicity included increase in age (OR 1.044, 95% CI 1.008 - 1.082, p = 0.016), ventricular arrhythmia (OR 2.757, 95% CI 1.262 - 6.024, p = 0.011), underlying lung disease (OR 3.885, 95% CI 1.584 – 9.528, p = 0.003) and cumulative dose of amiodarone (OR 5.457, 95% CI 1.515 – 19.660 p = 0.009).

Conclusion: The incidence of amiodarone pulmonary toxicity in Chinese patients in Hong Kong is estimated to be 2.2% in this study. Age, underlying lung disease, ventricular arrhythmia and cumulative dose of amiodarone are associated with the development of amiodarone pulmonary toxicity. It is worth conducting a prospective clinical study in future to validate the findings observed in this study.

Acknowledgements: I am grateful for the kind assistance and advice regarding statistical analysis from Mr. Dr. Hei Man Herbert Pang.

A CASE SERIES OF HEREDITARY CYSTIC LUNG DISEASE IN A CHINESE FAMILY
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Background and Aims: Birt-Hogg-Dubé syndrome is a rare autosomal dominant disease featuring multiple lung cysts and recurrent pneumothorax. Here we report a case series of a Chinese family diagnosed with this condition.

Methods: Six members of a Chinese family in Hong Kong were genetically confirmed to have Birt-Hogg-Dubé syndrome. Their clinical-radiological features were described.

Results: Their age range from 37 to 66 years. All of them were Chinese in ethnic origin. There were three males and three females. Five out of six did not smoke. Facial fibrofolliculomas could be identified in two out of three male patients, while none of the female patients demonstrated this skin lesion. All six patients had similar numerous bilateral thin-walled cysts of variable sizes surrounded by normal lung parenchyma on HRCT of Thorax (Figure 1). Their pulmonary function tests showed similarly...
A Familial Case of Birt-Hogg-Dube Syndrome (BHDS) Complicated with Bladder Cancer and Lung Cancer: A Case Report and Literature Review

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Background and Aim: BHDS is an autosomal dominant inherited disorder characterized by fibrofolliculomas, renal tumors, pulmonary cysts and pneumothorax. BHDS is a rare cause of pneumothorax and patients do not receive appropriate medical investigations. We herein report a familial case of BHDS.

Methods: An 89-year-old female was admitted for dyspnea. She had a past medical history of bronchial asthma, gastric cancer, and bladder cancer. She had no smoking history. Small papules on and around her nose and cheeks were noted. A chest CT demonstrated bilateral multiple lung cysts. The majority of cysts were located in the basilar medial regions. It also demonstrated a nodular opacity in the right lower lobe and bronchofiberscopic examination revealed adenocarcinoma. Her son, a 65-year-old male was consulted for pneumothorax. He had a past medical history of spontaneous pneumothorax, ureter cancer, and bladder cancer. He had a smoking history of 90 pack-years. He had multiple papules on the face and neck, and those pathological findings revealed fibrofolliculomas. A chest CT demonstrated pneumothorax in the left side and bilateral basally located lung cysts. We considered these cases to be BHDS because both patients met the criteria of European BHD Consortium.

Results: Folliculin (FLCN) mutations that may be tumor-suppressive are suspected to be causative of this syndrome. Its dysfunction might lead to tumors as reported by renal cancer. The mechanisms of the formation of pulmonary cysts, renal cysts, adenomas and/or carcinomas are under study. Because these two cases both had bladder cancer without specific risk factors, we suspect the causal relationship between BHDS and cancers.

Conclusion: It is reported that most cancers developed after appearing fibrofolliculomas or pneumothorax. If BHDS can be diagnosed earlier by these findings, an early detection and treatment of cancer may be possible.

AO047

A Rare Presentation of Bronchogenic Cyst with Atrial Fibrillation

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Introduction: 10 to 18% of Mediastinal masses are mediastinal cysts most commonly asymptomatic but may appear with infection or its pressure effects. Here we Report mediastinal cyst presented with Paroxysmal Atrial Fibrillation due to stretching of Left Atrial myocardium by its pressure effect which is very rare, only 2 cases a,b reported before

Case Discussion: A 53 years old male non-smoker with history of Parkinsonism came with complaints of dyspnoea, cough & fever. On evaluation, all routine labs were normal, chest x ray postero anterior view showing normal parenchyma but widened sub carinal angle. ECG showing Atrial fibrillation with sinus rhythm for which cardarone started, 2Decho showing compression of Left atrium, coronaries were normal on Angiography. Atrial Fibrillation and Difficulty breathing are not completely resolved so patient underwent Contrast Enhanced CT Chest (Figure 1) which was showing Unilocular single Bronchogenic cyst situated at subcarinal location with pressure effects on Left Atrium. Other causes of mediastinal cysts such as teratoma ruled out by Alpha feto protein and Beta HCG we thought of Bronchogenic cyst but for confirmation and to relieve pressure effects on Left Atrium surgical option chosen. After proper pre-operative Anaesthesia work up underwent Right thoracotomy cyst approached and dissected thick yellowish material removed (Figure 2) sent for Gene X Anaesthesia work up underwent Right thoracotomy cyst approached and dissected thick yellowish material removed (Figure 2) sent for Gene X
Respiratory Structure and Function

**AGREEMENT OF COMMONLY USED PREDICTION EQUATIONS FOR SPIROMETRY INTERPRETATION IN THAI PEOPLE**

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**Background and Aim:** Spirometry is the most common lung function test, which plays an important role in directing diagnosis of respiratory diseases and classifying their severity level. Reliable interpretation of spirometry results depends on lung function reference equations. Using inappropriate references potentially lead to errors in diagnosis and severity classification. The aim of this study was to investigate the agreement of spirometry interpretation among the Third National Health and Nutrition Examination Survey (NHANES III), Knudson, the Global Lungs Initiative 2012 (GLI 2012), and Siriraj reference equations for Thai people.

**Methods:** We conducted a retrospective study of 2,492 Thai people (age range 8-80 years old) who were referred by their physicians for spirometry testing at the Lung Health Center, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand during January 2005 to December 2015. The results of spirometry were classified as normal, spirometric restriction, obstruction, or mixed defect using the NHANES III, Knudson, GLI 2012, and Siriraj reference equations. Differences in classification for the diagnosis and severity devised by the four references were analysed using Nominal Analysis of Variance (NANOVA). Kappa statistic was used to investigate the agreement of interpretation among the four reference equations.

**Results:** The spirometry diagnosis and the severity classification were significantly different across the four sets of reference equations (p<0.001). The levels of agreement across the four sets of reference equations were moderate to good (Kappa values ranged from 0.56 to 0.77 for diagnosis and 0.67 to 0.82 for severity).

**Conclusion:** The results of this study suggest that the use of the NHANES III, Knudson, GLI 2012, and Siriraj reference equations alters interpretation of spirometry data in Thai people.

**A0049**

**NON-SPECIFIC VENTILATORY LIMITATION: PATIENT CHARACTERISTICS, ASSOCIATED DIAGNOSES AND RADIOLOGICAL CHANGES**

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**Background and Aim:** Non-specific ventilatory limitation (NSVL) is a non-specific finding of reduced FVC, normal FEV1/FVC ratio and normal total lung capacity (TLC). Although frequently attributed to obstructive airway disease such as asthma or chronic bronchitis, there is a paucity of study describing patients with NSVL, especially in the group with normal gas transfer. We aim to study the clinical characteristics of this respiratory function abnormality including prevalence, patient demographics, associated diagnosis and radiological changes.

**Methods:** We retrospectively screened 160 spirometry with restrictive ventilatory defect (FVC <80 %predicted) and concomitant assessment of lung volume (by body plethysmography or multi-breath nitrogen washout method) and carbon monoxide diffusion capacity (DLCO, by single-breath method) from January to October 2014. All tests were performed at the Respiratory Function Laboratory, Tan Tock Seng Hospital on calibrated equipment. 32 patients who had acceptable results, fulfilled criteria for NSVL (FEV1/FVC<70%, TLC ≥80 %predicted) and normal gas transfer (DLCO ≥80 %predicted) were identified for medical record review and final analysis.

**Results:** The patients were predominantly female (23; 72%) and non-smokers (29; 91%); median (interquartile range, IQR) age was 65 (59-71) years and body mass index was 25.1 (22.1-28.1) kg/m². Main lung function abnormalities were mild restrictive ventilatory defect (FVC 72, IQR 58-77 %predicted) and elevated residual volume (129, IQR 101-153 % predicted). The common associated diagnoses were asthma (11; 34%), bronchiectasis (4; 13%), small airway disease (3; 9%), interstitial lung disease (3; 9%) and pulmonary nodules (3; 9%). CT thorax, when performed (n=23), showed normal findings (9; 39%), mosaic attenuation (5; 22%) and bronchiectasis (4; 17%).

**Conclusion:** NSVL with normal gas transfer is not uncommon and affected patients are predominantly elderly, non-smoking and overweight female. Ventilatory impairment is mild and most patients have airway disease. Radiology is often normal but may demonstrate changes associated with gas trapping or airway disease.

**A0050**

**MEASUREMENT OF AIRWAY DIMENSIONS BY 3-D CT IN INFLAMMATORY BOWEL DISEASE PATIENTS**

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**Background and Aims:** An association between inflammatory bowel disease (IBD) and airway diseases is well described. However, it is unknown whether respiratory asymptomatic IBD patients have airway wall changes. Here, we evaluated the airway wall structure in IBD patients by 3-D CT analysis.

**Methods:** We conducted a hospital-based retrospective study. Subjects were recruited by medical records from January 2006 to December 2016 in our hospital. IBD patients were ulcerative colitis(UC) or Crohn’s disease(CD) and had undergone chest CT for various reasons. Subjects who had been taken screening chest CT but had not been detected any abnormalities, were defined as healthy controls. Airway dimensions were measured in the right upper and lower lobe segmental bronchi (B1, B5) as percentages wall area (%WA) and percentages wall thickness (%WT).

**Results:** One hundred thirty-nine IBD patients and 30 healthy controls were analyzed. IBD patients had a significantly greater %WA than healthy controls (58.9±6.2 vs54.0±7.4[p<0.01]) and a greater %WT compared to healthy controls (36.2±4.9 vs 32.6±5.0[p<0.01]). In IBD patients without definite abnormalities in lung fields(n=118), airway dimensions were increased compared with healthy controls (%WA; 59.0±6.2 vs 54.0±7.4[p<0.01],%WT; 36.3±4.9 vs 32.6±5.5 [p<0.01], respectively). However, there were no differences of airway dimensions between UC patients (n=79) and CD patients (n=60).

**Conclusions:** These findings suggest that airway wall thickness may occur in IBD patients, even in patients without respiratory symptoms.
HIGH SPEED, HIGH RESOLUTION IN VIVO DYNAMIC LUNG IMAGING USING A LABORATORY X-RAY SOURCE TO MEASURE REGIONAL LUNG FUNCTION AND PULMONARY VASCULATURE

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Background and Aims: Our laboratory has achieved fast lung imaging at high resolution in vivo using a high brightness laboratory X-ray source coupled with a high-speed detector. This system is used to image breathing mice at sufficient spatio-temporal resolution to track lung tissue patterns. This technique enables us to segment key features, such as the airways, lobes and pulmonary vasculature, without the use of contrast agents. Recent work into dead space ventilation in a mouse model of lung injury showed progressive increases in airway volume in response to mechanical ventilation (Kim et al., J Appl Physiol, 2017). Measurement of the pulmonary vasculature is based on the contrast-free angiography technique developed by our laboratory, in which diameters can be measured down to approximately 60 μm (Samarage et al., Med Phys, 2016).

Methods: We used a murine model of ventilator-induced lung injury whereby BALB/c mice were ventilated for either 2 or 5 hours (PIP = 20 cmH2O, zero PEEP). The imaging provides a displacement vector field for the entire 3D lung parenchyma, thus providing the ability to measure the tidal volume on a regional level (see panel A). Measurements of the pulmonary vasculature were obtained by applying a filter that detects tubular structures in the 3D image (panel B).

Results: Difference in tissue patterns in the CT slices after 5 hours mechanical ventilation were consistent with tissue injury (panels C, D). Although there was no evidence of change in global lung tissue expansion (ie tidal volume), regional contours showed decreases (relative to maximum) post-ventilation (panels E, F). Results from contrast-free vascular imaging in the same model showed global increases in the measured diameters of pulmonary vessels.

Conclusions: Our novel in vivo imaging technique provides high-resolution, non-invasive data on lung function and the pulmonary vasculature, and the ability to capture changes in these measures over time in the same animal and without contrast agents. Regional quantitative data on a lobar (or sub-lobar) level is also possible with this imaging technology and is the focus of ongoing work.

ACUTE CIGARETTE SMOKE EXPOSURE IMPAIRS AIRWAY CONTRACTION BUT NOT RELAXATION IN MOUSE PRECISION CUT LUNG SLICES

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Background and Aim: Cigarette smoke (CS) exposure has been linked to increased airway inflammation and loss of dilator sensitivity to β2-adrenoceptor agonists. We hypothesised that inflammation associated with acute CS exposure would induce similar changes in reactivity in mouse small airways ex vivo.

Methods: Male C57Bl6 mice (8-11 weeks) were exposed to room air (Air) or 9 cigarettes/day (CS) for 4 days. Separate mice were used for collection of bronchoalveolar lavage (BAL) for total/differential cell counts, or for preparation of precision cut lung slices (PCLS, 150 μm) for phase-contrast microscopy to analyse in vitro airway contraction to methacholine (MCh) or serotonin (5-HT), and relaxation to the β2-adrenoceptor agonist salbutamol.

Results: Total BAL cells were increased by ~100% with CS exposure, predominantly due to neutrophilia. Maximum contraction to MCh was attenuated by CS (% reduction in airway area: Air 59±7% (n=11); CS: 77±7% (p<0.05) with no change in potency, while contraction to 5HT was not significantly reduced (Air 53±17% (n=8); CS 40±9% (p>0.05), NS). Relaxation to 10-6 M salbutamol was similar between Air and CS (% relaxation: Air 68±15% (n=8); CS: 77±14% (n=5). The results are shown in Figure 1.

Conclusion: Despite marked lung inflammation, acute CS exposure reduced MCh contraction in small airways, without reducing dilator efficacy. Further studies are required in this model to define whether CS exerts differential effects on large airways to influence total lung function or whether prolonged CS exposure may be required to elicit changes in airway reactivity similar to those seen in chronic smokers.
Bronchoscopy and Interventional Techniques

AO053

DIAGNOSIS OF PERIPHERAL LUNG NODULE USING ENDOBRONCHIAL ULTRASOUND WITH A GUIDE SHEATH AND CT WORKSTATION : PRELIMINARY STUDY

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Background and Aims: Bronchoscopy is useful tool in the diagnosis of lung nodule. But the yield of peripheral lung lesion (PLL) is lower compared with central and intermediate lesion. Endobronchial ultrasoundography with guided sheath (EBUS-GS) has been used to overcome such limitation, however the diagnostic yield of transbronchial lung biopsy (TBLB) using EBUS-GS in PLL is not as high as expected. Accordingly we attempted to use CT work station to raise diagnostic yield of TBLB using EBUS-GS for PLL

Methods: From February to May 2017, 42 patients underwent EBUS-GS to diagnosis PPL at Ulsan University Hospital. The patients were randomized before EBUS-GS to group CW (the group using specific CT workstation to reconstruct bronchus anatomy) or non-CW (the group not using CT workstation).

Results: Of the 42 patients, 21 were in group CW. No statistically significant differences were found between group CW and non-CW in terms of the duration of EBUS-GS time (29.87 vs. 30.13 min, respectively, p=0.938), duration of navigation time (11.43 vs. 8.23 min, respectively, p =0.167). In CW group, EBUS probe was placed with the lesion in 76.2% which was higher than non CW group, 47.6% (p=0.057). The diagnostic yield of CW group was 71.4% and non CW was 80.9% respectively. which was higher than non CW group, 47.6% (p=0.057). The diagnostic yield of CW group was 71.4% and non CW was 80.9% respectively. No statistical difference to improve diagnostic yield.

Conclusions: CT workstation was a useful way to understand and reconstruct bronchus anatomy, but it did not shorten the procedure time. Even though it helps EBUS probe to be placed within the PPL but there is no statistical difference to improve diagnostic yield.

AO054

THE UTILITY OF NEW 25 GAUGE ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE IN LYMPH NODE STAGING

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Background and Aims: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is recommended not only for differential diagnosis but also for lymph node staging. However, standard 22 gauge needles are sometimes too rigid to approach some stations located at acute angle. On the other hand, new 25 gauge needle has been introduced to Japan around the end of 2016. This needle has advantages in flexibility and puncturability by its structure. We aimed to validate the clinical impact of this new needle in lymph node staging.

Methods: Consecutive patients who underwent EBUS-TBNA also served as lymph node staging of primary lung cancer in National Cancer Center Hospital from January 2016 to May 2017 were collected. The differences of diagnostic outcome between standard 22 gauge and new 25 gauge needles were analyzed.

Results: We analyzed 29 cases using 25 gauge and 75 cases using 22 gauge (104 cases in total). The distribution and size of lesions were well-balanced in both groups (p=0.649, p=0.846, respectively). While the 25 gauge group succeeded diagnosis in 2 cases and staging in 5 cases (100.0% vs. 90.7%). This failure was mainly caused by incomplete puncture for mediastinal lymph nodes. In contrast, while 124 punctures were attempted for 75 lesions and 110 core tissue were taken in the 25 gauge group, 272 punctures were attempted for 153 lesions and 237 core tissue were taken in the 22 gauge group. Therefore, sampling rate of core tissue was comparable in both groups despite the difference in needle thickness (88.7% vs. 87.1%, p=0.743).

Conclusions: We were able to successfully complete all EBUS-TBNA aimed lymph node staging using the new 25 gauge needle. This needle might be a preferable device for this setting.

AO055

UTILITY OF PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FOR RAPID EVALUATION IN TRANSBRONCHIAL BIOPSY SPECIMENS

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Background and Aim: Probe-based confocal laser endomicroscopy (pCLE) is a novel, non-invasive technology that provides real-time lung imaging during bronchoscopy. pCLE shows the elastic fiber network without the use of a fluorescent dye. Elastic fibers produce argon laser-induced autofluorescence at a wavelength of 488 nm, but tumor cells do not produce autofluorescence at a wavelength of 488 nm. As a result, the tumor cells cannot be observed directly. To diagnose benign and malignant lesion, elastic fiber and cell structures was evaluated with pCLE. However, there are no criteria to diagnose malignant lesion in peripheral lung tissue. Therefore, we stained transbronchial biopsy (TBB) specimens with acriflavine and evaluated TBB specimens with pCLE to diagnose peripheral pulmonary lesions.

Methods: After bronchoscopy, we stained TBB specimens with acriflavine and observed them using pCLE. We classified benign and malignant lesions by cell density and nuclear magnitude disparity.

Results: We defined the confocal laser endomicroscopic atypical classification (CLEA classification) from the findings of cells. Our sample size was 36 patients for whom benign and malignant specimens were differentiated using the CLEA classification. The sensitivity for malignancy was 91.3% and the specificity was 76.9%. Both inter-observer agreement (κ = 0.48) and intra-observer agreement (κ = 0.57) confirmed a moderate coincidence rate.

Conclusion: pCLE with acriflavine staining was useful for differentiating malignant from benign transbronchial biopsy specimens.
A REVIEW OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA) USE AT MULTIPLE CENTRES AS DIAGNOSTIC GUIDE FOR SARCOIDOSIS

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Background and Aims: Literature review demonstrated variable CD4/CD8 ratio in bronchoalveolar lavage for patients with sarcoidosis but there had been very few studies examining the CD4/CD8 ratio in mediastinal lymph node aspirates obtained by endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) for sarcoidosis. Our study aims to examine whether correlation exist between the CD4/CD8 ratio in EBUS-TBNA aspirate of mediastinal lymph nodes and the diagnosis obtained through histopathology in patients with confirmed sarcoidosis.

Methods: Our data set was obtained from electronic medical record and specialist letters for patients with EBUS procedure performed for mediastinal lymphadenopathy in last 3 years in Macquarie University Hospital, Concord Hospital, Nepean Hospital and Sydney Adventist Hospital (n=139). Our including criteria were set out as 1) clinical indication to perform EBUS-TBNA is sarcoidosis, 2)sufficient sample was sent for flow cytometry in addition to histopathology. Cases that did not fulfill the criteria were excluded from the study (n=86). Histopathology and cytology results were reviewed for correlation.

Results: Out of 39 patients suspicious for sarcoidosis, 18 patients were diagnosed with sarcoidosis through histopathology with granulomatous cells. CD4/CD8 ratio in mediastinal lymph nodes in those samples were elevated in 13 samples (72.2%), normal in 4 samples (22.2%) and low in 1 sample (5.6%). Statistically, there is no significant association between diagnosis of sarcoidosis and elevated CD4/CD8 ratio (p value=0.7342, Fisher exact test, 2-tailed).

Conclusions: CD4/CD8 ratio in mediastinal lymph node is highly variable and does not correlate with tissue diagnosis of sarcoidosis.

CRYOTHERAPY: NEW CONCEPT IN PEDIATRIC AIRWAY DISORDERS

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Background: Cryotherapy is an evolving therapeutic and diagnostic tool used during bronchoscopy. Through rapid freeze–thaw cycles, cryotherapy causes cell death and tissue necrosis or tissue adherence that can be used via the flexible or rigid bronchoscope. This extreme cold can be used through the working channel of the bronchoscope via a specialized cryoprobe or directly with the use of spray cryotherapy. These properties allow for multiple bronchoscopic techniques, each with its own equipment and procedural, safety, and efficacy considerations.

Aims: To investigate the efficacy and safety of bronchoscopic cryotherapy for pediatric airway disorders.

Methods: A total of 65 pediatric patients with airway disorders (stenosis, obstruction, foreign body aspirations as well as pulmonary atelectasis received bronchoscopic cryotherapy. Treatment efficacy was evaluated on bronchoscopy before cryotherapy and after the cryotherapy treatment.

Results: The results were amazing. All Patients had high degree of improvements. I used cryoprobe for removing of foreign bodies in 13 patients, open and dilate subglottic stenosis (in 8 patients), tracheal stenosis (in 12 patients), bronchial stenosis (in 33 patients) and control of telangiectasia bleeding sites in 3 patients.

Conclusions: Treatment with bronchoscopic cryosurgery is a safe and effective method to tracheal stenosis caused by granulation tissue.

THE UTILITY OF VIRTUAL FLUOROSCOPY DURING TRANSBRONCHIAL BIOPSY FOR NOT VISIBLE GROUND-GLASS NODULES ON X-RAY FLUOROSCOPY

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Background and Aim: Virtual fluoroscopy (VF) is a novel guided technique which can show the target lesion clearly on Ray Summation image similar to X-ray fluoroscopy. Endobronchial ultrasound with a guide sheath (EBUS-GS) is a better modality for imaging ground-glass nodules (GGNs). However the diagnostic yield is not ideal for GGNs that cannot be detected on X-ray fluoroscopy. We evaluated whether the addition of VF to EBUS-GS improved the diagnostic yield.

Methods: This study was a retrospective review of GGNs that were not detected on X-ray fluoroscopy during bronchoscopy. From September 2012 to February 2016, 74 cases with GGNs were not visible on X-ray fluoroscopy. The patients were divided into two groups whether we used VF or thin-section CT (TSCT) as a reference of bronchoscopy: VF group (n=35) and TSCT group (n=39). We compared the diagnostic yields between the two groups and performed multivariate analysis to determine the factors associated with increased diagnostic yield.

Results: The diagnostic yield was significantly higher in the VF group than in the TSCT group (77.1% vs 51.2%, p=0.030). There were no significant complications in both groups. In multivariate analysis, the positive bronchus sign and using of VF were the significant factors associated with successful bronchoscopic diagnosis (odds ratio: 5.41, 95% CI 1.36-21.40, and odds ratio: 3.68, 95% CI 1.16-11.60, respectively).

Conclusion: The addition of VF with EBUS-GS was advantageous for the diagnosis of GGNs that were not visible on X-ray fluoroscopy.
describe the patient experience of bronchoscopy as uncomfortable. Data relating to the patient experience is often used to determine whether a particular pharmaceutical agent reduces procedural discomfort. The aim of this systematic review was to determine the effectiveness of various pharmaceutical agents used during bronchoscopy on the patient experience, and highlight gaps in the evidence.

Methods: This systematic review was guided by Cochrane methodology (PROSPERO 2016: CRD42016037583). Eight data bases were searched: CINAHL, MEDLINE Complete, Cochrane, PubMed, Web of Science, EMBASE, PsycINFO and Scopus. Included RCTs were those that reported self-rated aspects of the patient experience and/or willingness to repeat the bronchoscopy.

Results: The search yielded twenty-five relevant RCTs. These studies reported data on a variety of psychological, physical, and patient satisfaction outcomes. The quality of the reviewed RCTs was often impaired: some studies were not blinded, methodology was unclear, and few studies reported protocol registration. There was inconsistent reporting of outcomes, use of measurement scales, and presentation in reports; making a meta-analysis impractical.

Conclusions: When pharmaceutical interventions were compared, some studies demonstrated improved patient outcomes. Propofol with hydrocodone resulted in improved patient comfort and reduced cough. Propofol compared to midazolam improved patient tolerance of the procedure and reduced breathlessness. Midazolam with dextromethorphan compared to midazolam alone reduced distress, discomfort and cough. Non-use of sedation resulted in negative psychological and physical effects. Overall, when compared to placebo, use of sedation improved patient comfort, tolerance and willingness to repeat the procedure but effects varied according to type of sedation.

ONE-YEAR OUTCOMES OF BRONCHIAL THERMOPLASTY FOR SEVERE UNCONTROLLED ASTHMA IN JAPAN
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Background and Aims: Bronchial thermoplasty (BT) has been approved as a non-pharmacologic treatment for severe uncontrolled asthma in Japan since September 2014. Previous trials demonstrated that BT led to improvement of asthma-related quality of life (QOL) and reduction of exacerbation. Until now, there has been few report on BT in Japanese asthmatic patients.

Methods: This study included adult Japanese patients who underwent BT for the treatment of severe uncontrolled asthma from February 2015 to April 2016. All subjects met European Respiratory Society/American Thoracic Society definition of severe asthma. The effectiveness and safety of BT, along with high-dose inhaled corticosteroids and long-acting β2 agonists, were assessed.

Results: Twelve subjects underwent three bronchoscopic procedures for BT. After every BT procedure, there was reversible local peribronchitis/bronchitis or atelectasis, which gradually improved within one week. Asthma-related QOL, asthma control, and forced expiratory volume in 1 second improved from 1 month until at least 1 year after BT. Ten patients (83.3%) had reduced frequency of severe exacerbation and 2 patients (16.7%) reduced their intake of maintenance asthma drugs after one year.

Conclusions: BT was a relatively safe procedure that improved airflow obstruction and asthma-related QOL and control, along with reduced frequency of severe exacerbation in Japanese patients with severe uncontrolled asthma.

DEVELOPMENT OF A NEW SHORT-TERM LUNG EMPHYSEMA MOUSE MODEL
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Background and Aims: Chronic obstructive pulmonary disease (COPD), including lung emphysema is one of the major health problems in the world. COPD is characterized by airflow limitation due to small airway disease and lung emphysema in consequence of alveolar destruction leading to airspace enlargement. There are many studies about the pathogenesis of lung emphysema, however the mechanisms of lung emphysema development are still unclear. The experimental animal model of lung emphysema may play an important role in elucidating the process of lung emphysema development. Animal models of lung emphysema by elastase administration or cigarette smoke (CS) inhalation have been developed. Elastase models are often criticized for having processed under nonphysiological conditions. Models using CS inhalation, however, requires long-term administration using special devices; generally, 8 weeks at least. Therefore, short-term and less nonphysiologic lung emphysema models are needed. Here, we developed a short-term lung emphysema mouse model using cigarette smoke extract (CSE).

Methods: CSE was made from smoke of combusted commercially available cigarettes, filtered through PBS. CSE or PBS was intratracheally administered using a micro sprayer to 15–16 weeks old male C57BL6 mice under anaesthesia for 6 weeks. The lung function was measured using flexiVent. In addition, histological findings and cell fractionation of bronchoalveolar lavage fluid (BALF) were evaluated.

Results: CSE increased lung capacity and lung compliance, significantly. In CSE group, the mean linear intercept length was significantly longer indicating lung emphysema, and the number of the cells in BALF was reduced. Cell fractionation did not differ between groups.

Conclusions: The short-term exposure of CSE developed lung emphysema in mice. This novel mouse model may contribute to further exploration of the underlying pathogenesis of lung emphysema.

THE EFFECTS AND MECHANISM OF ALENDRONATE FOR COPD ANIMAL MODEL
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Background: Alendronate (ALN), one kind of bisphosphonates, is always been used for osteoporosis. It can have the effect for osteoporosis in patients by inhibiting bone resorption of osteoclasts. Recent studies
found that ALN is one kind of the potent inhibitors to farnesyl diphosphate synthase which could regulate J2 receptor effectively in chronic obstructive pulmonary disease (COPD) patients. Our study is to investigate the effects of ALN on COPD rat model and the potential mechanism.

**Methods:** The establishment of COPD rat model was by cigarette smoking with a total body exposure method and air injection of lipopolysaccharide. A total of 36 female Wistar rats were randomly divided into three groups: normal, COPD and COPD-ALN groups. Pulmonary function tests were detected by the Double Chamber System. BALF, serum and lung tissues will be obtained. Cultured mouse airway smooth muscle (ASM) cells were stimulated by ALN 72h with different concentration. Western blotting, enzyme linked immunosorbent assay and immuno-fluorescence were used to detect related inflammatory cytokines and signaling pathway proteins.

**Results:** For animal models, the value of special airway resistance was gradually decreased with the increase of ALN concentration and the final decline was about 40%. Effective drug concentration range was from 0.625 to 5 mg/mL. What’s more, ALN could regulate the phosphorylation of expression extracellular regulated protein kinases1/2 (ERK1/2), myosin light-chain kinase (MLCK) and myosin light chain 20 (MLC20) in mouse ASM cells and tissues.

**Conclusion:** We found that ALN could improve the lung function. And ALN could regulate the contraction of airway smooth muscle by inhibiting Ras/ERK/MLCK/MLC20 pathway in COPD rat model. Although a clinical study should be conducted, ALN could be a novel therapeutic option for COPD.

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**AO063**

**AGING RELATED DNA METHYLATION IN PERIPHERAL BLOOD OF SMOKERS AND PATIENTS WITH COPD**

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**Background:** The incidence rate of COPD is increased obviously in aging population. Smoking is a risk factor of COPD occurrence.

**Aims:** In this study, we ought to determine whether there is difference of aging related gene methylation among non-smokers, smokers and COPD patients.

**Methods:** We selected ageing related genes: AREG, ATG3, E2F1, FOXO3, HDAC1, MMP2, NUF2, TGFB1, TP53 according to published literature. We assessed CpG sites methylation of promoter genes from peripheral blood in 18 non-smokers (42-68y, male), 21 smokers (40-66y, male) and 23 COPD patients (50-70y, male) using Illumina Nextseq500. The methylated levels of genes were compared. And the methylation association with age, smoking index, FEV1/predicted, scores of CATs and MMRC were evaluated.

**Results:** E2F1 promoter was lower methylated in smokers compared with non-smokers and COPD. Hyper-methylation of TGFB1 was tested in COPD compared with non-smokers and lower methylation of FOXO3 was tested in COPD compared with smokers. In non-smoker group, age and TP53 methylation have negative correlation. In smoker group, smoking index has correlation with the methylated levels of AREG and TP53. In COPD group, age has correlation with the methylated levels of FOXO3 and HDAC1. The percentage of FEV1/predicted has correlation with HDAC1 methylation. But genes methylation has no correlation with CATs and MMRC scores.

**Conclusion:** Our study suggests that E2F1, TGFB1, FOXO3 methylation may be used as epigenetic signatures in smokers and patients with COPD. AREG and TP53 methylation may have correlation with smoking index. HDAC1 methylation may have correlation with FEV1/predicted.

**AO064**

**ABNORMAL M1/M2 MACROPHAGE PHENOTYPE SWITCHING OCCURS DIFFERENTIALLY IN THE SMALL AIRWAY WALL AND LUMEN IN SMOKERS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)**

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**Background and Aims:** We explore potential dysregulation of macrophage phenotypes in COPD pathogenesis through integrated study of human small airway tissue, bronchoalveolar lavage (BAL) and an experimental murine model of COPD.

**Methods:** Small airway (SA) lung resections, and BAL smaples from normal controls (NC), smokers with normal lung function (NLFS), COPD current (CS) and ex-smokers (ES) were stained with CD163 antibodies for M2 macrophages and dual stained with anti-CD68- and anti-iNOS antibodies for M1. SA tissues sections were assessed: cells counted per mm² of SA wall and cells per mm for the epithelium respectively. Bronchoalveolar lavage (BAL) cyto-spin macrophages were enumerated by randomly selecting 12 fields and assessed per ml of original BAL fluid. BAL cytokines were measured using Millipore Magpix multiplexing.

**Results:** In NC SA wall there were fewer M1’s compared to NLFS (p<0.001) and COPD-CS (p<0.05), albeit a lesser extent in COPD-ES. Similarly, the epithelium had fewer M1’s in the NC compared to COPD-CS (p<0.001), yet again hardly any M2’s in the pathological groups (p<0.001). The BAL AMs were dominantly M2 in both smokers (p<0.001) and COPD (p<0.05) while percent M1’s decreased in COPDs compared to NC (p<0.01). BAL cytokine profile were dominantly M2, with an increase in CCL2, IL4, IL13 and IL10 in COPDs compared to NC (p<0.01) while no change in M1cytokines IP10, IFN-Υ and IL12 were observed.

**Conclusions:** In the SA wall the anti-inflammatory M2 macrophage phenotype which resides in normal airways are switched in COPD, so that the “inflammatory” M1 phenotype predominates. In BAL however, the profile shifted from a normal M1 to a more M2 phenotype in COPD, with similar cytokine profiles. These are important observations and warrant further studies.

**Grant Support:** Clifford Craig Foundation
Background and Aims: Cigarette smoke causes oxidative stress to the lungs inducing cellular transcriptome and proteome changes. Cells actively recycle damaged material using autophagy pathways through the fusion of autophagosomes and lysosomes forming an “autophagic flux”. However, accumulation or dysregulation of lysosomes leads to disrupted autophagy and consequently stressed endoplasmic reticulum (ER). The current study evaluates the presence of LAMP1+ lysosomes in the small airway (SA) epithelium of COPD patients and assess physiological outcomes.

Methods: SA lung sections from volunteers classified as nine non-smoking controls (NC), eleven smokers with normal lung function (NLFS), nine moderate COPD current smokers (CS) and ten ex-smokers (ES). Staining intensity of LAMP1+ cells was measured as objects per area of epithelium and SA wall using an imaging software Image ProPlus Version 7.0 and further represented as percent LAMP1+ expression in SA epithelium.

Results: Both COPD-CS and NLFS groups showed a significant increase in percent LAMP1+ lysosomes in the SA epithelium and sub-epithelium compared to NC (p<0.001) which significantly decreased in COPD-ES (p<0.05) but still higher than NC, suggesting both COPD and smoking effect. The normal airway epithelium was devoid of any detectable LAMP1 expression. In NLFS and COPD-ES the LAMP1+ epithelial lysosomes accumulated in the ER close to the nucleus, while in the COPD-CS the ER was disrupted and a more diffused LAMP1 expression was observed. The percent LAMP1 expression showed positive correlation to patient smoking history (pack-years) (Spearman’s rho (rs) 0.6, p = 0.002) while in COPD LAMP-1 negatively correlated to FEV1/FVC (rs -0.45, p = 0.03) and FEF25-75 (Spearman’s rho (rs) -0.5, p = 0.02).

Conclusions: Our data suggests that smoking actively stimulates lysosomal accumulation in the SA wall and is associated with decrease in lung function in COPD. The consequence of dysregulated lysosome in autophagy warrants further investigations.

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CILIARY DYSFUNCTION AND RESPIRATORY EPITHELIAL ULTRASTRUCTURAL ABNORMALITIES ARE FEATURES OF COPD IRRESPECTIVE OF EXACERBATION PHENOTYPE

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Background and Aims: Impaired mucociliary clearance may contribute to development of a frequent exacerbator phenotype, in patients with COPD. Aim of this study was to determine if COPD patients with the frequent exacerbator (FE) phenotype (defined by ≥2 exacerbations in the past year) have greater ciliary dysfunction and epithelial ultrastructural abnormalities compared to those with the infrequent exacerbator (IFE) phenotype and healthy subjects.

Methods: 16 COPD patients (FE, n=7 and IFE, n=9; mean±SD age = 63.7±3.9 years; 11 current smokers and 5 ex-smokers) and 12 healthy subjects (mean±SD age = 49.8±7.2 years, 6 current smokers and 6 ex-smokers) were studied. Subjects underwent bronchoscopic bronchial brushing from the bronchus intermedius. Assessment of ciliary beat frequency (CBF) and beat pattern (in terms of dyskinesia index, defined as the proportion of cilia with dyskinetic beat pattern) was performed using digital high speed video imaging. Epithelial ultrastructure was studied using Transmission Electron Microscopy (TEM).

Results: The CBF (median [IQR] of COPD FE (6.7 [6.3-6.9] Hz) and IFE (6.8 [5.7-7.2] Hz) were significantly lower compared to controls (8.5 [7.7-8.9] Hz; p<0.01). The dyskinesia index (median [IQR] of FE) was significantly higher in both groups of COPD patients (FE: 77.6 [68.6-97.2] % and IFE: 67.9 [59.1-88.9] %) compared to controls (14.5 [11.1-16.9] %); p<0.001 (Figure 1). Both smoker and ex-smoker COPD subgroups had significantly reduced CBF and increased dyskinesia, compared to controls. However, between FE and IFE phenotypes, there was no significant difference in CBF or dyskinesia index. Both FE and IFE COPD subgroups showed significantly higher ultrastructural abnormalities characterised by loss of cilia, extrusion of cells and cytoplasmic blebs (Table 1).

Conclusions: Dysfunctional cilia and epithelial ultrastructural abnormalities are features of COPD irrespective of exacerbation phenotype and smoking status. The clinical implications of dysfunctional cilia remain to be determined.

SPARC EXPRESSION IN AIRWAY SMOOTH MUSCLE CELLS IS REGULATED BY THE UNFOLDED PROTEIN RESPONSE AND MAY BE DIMINISHED IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Secreted protein acidic and rich in cysteine (SPARC) is a matricellular protein. It is implicated in the pathogenesis of a number of diseases, although its role in COPD is unknown. Endoplasmic reticulum (ER) stress and the unfolded protein response (UPR) contribute to COPD pathogenesis. Since TGF-β drives airway remodelling in
OPD and also induces ER stress, we determined whether TGF-β1 induces SPARC expression in airway smooth muscle (ASM) cells and whether this is related to ER stress. We also investigated whether SPARC expression is altered in ASM cells from COPD subjects.

Methods: ASM cells were stimulated with TGF-β1 (5, 10 ng/ml) for 24 or 72 h significantly enhanced cellular SPARC expression by approximately 4-fold. A significant increase in the concentration of soluble SPARC was also detected in culture supernatants: 136.5±16.1 ng/ml (SEM) and 744.9±402.3 ng/ml at 24h and 72h, respectively. TGF-β1 (10 ng/ml) enhanced the expression of ER stress markers GRP78 and IRE1α by approximately 2.5 and 5-fold, respectively. The chaperones 4-PBA and TMAO completely inhibited TGF-β1-induced SPARC, but had a less pronounced effect on SPARC secretion. Notably, SPARC secretion in COPD ASM cells was reduced when compared to non-COPD ASM cells, both at baseline (44.9±14.8 ng/ml vs 74.4±12.4 ng/ml, n=5-6) and in response to TGF-β1 stimulation (285.9±66.6 ng/ml vs 438.7±24.7 ng/ml, n=5-6), although this was not statistically significant.

Conclusions: Our studies suggest that the UPR regulates TGF-β1-induced SPARC expression in ASM cells and that SPARC secretion is reduced in COPD. Further investigation of the underlying mechanisms may provide new insight into COPD pathogenesis.

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Tuberculosis 2

PERFORMANCE OF DIFFERENT SETS OF SINGLE-NUCLEOTIDE POLYMORPHISMS (SNP) FOR TYPING MYCOBACTERIUM TUBERCULOSIS (MTB) STRAINS LINEAGE AND MODERN/ANCESTOR BEIJING SUBLINEAGE

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Background and Aims: Next-generation sequencing (NGS) provides high resolution molecular epidemiology of mycobacteria pathogen. Genetic diversity of MTB played an important role on transmissibility, virulence, drug resistance, and host response, with strains have been divided into seven major lineages. Lineage 2 (Beijing family) comprise pandemic strains found in South and East Asia, and further divided into modern/ancient sublineages. Different sets of single-nucleotide polymorphisms (SNP) have been proposed for typing MTB strains lineage and modern/ancient Beijing sublineage. We aimed to compare the performance of these different approaches in clinical isolates.

Methods: Using NGS, we studied 37 MTB strains isolated from 2015 to 2016 in Hong Kong, an intermediate TB-burden area, with 78 reference strains retrieved from GenBank were called variants from H37Rv (GenBank accession NC_000962.3) and classified by GATK. Different sets of SNPs were compared: (1) a reported robust SNP barcode for typing MTB; (2) reported specific SNPs for modern Beijing sublineage; (3) 21,805 SNP set from TGS-TB of short reads from NGS. Based on these previous researches, different sets of 21,805, 106 and 61 SNPs were used to construct phylogenetic trees independently by RAxML.

Results: We found that the phylogenetic tree constructed with 106 SNPs showed high concordance with lineage typing using polymerase chain reaction (PCR) typing as reference. In contrast, the two sets of 21,805 and 61 SNPs misled some of lineage typing when compared with PCR results. Modern/ancient Beijing sublineages also showed ambiguous results under these SNPs typing approaches.

Conclusions: In summary, a set of 106 SNPs may appear more suitable for typing MTB strains for lineage and modern/ancient Beijing sublineages simultaneously when using NGS data. Further studies are ongoing to correlate the different SNPs typing sets with specific epidemiological linkages.

Acknowledgment: We thank the Li Ka Shing Institute of Health Sciences for providing technical support.

STUDY OF DIAGNOSTIC UTILITY OF XPERT MTB/RIF TEST ON PLEURAL FLUID IN THE EVALUATION OF PATIENTS PRESENTING WITH PLEURAL TUBERCULOSIS IN NEPAL DEEBYA RAJ MISHRA1, NANDRA BHATTA1, MADHAB LAMSAL1, NARAYAN BHATTARAI1, ROBIN MASKEY1

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Background and Aim: Accurate diagnosis and early treatment of TB has the potential to reduce pleural TB-associated morbidity and mortality. Existing tests for the diagnosis of pleural TB have major limitations in terms of accuracy, time to diagnosis and drug resistance testing. A test which can diagnose pleural TB and detect resistance would be optimal for rapid diagnosis and treatment without delay. In this background, we looked at the diagnostic utility of Xpert MTB/RIF.

Methods: A prospective observational study was done in a tertiary care hospital in Eastern Nepal. 51 patients with clinico-radiologic suspicion of pleural TB were included. The results of pleural fluid Xpert MTB/RIF were compared with two Composite Reference Standards (CRS). CRS-1 consisted of positive pleural fluid smear, positive culture, positive histology of pleural biopsy and positive sputum results. CRS-2 included patients with CRS-1 and/or patients with high ADA values (>40 U/L) with response to Anti-tubercular treatment at 8 weeks of follow up.

Results: 36 patients were diagnosed as Pleural TB, 9 fulfilled CRS-1, Pleural fluid Xpert MTB/RIF was positive in 5 cases with CRS-1 and 9 cases with CRS-2. The sensitivity, specificity, positive predictive value and negative predictive value with reference to CRS-1 were 55.56%, 88.10%, 50% and 90.24% respectively. Using CRS-2 as reference, sensitivity, specificity, positive predictive value and negative predictive value were 25%, 93.33%, 90% and 34.15% respectively. 2 cases were diagnosed Xpert MTB/RIF Rifampicin Resistant on pleural fluid.

Conclusion: At a programmatic level, due to low sensitivity the Xpert Mtb/Rif test cannot be recommended as initial test of diagnosis in a high prevalence setting whereas a low negative predictive value precludes its use in a low prevalence setting. There are still exceptional circumstances where its use is justified.

DISEASE ACCURACY OF TWO NUCLEIC ACID AMPLIFICATION TESTS FOR RAPID DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSION

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Background: Tuberculous pleural effusion (TPE) occurs in up to 25% of TB patients. Owing to the pauci-bacillary nature of the pleural...
fluid, the diagnosis of TPE is a challenge. Newer diagnostic tools are required for the rapid diagnosis of TPE.

**Aim:** To compare the sensitivity and specificity of two commercially available nucleic acid amplification test Xpert MTB/RIF and Geno type MTBDRplus line probe assay (MTBDRplus) for the rapid diagnosis of TPE.

**Methods:** A prospective cross-sectional study was performed at Aga Khan University Hospital, Karachi, Pakistan from August 2014 to January 2016. Patients with suspected TPE were recruited on the basis of history, exudative lymphocytic nature of effusion and raised adenosine daminase level. Pleural fluid samples were tested for AFB smear, culture, Xpert MTB/RIF and MTBDRplus.

**Results:** We enrolled 99 patients with mean age of 50.4±20.3 years. Effusion size was mild in 18 (18.2%), moderate in 77 (77.8%) and massive in 4 (4.0%). Pleural fluid AFB smear was positive in 1 (1.01%), Xpert MTB/RIF was positive in 10 (10.1%) and MTBDRplus was positive in 6 (6.06%) cases. AFB culture was positive in 14 (14.14%) cases. Considering AFB culture as Gold standard, the sensitivity of Xpert MTB/RIF was found to be 57.14% (95% CI: 28.86 – 82.34%) and specificity was 97.65% (95% CI: 91.76 - 99.71%) and the sensitivity of MTBDRplus was 55.71% (95% CI: 12.76 – 64.86%) and specificity was 96.82% (95% CI: 93.62 - 99.90%). The sensitivity of Xpert MTB/RIF in TPE was significantly higher than MTBDRplus while the specificity was comparable among the two tests.

**Conclusion:** Xpert MTB/RIF has a significantly higher sensitivity for the rapid diagnosis of TPE as compared to MTBDRplus and AFB smear microscopy. Multicentre study with large sample size is needed to further evaluate the effectiveness of this method for the early diagnosis of TPE.

**THE CORRELATION BETWEEN XPERT MTB/RIF LEVEL CATEGORY WITH SPUTUM CULTURE CONVERSION TIME IN DRUG RESISTANT TUBERCULOSIS (TB) PATIENTS**

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**Background and Aims:** Sputum culture conversion is one of the predictors for the success of drug resistant TB treatment. We tried to determine the correlation between Xpert MTB/RIF level category with sputum culture conversion time in drug resistant TB patients.

**Methods:** This was a retrospective cohort study held in Dr. Moewardi hospital from September 2012 until October 2015. We analysed the data using SPSS version 18. The correlation between Xpert MTB/RIF level category with sputum culture conversion time were analysed using Spearman test.

**Results:** We obtained a total of 198 drug resistant TB patients. All of them had pulmonary TB with previous histories of category I anti-TB treatment as the highest cases. The Xpert MTB/RIF level category mostly belonged to low category (43.9%) group. Most of them (59.1%) obtained culture conversion in four to eight weeks after starting treatments. The Spearman test showed no correlation between Xpert MTB/RIF level category with sputum culture conversion time (CI 95%, r = 0.061, p = 0.392).

**Conclusions:** Xpert MTB/RIF level category showed no significant correlation with sputum culture conversion time in drug resistant TB patients statistically.

**AFB SMEAR M.TB ON ADULT PULMONARY TB PATIENTS WITH TYPE 2 DM AND WITHOUT: A CROSS SECTIONAL STUDY IN GENERAL HOSPITAL NORTH JAKARTA INDONESIA**

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**Background and Aims:** According to the Global Tuberculosis Report 2015, Indonesia ranked as second country in the world with the highest number of pulmonary tuberculosis cases. By 2015, the number of pulmonary TB new cases in Indonesia has increased to 330,910 cases of 2014 where 324,539 cases. DM is one of the most important factors that influence the occurrence worsening TB. Now is known that Diabetes Mellitus patients have body’s immune response disorder thereby facilitating M.tuberculosis infection and causing TB.

**Methods:** This research is a comparative study by cross sectional design. The sample in this research are adult pulmonary TB patients at General Hospital Grade C period October 1, 2013 – March 31, 2016 as much as 225 patients.

**Results:** Number of adult pulmonary TB patients were 225 patients. Of the 225 patients, found 81 patients with type 2 DM and 144 patients without type 2 DM. AFB smear results in patients with type 2 DM with smear 3+ was 14 (17.28%), 2+ was 15 (18.52%), 1+ was 15 (18.52%) and negative (−) was 37 (45.68%). AFB smear results in patients without type 2 DM with smear 3+ was 3 (2.08%), 2+ was 6 (4.17%), 1+ was 19 (13.19%), negative (−) was 112 (77.78%) and have no sputum was 4 (2.78%).

**Conclusions:** AFB smear positive found more in adult pulmonary TB patients with type 2 DM compared to TB patient without type 2 DM. It also found statistically significant between type 2 DM with the AFB smear results on adult pulmonary TB patients (p value: < 0.005; OR: 0.210).
ROLE OF CBNAAT IN THE EARLY DETECTION OF RIFAMPICIN RESISTANCE IN RETREATMENT CASES OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

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Background and Aim: India is the highest tuberculosis burden country in the world. The global incidence of multidrug-resistant TB (MDR-TB) is 630,000 cases. India constitutes one tenth of the global burden with 64,000 cases, presently. Though the conventional drug susceptibility testing (DST) is considered the “Gold standard” for the detection of drug-resistant TB, it is time-consuming taking about 6-8 weeks. Cartridge-based nucleic acid amplification test (CBNAAT) not only detects M.tuberculosis but also detects rifampicin resistance in a very short period of 2-3 hours only. We conducted this study to know the usefulness of the test in early detection of rifampicin resistance in retreatment cases of pulmonary and extra pulmonary tuberculosis.

Methods: This study was conducted in the department of TB and respiratory diseases, J.N. Medical college, AMU, Aligarh, India from April 2016 to July 2017. Sputum samples of retreatment cases of pulmonary tuberculosis patients and needle aspirates, fluids and biopsy material, etc. from extra pulmonary sites were subjected to CBNAAT for detection of M. tuberculosis and rifampicin resistance.

Results: A total of 1381 samples taken from retreatment cases of pulmonary and extra pulmonary tuberculosis patients were subjected to CBNAAT. M.tuberculosis was detected in 752 (53.75%) out of 1213 sputum samples of pulmonary tuberculosis patients. Out of these 752 cases, rifampicin resistance was detected in 117 (15.7%) cases. A total of 168 different samples from extra pulmonary sites were examined. Out of these M.tuberculosis was detected in 67 (39.8%) samples and rifampicin resistance was detected in 15 (19.4%) samples.

Conclusion: We found a very high rate of rifampicin resistance, 18-19%, in retreatment cases of tuberculosis. CBNAAT was found to be a extremely useful tool for early detection of rifampicin resistance.

Respiratory Infections (non-tuberculosis) 2

A SINGLE CENTRE, PROSPECTIVE, LONGITUDINAL STUDY OF THE HUMAN RESPIRATORY VIROME AFTER LUNG TRANSPLANTATION

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Background: The pulmonary component of the human respiratory virome (a subset of the human microbiome) is transplanted into the recipient at lung transplantation (LTX). We explored the role of community acquired respiratory viruses (CARV) within the transplanted pulmonary virome.

Methods: Single centre, prospective, longitudinal study of viruses in recipient nasopharyngeal swabs prior to LTX, swabs of explanted lungs, donor lungs prior to implantation and bronchoalveolar lavage (BAL) on post-operative days (POD) 1, 7, 21, 42, 63, 84. Nucleic acids were isolated, followed by RT-qPCR for CARV (human rhinovirus (HRV), respiratory syncytial virus, influenza A and B, parainfluenza virus (PIV) 1, 2, 3, and human metapneumovirus).

Results: 47 consecutive LTX were recruited (bilateral: heart lung: lung+iver = 44:1:2). Average age 45±14 years, mean ±SD (range 20-63) (M±3). Follow up: 185±100 days, range 11-352 with 94% crude survival. Indications: emphysema (n=19), cystic fibrosis (n=9), chronic lung allograft dysfunction (n=7), pulmonary fibrosis (n=7) and other (n=6). Explanted lung swabs were positive for viruses in 14/40 (influenza A=11, B=3, HRV=2) despite recipient vaccination and negative recipient NPS. POD1 BAL showed influenza A (n=11), HRV (n=6) and PIV (n=1). Donor swabs showed influenza (A=1, B=1), and HRV (n=2). Donor transmission of influenza was observed. 40/47 recipients were viral positive in BAL (26/40 on multiple BAL) and viruses persisted for 3-12 weeks. Concurrent surveillance transbronchial biopsies revealed acute cellular rejection Grade A1 (n=12), Grade A2 (n=3) and Grade B1R (n=6) but no relationship with viral detection was observed.

Conclusions: Frequent donor transmission and early acquisition of CARV (particularly Flu A) support the importance of respiratory virome surveillance after LTX to direct acute therapies. While a direct relationship with acute rejection was not detected, ongoing data collection will facilitate analysis of long term clinical outcomes related to the changing dynamics of the pulmonary microbiome after lung transplantation.

THE FIRST CASE OF COMMUNITY-ACQUIRED INVASIVE PNEUMONIA DUE TO K2 SEROTYPE HYPERVIRULENT KLEBSIELLA PNEUMONIAE IN AN ADULT PATIENT

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Background and Aims: The incidence of hypervirulent Klebsiella pneumoniae [hvKP] infection has been increasing particularly in Asian countries. It causes severe and metastatic infections such as pyogenic liver abscesses, bacteremia, meningitis, osteomyelitis, and endophthalmitis even in healthy individuals; however, pneumonia due to this strain is not common.

Methods: A 79-year-old Japanese woman with dementia, primary alderosteronism, and bed-ridden status after cerebellar hemorrhage, was admitted to our hospital complaining of three days of fever, productive
cough, and respiratory distress. On arrival, her vital signs indicated sepsis: blood pressure 99/69 mmHg, heart rate 130 beats/min, and respiratory rates 25 breaths/min. Physical examination revealed holo-crackle on auscultation. Computed tomography revealed lobar pneumonia and multiple infiltration particularly in lower lobes. Ampicillin/sulbactam (ABPC/SBT) was started on the diagnosis of aspiration pneumonia immediately. However, in the following day, both sputum and two sets of blood culture illustrated the hypermucoviscous phenotype. Colonies on sheep blood agar illustrated the hypermucoviscous and a string test showed over 5 mm in length, consistent with hvKP. Genetic analysis identified this strain as K2 serotype and having rmpA gene. ABPC/SBT was switched to ceftriaxone and the patient was recovered promptly without recurrence.

Results: Although previous investigations reported the emergence of hospital-acquired or ventilator-associated pneumonia caused by hvKP, there was only one report on community-acquired pneumonia due to hvKP in China. Difference between this previous case and the present case are summarized in Table 1, and characteristics of those strains are completely different.

Conclusion: We presented the first identified case of community-acquired pneumonia due to serotype K2 hvKP. Although only a small number of pneumonia caused by hvKP has been reported, clinicians need to be aware of the emerging of this strain, as it has many virulence factors in addition to hypermucoviscous phenotype.

A0074

CLINICAL CHARACTERISTICS OF CORYNEBACTERIUM PNEUMONIA PATIENTS: A RETROSPECTIVE, SINGLE CENTER INVESTIGATION

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Background and Aims: Cases of Corynebacterium pneumonia (CP) were rarely reported, and risk factor and prognosis of CP were still unknown. Our aim is to elucidate the clinical features and outcomes of CP.

Methods: This is a hospital-based retrospective study at Kameda Medical Center, a tertiary hospital with 917 beds in Chiba, Japan. We identified pneumonia patients with Corynebacterium sp. dominantly detected in sputum whose smear was Geckler’s classification number 3 or more from October 2013 to September 2016. We collected patients’ characteristics, clinical course and mortality, retrospectively.

Results: 17 cases of CP were eligible. The mean age was 73 years and 14 cases were male. The mean performance status (PS) was 2. The comorbidity was as followed: cerebrovascular disorder (CVD) 7 cases, malignancy 7 cases, 5 cases and 12 cases were each community onset pneumonia and hospital-acquired pneumonia (HAP) including 4 cases of ventilator-associated pneumonia and 5 cases of aspiration pneumonia. C. striatum (n=11) was the most frequent, and the rest 6 strains were other three species. 30-day mortality was 47% (8 cases). Penicillin resistant strains were 12 (71%). All strains were vancomycin (VCM) susceptible, and cases who underwent VCM combination therapy was 9 and 30-day mortality was 56% (5 cases). Those who did not underwent VCM combination therapy was 8 and 30-day mortality was 38% (3 cases).

Conclusions: CP patient was characterized by elderly, male, poor PS, past medical history of CVD, HAP, high mortality, and high prevalence of penicillin resistance. Although VCM showed susceptibility, antibiotic combination therapy containing VCM could not reduce 30-day mortality.

NODULAR BRONCHIECTASIS WITH POSITIVE RESULTS FOR SERUM ANTIBODY TO MYCOBACTERIUM AVIUM COMPLEX, WITHOUT AN EARLY DEFINITE DIAGNOSIS OF PULMONARY MYCOBACTERIUM-AVIUM-COMPLEX DISEASE

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Background: Nontuberculous mycobacterial pulmonary diseases have been increasing in many countries, and in Japan, 90% of them are caused by the Mycobacterium avium complex (MAC). In Japan, measurement of the serum IgA antibody to the MAC-specific glycopeptidolipid core antigen has been routinely used to diagnose MAC pulmonary disease (MAC-PD) rapidly, and has been reported to have moderate sensitivity (50-85%) and high specificity (95-100%). However, in clinical practice, it is difficult to establish a definitive diagnosis of MAC-PD, even in positive cases.

Aims: This retrospective study investigated the final diagnosis and prognosis of patients suspected of having MAC-PD.

Methods: Of the patients who were referred to our department between December 2013 and December 2016 and were HIV-negative and diagnosed with bronchiectasis via chest computed tomography (CT), 301 tested positive for the serum glycopeptidolipid antibody. Of these, 146 were diagnosed with MAC-PD within two months of the initial visit. The remaining undiagnosed 155 patients were selected for review.

Results: Thirty-one patients were male and 124 were female; the mean age was 69 years. In most cases, high-resolution CT scans showed nodular bronchiectatic changes in the right middle lobe and lingula, which were consistent with MAC-PD. There were no cystic fibrosis cases. During the average nine-month observation period, 12 patients were definitively diagnosed with MAC-PD and 34 patients were diagnosed with “probable” MAC-PD, of which only one sputum culture yielded MAC. Five patients were diagnosed with other nontuberculous Mycobacterium diseases. The disease etiology could not be determined in the remaining 104 patients. There were no deaths related to pulmonary lesions, and serial chest radiographs revealed most pulmonary lesions were stable.

Conclusions: If an early diagnosis of MAC-PD was not made in patients with nodular bronchiectatic pulmonary diseases who tested positive for serum MAC antibodies, later diagnosis was difficult, but short-term prognosis was good.

PROGNOSTIC VALUE OF A B-TYPE NATRIURETIC PEPTIDE IN PATIENTS WITH PNEUMONIA: A PROSPECTIVE COHORT STUDY

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Background and Aim: Pneumonia is a major medical problem and is the leading infectious cause of death in developed countries, especially among the elderly. To date, no systematic assessment has used B-type natriuretic peptide (BNP) levels as a prognostic marker for pneumonia.
We validated the usefulness of BNP as a prognostic marker for pneumonia.

Methods: We conducted a prospective cohort study at Kanazawa Medical University Himi Municipal Hospital. We enrolled patients admitted between 1 January 2012 and 31 October 2016 with a diagnosis of community-acquired pneumonia (CAP), non-CAP, aspiration pneumonia (AP) and healthcare-associated pneumonia (HCAP) whose BNP levels had been determined within the first 24 hours of admission. Data on age, sex, outcome (dead or alive), and measured levels of BNP, C-reactive protein (CRP), creatinine and fasting plasma glucose were collected from all included patients. We applied univariate analysis to compare these data and outcome to all included patients, CAP, and non-CAP.

Results: A total of 543 patients were enrolled in this study. The mean age of all patients (328 males) was 82.5 ± 9.8 years. Of 543, 205 were diagnosed with CAP and 338 with non-CAP. Age and measured levels of BNP and creatinine were significantly higher in non-survivors than in survivors for all included patients (p < 0.01, < 0.001, < 0.001, respectively). A similar situation was found in age and measured levels of BNP, CRP, creatinine, and fasting plasma glucose for CAP (p < 0.02, < 0.001, 0.002, < 0.001, < 0.001, respectively) and in measured levels of BNP (p < 0.001) for non-CAP. No significant difference was observed with respect to the other markers.

Conclusion: BNP levels may be a useful single prognostic marker for CAP and non-CAP. As such, systematic screening of BNP in hospitalised elderly patients with pneumonia may help identify those with a poor prognosis.

PROGNOSIS FACTORS OF PNEUMOCYSTIS JIROVECII PNEUMONIA IN NON-HIV INFECTED PATIENTS

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Background and Aim: Pneumocystis jirovecii pneumonia (PCP) is a life-threatening disease. The incidence of PCP has been increasing in recent 10 years among non-HIV infected population. We aim to identify the prognostic factors of non-HIV infected patients with PCP.

Methods: The PCP was diagnosed by clinical symptoms, radiographic changes and positive quantitative PCR (qPCR) results at National Taiwan University Hospital from October 2015 to October 2016. The cycle threshold (Ct) values obtained by qPCR were used to semi-quantitate the fungal burden. Clinical characteristics, management, outcomes and risk factors for mortality of these patients with PCP were evaluated.

Results: During the study period, 109 patients with PCP were included in this study. The common underlying diseases were hematological malignancy (26.6%) and HIV infection (22.9%). The non-HIV-infected patients were older (P < 0.001), had lower fungal burden (P < 0.002), longer duration between initial radiographic presentation and initiation of anti-PCP treatment (P < 0.001), higher rate of respiratory failure (P < 0.001) and 60-day mortality (P < 0.006). Among non-HIV-infected patients with PCP, multivariate analysis revealed lymphopenia (odds ratio, OR = 3.24, 95% confidence interval, CI = 1.07-9.79; P = 0.037), adjunctive steroid use (OR = 6.23, 95% CI = 1.17-33.14; P = 0.032), pneumothorax (OR = 10.68, 95% CI = 1.00-113.93; P = 0.050) were related to higher 60-day mortality.

Conclusion: Lymphopenia, adjunctive steroid use and pneumothorax were independent risk factors of poor prognosis in non-HIV infected patients with PCP.

IMPACT OF ADENO-TONSILLECTOMY ON NEURO-COGNITIVE AND BEHAVIOURAL FUNCTIONS IN CHILDREN WITH SLEEP DISORDERED BREATHING

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Background and Aims: Adeno-tonsillectomy (AT) is the treatment of choice for paediatric sleep-disordered breathing (SDB). However, the effect of AT on neuro-cognitive and behavioural (NCB) abnormalities in these children is not clear. The aim was to evaluate NCB functions in a cohort of children with SDB using validated instruments, before and after AT.

Methods: We enrolled children (6-18 years) who underwent AT for SDB diagnosed after overnight polysomnography (PSG) over a period of one year. NCB evaluation using Wechsler Intelligence Scale (WIS) for Indian Children and The Conners 3-Parent version of the Parent Conner Scale (PCS) was done in all children prior to and after 6 months of AT. PSG was repeated after 3 months of AT.

Results: A total of 33 children underwent AT for SDB (males=26;7, mean age 9.0 ± 2.97 years). NCB evaluation, before and after AT, could be completed in 31 children. There was a significant improvement in mean apnea hypopnoea index (AHI) after 3 months of AT (7.88 ± 7.91 vs 2.03 ± 3.10, p < 0.001). Obstructive sleep apnoea (AHI≥5) was seen in 33 (100%) children preoperatively and 15 (46.9%) postoperatively (p < 0.001). There was a significant improvement in mean Verbal-IQ (92.57 ± 12.73 vs 97.40 ± 12.46, p < 0.001), Performance-IQ (97.83 ± 13.03 vs 105.38 ± 13.80, p < 0.001) and Total-IQ (95.19 ± 11.85 vs 101.42 ± 11.86, p < 0.001) MIS scores after 6 months of surgery. In PCS, there was a significant improvement in inattention (62.97 ± 11.70 vs 51.26 ± 18.53, p < 0.001) and learning problem (64.61 ± 18.76 vs 51.32 ± 17.70, p < 0.01) scores after 6 months of AT. However, the number of children in clinical range for any NCB dysfunction in either of the scales did not change significantly after AT.

Conclusions: AT has a favourable impact on sleep parameters and NCB functions in children with SDB. However the improvement is incomplete and most of these children continue to have residual dysfunction in sleep and NCB parameters even after 6 months of surgery.

LONGITUDINAL ASSESSMENT OF SLEEP ABNORMALITIES IN PATIENTS WITH SEVERE CYSTIC FIBROSIS

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Background and Aim: A number of devices, including overnight oximetry and polysomnography (PSG), can be used to assess nocturnal respiration, sleep and other respiratory events. We have recently used a novel non-invasive device (the Sonomat®), which can also assess adventitial sounds. This study compares the changes in PSG and Sonomat recordings in adults with cystic fibrosis (CF) who have clinically deteriorated over a 2 year period.

Respiratory Neurobiology and Sleep

AO077

AO078

Impact of Adeno-Tonsillectomy on Neuro-Cognitive and Behavioural Functions in Children with Sleep Disordered Breathing

AO079

Longitudinal Assessment of Sleep Abnormalities in Patients with Severe Cystic Fibrosis
Methods: Overnight studies, using PSG and the Sonomat, were performed in a cross-sectional study of 40 patients with CF. Following clinical deterioration, 8 subjects underwent repeat studies after 1-2 years. Parameters assessed using the PSG included: sleep efficiency, arousal index (AI), respiratory disturbance index (RDI), mean nocturnal oxygen saturation (SpO2), nadir SpO2 and mean oxygen desaturation. Using the Sonomat, recorded sounds were classified as coughs or crackles based on the spectrographic variations in frequencies, intensity and timing of the sound during the respiratory cycle. Total duration (as % total sleep time) of these sounds was used to quantify recorded sounds.

Results: Eight subjects (2 male; aged 29.5 ± 5.4 years (mean±SD); FEV1 of 45.0 ± 11.9 % predicted) were studied twice. There was a statistically significant increase in mean oxygen desaturation (baseline to second study) from 1.4 ± 1.9% to 4.0 ± 2.1% (p=0.01). There was a trend to reduced minimum SpO2 between the baseline and second study (89.0 ± 4.6% versus 82.8 ± 8.9%; p=0.065). There was no statistically significant difference in any of the other PSG parameters. The Sonomat demonstrated that crackles duration increased from 21.2 ± 15.4% at baseline to 78.6 ± 15.5% at the second study (p=0.001). However, cough duration did not change between the two studies.

Conclusions: Using the Sonomat to analyse recorded sounds, the significant increase in the presence of crackles was consistent in all subjects following clinical deterioration. As expected with deteriorating lung function, oxygen desaturation worsened over time in subjects with severe CF lung disease. However, there was no change in the other PSG markers of sleep quality despite the deterioration in lung function. We speculate that sequential use of the Sonomat to assess sleeping adventitious sounds may be useful to detect deteriorating lung function.

EVIDENCE OF ASSOCIATION BETWEEN GABBR2 GENE POLYMORPHISM AND OBSTRUCTIVE SLEEP APNEA SYNDROME IN ASTHMA PATIENTS
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Background and Aim: Existing data suggest possible involvement of gamma-aminobutyric acid (GABA)-ergic system in the pathogenesis of obstructive sleep apnea (OSA). Particularly, baclofen – selective agonist of GABAB receptors was shown to increase the rate of apnea-hypopnea events during sleep. In addition, GABBR1 gene polymorphisms were found to be associated with OSA. The aim of the present study was to investigate the effect of GABBR1 and GABBR2 polymorphisms on the predisposition to OSA in asthma patients.

Methods: The study enrolled 104 patients with persistent mild-to-moderate asthma. OSA was assessed by overnight cardiorespiratory monitoring. GABBR1 rs1805056 (Ala20Val) and rs2267633 (UTR-3 c.-4797C>T) and GABBR2 rs10985765 (Thr869Ala) and rs35400353 (UTR-5 c.-161_-159delCGC) polymorphisms were genotyped by PCR-RFLP analysis.

Results: OSA was observed in 34.6% of asthma patients. We did not find any association of OSA with GABBR1 gene polymorphisms. However, GABBR2 rs35400353 polymorphism significantly influenced OSA rate in asthma patients. Homozygous deletion genotype (DD) occurred more frequently in the group with OSA (87.9% vs. 62%) while heterozygous (ID) genotype was more common among patients without OSA (38% vs. 12.1%), p=0.007. This effect remained significant (OR 5.6, 95%CI (1.6; 19.8)) after adjustment for age and gender covariates, which also had a notable influence on the risk of OSA. Homozygous genotype without deletions (II) was not observed in our sample. Apnea-hypopnea index was higher in DD than in ID genotype carriers (3.2 (1.4; 5.4) vs. 2.1 (0.6; 4.3), p=0.014). Furthermore, rs35400353 influenced OSA severity – DD genotype was found in 84% of mild OSA and in 100% of moderate and severe OSA (p=0.04). GABBR2 rs10985765 polymorphism had some tendency to be linked with OSA (p<0.04 for alleles), yet most associations were insignificant.

Conclusion: rs35400353 polymorphism in GABBR2 appears to influence the risk of OSA in asthma patients. Further study in larger sample size is needed to replicate this finding.

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PRODROMAL OBESITY HYPVENTILATION SYNDROME - EARLY DETECTION OF HYPVENTILATION IN THE VERY OBESE POPULATION
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Background and Aims: Prodromal obesity hypoventilation syndrome (pOHS) refers to the presence of nocturnal hypoventilation (NH) without awake hypercapnia. This study evaluates the characteristics and prevalence of pOHS in the very obese population and further investigates simple measures to detect hypoventilation prior to the development of awake hypercapnia.

Methods: 89 consecutive patients with a BMI >40 kg/m2 without known lung or neuromuscular disease were recruited from local sleep and obesity clinics. Anthropometrics, spirometry, daytime pulse oximetry, supine and upright arterialised capillary blood gases (cABG) and slow vital capacity obtained in random order, as well as in-lab polysomnography and nocturnal transcutaneous carbon dioxide monitoring (TcCO2) were performed on all patients.

Results: 21 patients (24%) were diagnosed with pOHS, 54 patients (61%) with obstructive sleep apnoea (OSA) without hypoventilation, 2 patients (<1%) without sleep disordered breathing and 12 patients (13%) with OHS. The mean BMI, age and gender (%male) of the overall cohort were 54 kg/m2, 49 years and 37% respectively. Compared with OSA, patients with hypoventilation (OHS + pOHS) demonstrated significant differences in daytime pulse oximetry (SpO2), slow and forced vital capacities, anthropometrics and body mass index (BMI). The pOHS group however only showed significant differences in neck (pOHS: 51 v OSA: 47cm; p=0.01), sagittal height (31 v 28cm; p=0.01), BMI (57 v 51 kg/m2; p=0.008) and SpO2 (94 v 96%, p=0.007), compared with OSA. Combining SpO2 and BMI yielded an area under the ROC curve of 0.8. Only patients with hypoventilation, including the pOHS group, showed a rise in cABG carbon dioxide levels (PaCO2) in a supine v upright position (pOHS: 44 v 41mmHg; p=0.001).

Conclusions: Prodromal OHS can be recognised early with simple measures in an outpatient setting particularly with BMI and SpO2. A higher supine versus upright PaCO2 is also helpful.
EFFECTS OF HIGH FLOW OXYGEN THERAPY ON OXYGEN SATURATION INDEX IN PATIENTS WITH ACUTE ISCHEMIC STROKE
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Background and Aims: Hypoxemia is associated with neurological deterioration in stroke patients. Severity of stroke may affect the benefit of oxygen supplementation. Abnormal breathing patterns among stroke patients increase the risk of hypoxemia. High flow nasal cannula (HFNC) has benefits of positive airway pressure throughout the breathing cycle. We aimed to assess the effect of HFNC on oxygen desaturation index (ODI) and neurological outcomes in stroke patients with moderate and severe severities.

Methods: We conducted a single-center, prospective, RCT. The patients with acute ischemic stroke admitted in a stroke unit within 72 hours after the onset were enrolled. Inclusion criteria were stroke patients with moderate and severe severities and low risk of prior OSA. The eligible patients were randomly assigned to high flow, low flow and no oxygen groups. The primary outcome was ODI in the first day of treatment, while secondary outcomes were 1) numbers of patients with oxygen desaturation, and 2) NIHSS change at seventh day of admission.

Results: Form a total of 30 patients, 10 patients were randomized into each group. The median ODI was 6.2 in the high flow oxygen group, 1.1 in the low flow oxygen group, and 5.0 in the no oxygen group (p=0.002), but there was no difference in numbers of patients with oxygen desaturation. Moreover, the NIHSS change at 7 days after randomization were 1.5, 3 and -0.5 in the high flow oxygen, low flow oxygen and no oxygen group respectively (p=0.011). Furthermore, the low flow oxygen group had the highest proportion of the patients with clinically significant neurological recovery.

Conclusion: In acute ischemic stroke patients with moderate and severe severities, low flow oxygen therapy significantly reduced ODI and improved neurological recovery compared to high flow oxygen therapy and no oxygen. Benefit effect of oxygen supplementation in acute stroke patients should be confirmed in further study.

ASSESSMENT OF SOFT PALATE MUSCLE FATIGUE AND ITS EFFECT ON VELOPHARYNGEAL UPPER AIRWAY DYNAMICS
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Background and Aims: Velopharynx is the most collapsible segment of the upper airway (UA), thus soft palate muscles are crucial in the maintenance of UA patency. The aim of this study was to investigate the endurance properties of the soft palate muscles using a dedicated fatigue protocol, as well as to quantify the effects of such protocol on velopharyngeal UA dynamic properties in OSA patient and control subjects.

Methods: 5 OSA (AHI ≥ 15 /h) and 6 control (AHI < 15 /h) subjects were recruited to perform a soft palate fatiguing protocol (until exhausted), in which maximal cheek-bulging manoeuvres were performed for 5 s every 10 s to generate the previously determined maximal intra-oral positive pressure while keeping the jaw opened with a mouth piece, until the peak pressure cannot reach 85% of baseline maximal pressure for 2 consecutive trials. UA dynamic properties were measured by inspiratory phrenic nerve magnetic stimulation (PNMS) performed before, immediately and every 3 minutes after the fatigue protocol for 30 minutes' recovery time. Inspiratory UA closing pressure was estimated by modeling the flow/velopharyngeal pressure relationship in response to phrenic twitches.

Results: There was no significant difference in endurance time and muscle total work for the fatiguing trial between the 2 groups. Overall, the PNMS-induced maximal instantaneous airflow was not significantly different before and after the fatiguing trial. Linear velopharyngeal resistance significantly increased 3 mins after the fatigue trial when compared with the baseline (5.61±3.83 cmH2O l−1 s−1 vs. 2.23±1.34 cmH2O l−1 s−1, p=0.01), and didn’t recover within 30 minutes. In OSA group, Pcrit measured after fatigue tended to be higher than the baseline (-3.9±2.1 cm H2O vs. -6.8±2.5 cm H2O, p=0.08). This is not observed in controls.

Conclusions: The cheek-bulging manoeuvre can induce soft palate muscle fatigue and alters velopharyngeal mechanical properties. Such effects may be more prominent in OSA patients.
ACCEPTANCE OF UPPER AIRWAY MUSCLE TRAINING FOR TREATMENT BY OBSTRUCTIVE SLEEP APNEA: RESULTS OF A PROSPECTIVE SURVEY
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Background and Aims: Obstructive sleep apnea (OSA) is associated with a variety of adverse health outcomes. Upper airway muscle training (UAMT) represents a novel, effective treatment approach for OSA. This study was aimed at investigating the attitude towards UAMT and to evaluate to what extent physiological and sociodemographic factors may influence them.

Methods: 158 consecutive newly diagnosed OSA patients were recruited to complete a self-administered questionnaire, including assessment of their interest towards UAMT, anticipated ability to complete such therapy, as well as information about factors that could influence these attitudes. Socio-demographic information and sleep recording data were also obtained.

Results: The majority of patients were interested in such program (82.9%) and mentioned their anticipated ability to complete it 1 hour/day for 1 month (72.1%), especially if applied later only 2-3 times/week (82.9%). 55.0% of them indicated that requirements of training schedule and duration might influence their choice. Patients with low Socioeconomic status (SES) or female gender were more prone to complete such program (p<0.05). Multivariate analysis revealed that age (OR: 1.04, 95% CI: 1.01-1.07; P=0.02) was an independent determinant for interest to complete it, along with a preference over conventional therapies. Attitudes towards such therapy are sensitive to factors such as gender, age, severity of OSA and SES level.

Respiratory Infections (non-tuberculosis) 3

ANALYSIS OF MUTATION ASSOCIATED WITH MACROLIDE RESISTANCE IN BORDETELLA PERTUSSIS IN OKINAWA, JAPAN
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Background and Aims: The first resistant strain of Bordetella pertussis to erythromycin was reported in US in 1994. After that, several countries such as China, France, and USA have reported some cases of macrolide-resistant B. pertussis infections. All of these studies have shown that target site modification in B. pertussis such as transition mutation at position 2047 (AtoG) of Sanger Center sequence of B. pertussis 23S rRNA gene (binding site of macrolide in bacteria) was the only mechanism to develop resistance against macrolide. In this study, we aimed to identify mutational change at that position of B. pertussis isolates to evaluate the macrolide resistant strain of Bordetella pertussis in Okinawa.

THE IMPACT OF CIGARETTE SMOKE EXPOSURE ON LUNG FIBROBLASTIC RESPONSE AFTER INFLUENZA PNEUMONIA
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Methods: From 2012 to 2017 February, 11 nasopharyngeal swab samples collected prospectively from pertussis suspected patients were diagnosed as B. pertussis positive samples through PCR using Seeplex® pneumobacter ACE detection kit (Seegene, Seoul, Korea). Subsequently, polymerase chain reaction primers 1970U and 2408L were used to amplify a region of 23S ribosomal RNA gene to look for mutation. After amplification, 521 bp PCR product generated in 9 samples were then subjected to be sequenced to detect A to G transition mutation at position 2047 associated with macrolide resistance in B. pertussis.

Results: In comparing to the GenBank sequences of the B. pertussis reference strain Tohama (accession number N68332), no mutation at macrolid binding site (A2047G) was detected in any strains.

Conclusion: Although no evidence of mutation was found in the strains tested from Okinawa, monitoring of antimicrobial resistance is necessary to evaluate the individual treatment failure.

MACROLIDES PROTECT AGAINST PSEUDOMONAS AERUGINOSA INFECTION VIA INHIBITION OF INFLAMMASOMES
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Background and Aims: Macrolides antibiotics have been effectively used in many chronic diseases, especially with Pseudomonas aeruginosa (P. aeruginosa) infection. The mechanisms underlying the therapeutic effects of macrolides in these diseases remain poorly understood.

Methods: We established a mouse model of chronic lung infection using P. aeruginosa agar-beads, with azithromycin treatment or placebo. Lung injury, bacterial clearance and inflammasome-related proteins were measured. In vitro, the inflammasomes activation induced by flagellin or ATP were assessed in LPS-primed macrophages with or without macrolides treatment. Plasma IL-18 levels were determined from patients who were diagnosed with bronchiectasis isolated with or without P. aeruginosa and treated with azithromycin for three to five days.

Results: Azithromycin treatment enhanced bacterial clearance and attenuated lung injury in mice chronically infected with P. aeruginosa, which resulted from the inhibition of caspase-1-dependent IL-1β and IL-18 secretion. In vitro, azithromycin and erythromycin inhibited NLRC4 and NLRP3 inflammasomes activation. Plasma IL-18 levels were higher in bronchiectasis patients with P. aeruginosa isolation compared with healthy controls. Azithromycin administration markedly decreased IL-18 secretion in bronchiectasis patients.

Conclusions: The results of this study reveal that azithromycin and erythromycin exert a novel anti-inflammatory effect by attenuating inflammasomes activation, which suggests potential treatment options for inflammasome-related diseases.
Background and Aim: Influenza is one of the major global health problems. Pneumonia secondary to influenza is the major cause of mortality from this. During the resolution of pneumonia, loss of lung function combined with fibrotic change can happen, however the mechanism is still unclear. Furthermore, little is known about the effect of smoking on influenza pneumonia. In this study, we evaluated the impact of smoke exposure on the pulmonary fibroblastic response after influenza infection.

Methods: Male 10-11 weeks C57BL/6J mice were used for experiments. After 2 weeks of exposure to smoking (smoking group) or air (non-smoking group), mice were infected with H1N1 in bronchoalveolar fluid (BAL). Primary fibroblasts were isolated from the lung of mice.

Results: The amount of collagen in right lung increased after influenza infection, however the amount between the smoking and non-smoking group were not different up to 15 days. Interestingly, collagen increased more in the smoking group, causing significant higher amount in compared to the non-smoking group on 30 days after infection (465.8 ± 24.01 ug vs. 295.4 ± 23.4, P = 0.036). Mean linear intercepts and lung volume were also increased in the smoking group compared to non-smoking group. Active TGFβ1 levels in the BAL fluid increased in both groups after infection. The level was greater in non-smoking group at an early phase (day 2), but the level was greater in smoking mice at a later phase (day 24). In ex-vivo model, fibroblasts isolated from the smoking group infected with influenza showed rapid proliferation with increased expression of various growth factors and stress fibers.

Conclusion: Smoking changes the fibroblastic process after influenza infection. It induced more fibrosis with a delayed increase in TGFβ1 and transformed characteristics of fibroblast.
CLINICAL INVESTIGATION FOR THE EFFICACY OF PULSE OXI-CAPNOMETER®-CAPNO-EYE® IN RESPIRATORY FAILURE PATIENTS—COMPARISON BETWEEN PACO₂, PCO₂, PTCCO₂ AND ETCO₂

SHOTA FUJIMOTO¹, MANABU SUZUKI¹, RITSU IBUSUKI¹, KENTARO TAMURA¹, SACHI MATSUBAYASHI¹, NAOKO NAGANO¹, YOSHIE TSUJIMOTO¹, TAMAKI KAKUWA¹, TOMOYUKI SUZUKI¹, KEITA SAKAMOTO¹, AYAKO SHIOZAWA¹, KONOMI KOBAYASHI¹, SHOTA YAMAMOTO¹, ERIKO MIYAWAKI¹, MASAO HASHIMOTO¹, SATORU ISHIHITA², ERIKO MORINO², JIN TAKASAKI², GO NAKA², TERUHIKO TSUJIMOTO², TAMAKI KAKUWA², TOMOYUKI SUZUKI², KEITA HARUHITO SUGIYAMA²

1Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, 2Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

AO091

Background and Aim: We report our experience of utilizing a novel pulse oximeter-capnometer “Capno-Eye®,” which enables measurement of end tidal carbon dioxide (EtCO₂) and transcutaneous pulse oximetry oxygen saturation at patients’ bed side. It is an instrument which can measure EtCO₂ non-invasively. Subjects would hold mouthpiece in their mouth and breathe quietly for six times. Evaluation of hypercapnia and hypoxemia is essential when we treat patients suffering from respiratory diseases, especially in patients with hypercapnic respiratory failure. Therefore, arterial blood sampling would be required, sometimes repeatedly, however which is an invasive medical procedure.

Methods: We recruited the respiratory failure patients and measured EICO₂ using by Capno-Eye®. At the same time, we measured partial pressure of arterial carbon dioxide (PaCO₂), partial pressure of venous carbon dioxide (PvCO₂) and percutaneous carbon dioxide partial pressure (PtcCO₂) by using TCM/TOSCA®. After then, we analyzed relationships among them. We collected a total of 60 samples. We had 30 cases each for type 1 and type 2 respiratory failure and measured data were compared between two groups respectively.

Results: Thirty patients of type 1 and 18 patients of type 2 participated this study. Some patients of type 2 were measured more than once. A significant relationship was found between PaCO₂ and EICO₂ and between PaCO₂ and PtcCO₂. The correlation coefficients were statistically analyzed by using Pearson’s product-moment correlation coefficient. PaCO₂ and EICO₂ were highly correlated (correlation coefficient: 0.886, 95% CI 0.815 - 0.931, p < 0.001). PaCO₂ and PtcCO₂ were also correlated (correlation coefficient: 0.91, 95% CI 0.853 - 0.945, p < 0.001).

Conclusion: “Capno-Eye®” is an easy-to-use and non-invasive device. Although TOSCA® showed more accuracy than Capno-Eye®, it needs high cost and more time and labor. These results suggested “Capno-Eye®” might be useful in daily medical practice.

OBESITY IS AN INDEPENDENT RISK FACTOR FOR OBSTRUCTIVE SLEEP APNEA IN CHILDREN

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AO092

Aim: To inspect into the risk factors and their correlation of obstructive sleep apnea(OSA) in children.

Method: 451 children aged from 12 to 15 in People’s Hospital of Dong-guan city and Nanfang Hospital of Southern Medical University from June 2013 to December 2013 were involved and divided into OSA group and control group according to International standard of OSAHS children. All of them performed night-time polysomnography (PSG) monitoring; moreover, other related data was recorded, including body mass, BMI, stature, neck circumference, neck length, inherited conditions, apnea-hypopnea index(AHI), the number of snoring and the proportion of limb spasms.

Result: In this study, 451 children, 181 (40.1%) girls and 370 (59.9%) boys, divided into OSAHS group (n = 86), control group (n = 365), aged (13.67 ± 0.60) years. The proportion of obesity (26.7% vs. 3.6%, P < 0.05), the average body mass, BMI, stature, AHI, the proportion of snoring and limb spasm and neck circumference-to-neck length ratio were significantly higher in OSA group than in controls. There was a significant correlation between AHI and BMI (r = 0.519, P < 0.001), snoring, neck circumference, neck length and neck circumference (r = 0.442, P < 0.001) and neck length. In the subgroup study for different degree of obesity, the correlations were all significant, obesity (r = 0.408, P < 0.001), overweight (r = 0.462, P < 0.001). Multivariate logistic regression analysis showed that obesity, neck circumference and the number of snoring were the independent risk factors for OSA in children, with the highest risk factor for obesity (P <0.001, OR = 3.778, 95% CI = 1.618 - 8.822).

Conclusion: The independent risk factors for OSA in children includes obesity, the number of snoring and neck circumference and the severity of obesity is significantly related to the severity of OSA in children.
occurred in 28.2% of subjects at median of 11 months after treatment completion. None of the IgG4-RLD had mortality. 

**Conclusion:** Most of IgG4-RLD patients showed favorable outcome of treatment, although relapse was frequent.

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**AO095**

**SIMPLE PLEURAL MANOMETRY USING EXISTING PLEURAL DRAINAGE SYSTEM: EXPERIENCE OF TWO CASES OF PLEURAL EFFUSIONS WITH POST-DRAINAGE UNEXPANDABLE LUNG AND PNEUMOTHORAX EX VACUO**

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**Background and Aim:** Pleural pressure (PP) is rarely measured due to limited access to specialised measurement equipment. Although the clinical role of pleural manometry remains to be defined, it allows objective diagnosis of unexpandable lung. We aim to describe a simple pleural manometry using existing pleural drainage system in two cases of post-drainage unexpandable lung and pneumothorax ex vacuo.

**Methods:** Pleural catheter (PC) was connected to two 3-way stopcocks, existing drainage tube arranged in ‘U’ shape (with sterile water column as a manometer) and a Redax 2-compartment drainage bottle in series. PP is estimated by measuring the displacement of the water column in centimetre. The PP was recorded at baseline and following 50mLs pleural aspiration (see Figure 1). PP was recorded at baseline and following 50mLs pleural aspiration (see Figure 1).

**Results:** The patients were: 1) a 71-year-old man with malignant and parapneumonic effusion and 2) a 59-year-old man with bilateral chronic pleural effusions due to possible uraemic pleuritis and hypoalbuminaemia. The patients had PC drainage for 7 and 13 days respectively with little improvement in breathlessness. In both cases, post-drainage chest X-rays showed unexpanded lung with pneumothorax. PP was progressively more negative relative to cumulative volume of air aspirated. When PP dropped to <-20 cmH2O with <300mLs total volume aspirated in both cases, the procedures were terminated and PP equalised to atmospheric pressure. Calculated pleural elastance was 70 cmH2O/L and 76 cmH2O/L for the patients respectively. PCs were subsequently removed. The patients were asymptomatic throughout PP measurement.

**Conclusion:** PP can easily be measured in pneumothorax ex vacuo using existing pleural drainage system. Pleural manometry confirmed unexpandable lung, absence of air leak and facilitated clinical decision making. In these patients, pleural elastance is elevated and large volume aspiration should be avoided as it is potentially unsafe.

**Figure 1. Simple bedside pleural manometry set up and measurement.**

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**RELATIONSHIP OF PLEURAL FLUID PH AND GLUCOSE: A MULTI-CENTRE STUDY OF 2971 CASES**

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**Background:** Pleural effusion has over 60 differential diagnoses. Pleural fluid pH and glucose levels are both reduced in inflammatory and/or metabolically active conditions. Measurements of pH are susceptible to collection methods whereas pleural fluid glucose concentrations may be influenced by corresponding serum glucose levels. Whether pleural fluid pH and glucose correlate with each other and provide duplicate information or contribute independent knowledge is unclear.

**Aims:** To investigate the relationships between pleural fluid pH and glucose levels in unselected pleural effusions, incidences and circumstances of discordance in their levels.

**Methods:** Pleural fluid pH and glucose data were collated from three centres in Spain, UK and Australia. Polynomial regression was conducted to assess the relationship between pH and glucose. The concordance between pH and glucose for varying cut-off levels was also demonstrated.

**Results:** Pleural fluid samples (n=2971) were separated into four categories: malignant (n=1045), bacterial infection (n=1133), TB pleuritis (n=544) and other benign effusions (n=1133) based on clinical diagnoses. The median pH was 7.43 (range 5.04-8.50) and glucose levels was 5.99 (range 0-29.4) mmol/L. A predictive curve of pH against glucose was developed (Figure 1). Most (91.6%; n=2720) of the samples were concordant in pH and glucose levels (i.e. both below or above the cutoffs of 7.20 and 3.3mmol/L respectively). Concordance was the lowest in the TB group (80.7%) and highest in the other benign pleuritis group (98.2%). Patients with a low pH but high glucose (n=99) were more likely to have bacterial pleural infection and 31% were diabetic (vs 8% of the group with low glucose and high pH, p<0.001).

**Conclusion:** Pleural fluid pH and glucose correlate in a non-linear fashion. Our findings suggest that either test below its cut-off level can be used to guide treatment of infection. Pleural fluid glucose should be interpreted with care in patients with hyperglycemia.

**Figure 1. Predictive curve of pH against glucose.**
Background and Aim: Since asthma and chronic obstructive pulmonary disease (COPD) have often been viewed as distinct diseases, clinical studies frequently focus on each disease separately, limiting the possibility of identifying overlapping mechanisms. NOVELTY (a NOVEL observational longitudinal study) is a prospective, global study enrolling ~15,000 patients aged ≥12 years with asthma and/or COPD. NOVELTY aims to describe patient characteristics, treatment patterns, and illness burden over time, and to identify phenotypes and endotypes associated with differential outcomes. Electronic medical records (EMRs) were analyzed to understand the potential US patient population for NOVELTY, and assess EMRs as a potential data source.

Methods: EMR data were collected over a 12-month period from four healthcare systems in the Anolinx eResearch Network (A-EMR 1-4; Table 1), and from the QuintilesIMS US EMR database (IMS EMR; Table 2). Patients with asthma and/or COPD were identified using International Classification of Diseases-9. Severity was classified using treatment/lung function-based algorithms.

Results: EMRs from 654,122 patients with asthma, 735,453 with COPD, and 83,857 with both diagnoses were identified. In patients with asthma, 23.5%, 1.5%, and 0.1% had mild, moderate, severe and very severe disease, respectively (73.8% unclassifiable). In patients with COPD, 26.7%, 12.0%, and 21.9% had mild, moderate and severe/very severe disease, respectively (39.3% unclassifiable). Many respiratory-relevant variables were infrequently recorded, or were not in searchable formats (Tables). Patient-reported outcomes (PROs) were not documented.

Conclusion: EMR analysis revealed US patient numbers potentially eligible for NOVELTY. Disease severity was unclassifiable for many patients, suggesting that treatment or lung function data were not readily available in EMRs. Several key variables (e.g. lung function; PROs) were not available with sufficient completeness and frequency over time. Primary data collection for NOVELTY will therefore use electronic case report forms, with EMRs providing supplementary data.

Study Funding: AstraZeneca.

Table 1. EMR completeness for demographic variables: patients (%) with ≥1 data point over 12 months

<table>
<thead>
<tr>
<th>Scope of database</th>
<th>A-EMR Asthma, COPD</th>
<th>A-EMR 2 Asthma, COPD</th>
<th>A-EMR 3 Asthma, COPD</th>
<th>A-EMR 4 Asthma, COPD</th>
<th>IMS EMR Asthma, COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;750 physicians</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
</tr>
<tr>
<td>&gt;1,700 hospitals, clinics, and other facilities</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
<td>100, 100</td>
</tr>
<tr>
<td>&gt;2,500 physicians</td>
<td>94, 95</td>
<td>94, 95</td>
<td>94, 95</td>
<td>94, 95</td>
<td>77, 80</td>
</tr>
<tr>
<td>&gt;50 private practices, outpatients/ambulatory clinics only</td>
<td>90, 92</td>
<td>90, 92</td>
<td>90, 92</td>
<td>90, 92</td>
<td>90, 92</td>
</tr>
<tr>
<td>&gt;40,000 physicians</td>
<td>98, 97</td>
<td>98, 97</td>
<td>98, 97</td>
<td>98, 97</td>
<td>98, 97</td>
</tr>
</tbody>
</table>

*Data recorded in EMRs in unstructured format, unable to be collected at a system-wide level for this analysis. BMI, body mass index; COPD, chronic obstructive pulmonary disease; EMR, electronic medical record.

Table 2. EMR completeness for disease-related variables: patients (%) with ≥1 data point over 12 months

<table>
<thead>
<tr>
<th>Disease-related variables</th>
<th>A-EMR Asthma, COPD</th>
<th>A-EMR 2 Asthma, COPD</th>
<th>A-EMR 3 Asthma, COPD</th>
<th>A-EMR 4 Asthma, COPD</th>
<th>IMS EMR Asthma, COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbations</td>
<td>38, NR</td>
<td>23, NR</td>
<td>36, NR</td>
<td>32, NR</td>
<td>10, 11</td>
</tr>
<tr>
<td>Prescriptions</td>
<td>73, 66</td>
<td>&gt;75, &gt;75</td>
<td>27, 69</td>
<td>100, 100</td>
<td>44, 45</td>
</tr>
<tr>
<td>Allergy history</td>
<td>100, 100</td>
<td>&gt;90, &gt;90</td>
<td>97, 98</td>
<td>&gt;80, &gt;80</td>
<td>NR, NR</td>
</tr>
<tr>
<td>Blood eosinophils</td>
<td>59, 70</td>
<td>&gt;70, &gt;70</td>
<td>41, 55</td>
<td>&gt;60, &gt;60</td>
<td>11, 11</td>
</tr>
<tr>
<td>FEV1</td>
<td>*, *</td>
<td>*, *</td>
<td>*, *</td>
<td>*, *</td>
<td>NR, NR</td>
</tr>
<tr>
<td>FVC</td>
<td>*, *</td>
<td>*, *</td>
<td>*, *</td>
<td>*, *</td>
<td>NR, NR</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>22, 34</td>
<td>21, 21</td>
<td>20, 36</td>
<td>10, 10</td>
<td>NR, NR</td>
</tr>
</tbody>
</table>

*Data recorded in EMRs in unstructured format, unable to be collected at a system-wide level for this analysis. COPD, chronic obstructive pulmonary disease; EMR, electronic medical record; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NR, not recorded.
INTERSTITIAL LUNG DISEASE 1

BASELINE RISK FACTORS FOR USE OF NON-INVASIVE VENTILATION IN A COHORT OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Background: Respiratory failure due to neuromuscular weakness is the most common cause of death in Amyotrophic Lateral Sclerosis (ALS). Non-invasive ventilation (NIV) can improve quality of life and potentially improve survival. Due to variable progression of ALS, the onset of respiratory weakness remains uncertain. Predicting non-invasive ventilation use may help deliver early interventions in ALS. In this study, we sought to determine the baseline risk factors for eventual initiation of NIV.

Methods: We performed a retrospective cohort study of 572 patients who met El Escorial criteria for ALS. All patients were seen in a multidisciplinary Neurology clinic at the University of Pennsylvania. Outpatient visits occurred approximately every three months between May 2010 and October 2016. Study variables included a variety of demographics and longitudinal data. We used Cox proportional hazard models, censoring at date of death or last visit date.

Results: There were 812 person-years of follow-up time, and 45.5% (n=260) were initiated on NIV during the study period. In a multivariate analysis, factors significantly associated with risk of NIV included older age at diagnosis (per 10 years, HR 1.27, p<0.001), fewer years between symptoms and diagnosis (HR 0.73, p<0.001), underweight BMI (HR 2.18, p<0.007), African-American race (HR 1.83, p=0.006), lower decile of percent predicted FVC (HR 1.15, p<0.001), history of hypertension (HR 1.34, p<0.001), lumbosacral symptom onset (reference: bulbar, HR 1.67, p=0.040), and El Escorial criteria of Suspected ALS (HR 0.62, p=0.027) or Possible ALS (HR 0.67, p<0.001) with a reference of Definite ALS.

Conclusions: We identified baseline risk factors that were significantly associated with initiation of NIV in ALS. To our knowledge, this is the largest cohort study of ALS patients to identify risk factors for respiratory insufficiency. These factors may reveal important mechanisms of respiratory failure in ALS, which could be targeted with novel therapies.

Distribution of honeycombing area using quantitative CT analysis effects the mortality in IPF

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Background and Aims: In idiopathic pulmonary fibrosis (IPF), the relationship between the distribution of fibrotic changes and their progression are unknown. We hypothesized that the distribution of honeycombing area in upper and lower lung area using quantitative computed tomography (CT) analysis might predict mortality in IPF.

Methods: Chest high-resolution CT (HRCT) and pulmonary functional tests (PFTs) of 229 clinical IPF patients were retrospectively evaluated. Survival was assessed through April 30, 2017. We measured the honeycombing area as CT Honeycombing Area (HA) and the percentage of HA of whole lung area as %HA quantitatively using a computer-aided system. The upper and lower lung area were derived by the tracheal bifurcation. The percentage of upper-HA or lower-HA to upper lung area or lower lung area were calculated as %U-HA or %L-HA respectively. The ratio of %L-HA to %U-HA were also calculated as %HA ratio. PFTs were obtained within 3 months of each HRCT scans.

Results: The median (25th, 75th percentiles) age, %FVC, %DLC, composite physiologic index (CPI), and GAP (gender, age, and physiology) stage were 72 (65.5, 77), 76.2% (62.6%, 90.9%), 68.9% (52.1%, 86.6%), 32 (17.4, 44.1), and 1 (1, 2) respectively. In quantitative CT analysis, the median (25th, 75th percentiles) %HA, %U-HA, %L-HA, and %HA ratio were 2.1% (0.9%, 3.7%), 0.8% (0.3%, 1.9%), 2.5% (1.1%, 4.4%), and 3.0 (1.6, 5.3), respectively. In univariate analysis, %HA and %HA ratio were significant (HR: 1.34; p<0.001, and HR: 0.89; p=0.0005, respectively). In multivariate analysis with BMI and GAP stage, %HA ratio was also significant (HR: 0.91; p=0.011). Patients with %HA ratio smaller than 3 had significantly lower survival rate than patients with %HA ratio greater than 3 (log-rank: p=0.0003).

Conclusions: The lower/upper ratio of honeycombing area by quantitative CT analysis might be a good indicator of mortality in IPF patients.

Antifibrotic drug target protein (RXFP1) is expressed in idiopathic pulmonary fibrosis lungs

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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic disease of the lungs of unknown aetiology. Once diagnosed, it is usually fatal within 2.5-3.5 years. There is no effective treatment apart from lung transplantation and even then there is a 40% chance of rejection (chronic lung allograft dysfunction; CLAD). This too is characterized by fibrosis, especially around the airways in the transplanted lung. Due to its potent anti-fibrotic effects the relaxin / RXFP1...
Abstracts

AO100

BLEOMYCIN-INDUCED LUNG EPITHELIAL CELL INJURY IS ASSOCIATED WITH G2/M CELL CYCLE ARREST VIA SCHLAFEN AXIS
SOOJIN JANG1, HANBYEOL LEE1, JOOYEON LEE1, SE MIN RYU1, SUNG-MIN PARK1, KYUNG-HAK LEE1, SEONG-JOON CHOE1, SE-RAN YANG1
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Background and Aims: Idiopathic Pulmonary Fibrosis (IPF) is a fibrotic lung disease with progressive restrictive-ventilatory limitation and its declining lung function causes an emerging problem of public health. Pulmonary type II epithelial cells (AE II cells) are thought to play a critical role with the secretion of surfactant protein and differentiation into type I cells during epithelial repair. However, it still remains unknown whether bleomycin (BLM) which is able to cause cellular damage induces cell cycle arrest in AE II cells. Therefore, we determined whether bleomycin affects cellular proliferation and its involved mechanisms in mouse AE II cells.

Methods: MTT assay: BLM-induced MLE-12 cells were analyzed by MTT reagent. qRT-PCR: Total RNA is isolated by MLE-12 cells. We used SYBR Green and calculated by 2^(-ΔΔCt) methods. ELISA: Level of cytokine is measured by Duoset ELISA kit. Immunocytochemistry, PI staining

Results: In ELISA assay, treatment of BLM significantly increased TGF-β, TNF-α, and IL-6 pro-inflammatory cytokines in a dose-dependent manner. In addition, BLM exposure resulted in up-regulation of p21, p53 and Schlafen (SLFN) family by real-time RT-PCR analysis. Morphologically, the enlargement and flatten of the nucleus was found and G2/M cell cycle arrest in PI staining.

Conclusions: Taken together, BLM-induced G2/M phase arrest via SLFN signaling, flat cells in morphology and increased inflammation. Therefore, our findings suggest that BLM decreased the proliferation of AE cells and the related cell cycle arrested is associated with p21-p53-SLFN axis.

AO101

IDIOPATHIC PULMONARY FIBROSIS IN NEVER SMOKERS
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Background and Aims: Several previous studies demonstrated the possible involvement of smoking in the pathogenesis of idiopathic pulmonary fibrosis (IPF). However, we often encounter IPF patients who had never smoked. We conducted a retrospective study to investigate the characteristic features of IPF in never smokers.

Methods: To exclude the influence of emphysema on the clinical features of IPF, this study included only IPF patients with high resolution computed tomography (HRCT) findings of definite usual interstitial pneumonia pattern without obvious emphysema.

Results: A review of medical records identified 39 IPF patients without emphysema on HRCT; 15 of 39 these patients had never smoked. There were more women in the group of never smokers than in the group of smokers (73.3% vs. 0.0%, p < 0.01). There were no significant differences between the two groups in terms of mean age, findings on pulmonary function testing, serum KL-6 and SP-D levels, frequency of positive serum autoantibodies, frequency of acute IPF exacerbation, and mortality rate from IPF-related conditions, such as acute exacerbation, chronic respiratory failure, and lung cancer.

Conclusions: The clinical features of IPF in never smokers were not different from those in smokers, except for the preponderance of women. Based on these results, smoking appears to be not directly related to the pathogenesis of IPF, although it can alter the clinical features of IPF through development of emphysema, as reported by previous studies on combined pulmonary fibrosis and emphysema. The limitation of this study was its single-center design involving a small number of patients. Further investigations on a larger number of patients will be needed to clarify the role of smoking status in the pathophysiology of IPF.

AO102

JAPANESE FIRST GUIDELINE FOR THE TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS 2017
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Aim: To improve clinical outcomes for idiopathic pulmonary fibrosis (IPF), the Japanese Guideline for Treatment of Idiopathic Pulmonary Fibrosis 2017 was developed to standardize treatment and management of IPF.

Methods: The Japan Ministry of Health, Labour and Welfare Research Committee on Diffuse Pulmonary Disorders used the GRADE system to develop the first edition of a clinical practice guideline that includes clinical questions (CQs) and recommendations. The committee also formulated clinical questions, particularly on the chronic stable phase and on cases with acute exacerbation or comorbid lung cancer, which are decisive for poor prognosis but are not described in the IPF guideline of ATS/ERS/JRS/ALAT.
Results: The nine sub-CQs addressing treatment and management recommendations for progressive IPF include corticosteroids alone, immunosuppressants combined with corticosteroids, inhaled N-acetylcysteine monotherapy, pirfenidone, nintedanib, pirfenidone combined with inhaled N-acetylcysteine, pirfenidone combined with nintedanib, long-term oxygen therapy, and pulmonary rehabilitation. The five sub-CQs for acute exacerbation of IPF include corticosteroid pulse therapy, immunosuppressants, sivelestat sodium hydrate, direct hemoperfusion with a polymyxin-B–immobilized fiber column, and recombinant human soluble thrombomodulin. The three sub-CQs for coexisting IPF and lung cancer include surgical therapy, perioperative prophylactic treatment, and chemotherapy. For all CQs except pirfenidone and nintedanib, the certainty/quality of evidence was low or very low and the strength of the recommendations was weak. In addition to recommendations for CQs, the guidelines include a summary of evidence, a discussion by the guideline development group, and a list of studies evaluated.

Conclusion: The new clinical practice guideline for refractory IPF is expected to standardize IPF treatment and management and improve IPF outcomes among patients just below the PBS threshold.

AO103

ELIGIBILITY FOR ANTI-FIBROTIC TREATMENT IN IDIOPATHIC PULMONARY FIBROSIS (IPF) DEPENDS ON THE PREDICTIVE EQUATION USED IN PULMONARY FUNCTION TESTING

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Background: Pharmaceutical Benefit Scheme (PBS) prescription of Nintedanib for IPF is publically funded in Australia for patients with a diffusion capacity of carbon monoxide (DLCO) corrected for haemoglobin (DLCO/Hb) ≥30% predicted, forced vital capacity (FVC) ≥50% predicted, and FEV1/FVC ratio >0.7(3). These restrictions reclass inclusion criteria of the ‘INPULSIS’ trial; however the PBS does not stipulate which reference equation should be used; multiple equations exist and are used in development group, and a list of studies evaluated.

Methods: DLCO/Hb measurements from our Pulmonary Function laboratory database were analysed using seven reference equations. Difference between the %pred DLCO/Hb for each equation was calculated, with particular reference to the classification of patients above or below the PBS threshold.

Results: 12,583 (5,999 male) DLCO/Hb values were analysed. Comparing to our standard reference equation (ROCA (1)) there was a mean percentage predicted DLCO/Hb difference of –4.0% for Crapo, +10.0% for Thompson (2), -7.0% for Knudson, -6.0% for Paoletti, +5.0% for Cotes, and +17.0% for Miller. For females compared to ROCA (1) there was a mean percentage predicted DLCO/Hb difference of -3.4% for Crapo, +12.4% for Thompson, -4.0% for Knudson, -6.3% for Paoletti, +3.8% for Cotes, and +13.4% for Miller.

Conclusion: There is significant variability in the %pred value for DLCO between the seven equations analysed. This variability impacts access to subsidized treatment for IPF in Australia. Centres treating IPF should be aware of the potential benefit in using multiple predicted equations for patients just below the PBS threshold.
Background: In 2016, a new conceptual framework for acute respiratory deterioration (ARD) and a revised definition for an acute exacerbation (AE) in idiopathic pulmonary fibrosis (IPF) were proposed.

Aim: To investigate incidence, risk factors and impact of AE in IPF by revised definition, and compare them with those by the past definition.

Methods: This was a retrospective review of 445 patients with IPF (mean age 66.4 years, 76.4% was male and 37.1% were biopsy-proven). AE was classified as idiopathic (I-AE) or triggered AE (T-AE).

Results: The median follow-up period was 29.6 months. ARD requiring hospitalisation occurred in 129 patients (28.9%). AE in 78 (17.3%) (I-AE in 65, T-AE in 13). The 1- and 3-year incidences of AE were 7.6 and 20.9%, respectively. Increased age, low forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide (DLco) were significant risk factors for AE. The in-hospital mortality rate was 44.8%, the 1- and 5-yr survival rates from the initial diagnosis were 79.2% and 17.1%. AE was a significant predictor (HR 1.838, p<0.001) of poor survival after initial diagnosis, along with increased age, low FVC and DLco. Compared to the results of the past definition of AE (the 1-year incidence, 5.2%; in-hospital mortality rate, 52.7%), the revised definition increased the incidence by 2.4%, and decreased in-hospital mortality by 7.9%.

Conclusion: The 1- and 3-yr incidences of AE were 7.6 and 20.9%, respectively. Increased age, low FVC and DLco were risk factors. AE had a serious impact on the overall survival of the patients with IPF.

COPD 3

THE PREVALENCE OF COPD IN ENGLAND: AN ONTOLOGICAL APPROACH TO CASE DETECTION IN PRIMARY CARE
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Background and Aims: Estimates of the true prevalence of COPD in England vary considerably due to difficulties in structured case finding. Coded data from primary care computerised medical records (CMR) can be used to monitor disease prevalence, however reliance upon diagnostic codes alone is likely to lead to missed cases. The aim of this study was to develop a structured ontological approach to COPD case detection and implement it in a large primary care database to estimate the prevalence of COPD in England.

Methods: A three layer iterative process was developed (see Figure 1). Disease concepts were placed into an ontology and relevant CMR codes assigned. A logical data extraction was then performed to test the ontology in a primary care cohort of 1,595,537 patients and COPD prevalence in different subgroups was estimated.

Results: Use of the ontological approach yielded a prevalence of COPD of 3.4% in the total study cohort, 6.1% in those aged >=35 and 7.3% in smokers (see Figure 2). This is significantly higher than the current UK estimate of 1.9%. The ontological approach identified an additional 23,714 cases compared with using diagnostic codes alone.

Conclusions: In this paper, we demonstrate a robust reproducible method for COPD case detection in routinely collected primary care data. Our calculated prevalence was higher than existing UK estimates, suggesting that the burden of COPD in England is higher than currently predicted.

FEASIBILITY ANALYSIS OF NEBULIZED BUDENSONIDE USED FOR COPD EXACERBATIONS INITIAL TREATMENT: A POST HOC ANALYSIS OF A NON-INTERVENTIONAL, RETROSPECTIVE, OBSERVATIONAL STUDY
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Background and Aims: Corticosteroids is one of classes of medication most commonly used for COPD exacerbations. But the effect of different corticosteroids as initial treatment has been unclear yet. This post-hoc analysis aims to explore corticosteroids initial treatment indicators from baseline features and assess the clinical outcome of patients with COPD exacerbations treated by nebulization budesonide and systemic corticosteroids as initial treatment in order to understand the option of corticosteroids during COPD exacerbations.

Methods: Data were pooled from 3121 subjects who had participated in a retrospective, multicentre, noninterventional study (NCT02051166), which was designed to collect data from patients hospitalized for COPD exacerbations from January 2014 to September 2014 in China. Subjects included in this post-hoc analysis had received initial treatment with nebulization budesonide or systemic corticosteroids after hospitalization. According to sequential treatment regimen adjustment, these subjects were classified into four groups: Dose maintenance or reduction for nebulization budesonide (n=1443); Dose escalation for nebulization budesonide (n=756); Dose reduction for systematic corticosteroids (SCS) (n=518) and Dose maintenance or escalation for SCS (n=404). Clinical outcome were assessed.

Results: Baselines characteristics were similar among four groups, except that the average PaCO2 values (SD) at the first test during hospitalization were 48.0(14.32), 51.3(15.60), 52.7(18.97) and 51.2(18.87) mmHg, respectively. During the treatment course, rate of endotracheal intubation were 48.0(14.32), 51.3(15.60), 52.7(18.97) and 51.2(18.87) mmHg, respectively. During the treatment course, rate of endotracheal intubation were 1.8%, 3.3%, 2.5% and 3.2%, respectively. In-hospital mortality rate were 0.7%, 1.9%, 1.2% and 2.7%, respectively. Mean hospitalization duration (SD) were 11.5(5.84), 13.9(7.84), 13.3(5.41) and 11.3(4.90) days, respectively. During hospitalization, rate of new onset pneumonia in 4 groups were 1.2%, 3.5%, 2.9% and 2.7%, respectively.

Conclusions: Clinical outcome after received with nebulized budesonide or SCS as initial treatment were similar among AECOPD patients. Thus, it seems quite feasible for Nebulization Budesonide as the initial treatment for patients with COPD exacerbations.

ESTIMATING THE NUMBER OF PATIENTS NEEDED TO TREAT (NNT) WITH INDACATEROL/GLYCOPORYRONIUM TO PREVENT COPD EXACERBATIONS: RESULTS FROM THE FLAME STUDY

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Background and Aims: The FLAME study demonstrated that indacaterol/glycopyrronium (IND/GLY) is superior to salmeterol/fluticasone (SFC) in reducing the rate and risk of exacerbations. Here, we determined the number needed to treat (NNT) for IND/GLY to prevent one COPD exacerbation, to prevent one case of repeat exacerbation, and to prevent a patient from having an exacerbation during one year versus SFC.

Methods: FLAME was a 52-week, multicentre, randomised (1:1), double-blind, double-dummy, parallel-group study which compared IND/GLY 110/50 μg o.d. and SFC 50/500 μg b.i.d. Annualised and Kaplan-Meier (KM) event rates of exacerbation during the 52-week treatment period from the FLAME study were used to estimate the NNT for IND/GLY versus SFC.

Results: Based on the annualised exacerbation event rates, the NNT for IND/GLY versus SFC was 4.76 to prevent one moderate or severe exacerbation. The NNT with IND/GLY versus SFC was 50 to prevent one severe exacerbation requiring hospitalisation. To prevent one incidence of repeat exacerbations (≥ 3 exacerbations of any severity; mild, moderate or severe) for one year, the NNT with IND/GLY was estimated to be 31.58 versus SFC. Furthermore, the NNT with IND/GLY versus SFC was 15 to maintain a patient free from moderate or severe exacerbations for one year, as calculated from KM event rates.

Conclusion: Number needed to treat calculations confirms the efficacy advantage of indacaterol/glycopyrronium compared with salmeterol/fluticasone in preventing COPD exacerbations in patients with moderate-to-very severe airflow limitation.

REFERENCE

ONCE-DAILY INHALED UMECLIDINIUM/VILANERTOL COMBINATION THERAPY COMPARED WITH PLACEBO ON EXACERBATIONS IN CHINESE PATIENTS WITH COPD

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Background and Aims: Inhaled combination long-acting muscarinic antagonist and long-acting β2-agonist is recommended for the treatment of COPD according GOLD 2017, and has been demonstrated to reduce COPD exacerbations. To investigate the time to first COPD exacerbation following uemclidinium(UMEC)/vilanterol(VI) 62.5/25mcg treatment in Chinese COPD patients.

Methods: A 24-week, randomized, double-blind, placebo-controlled, study (ClinicalTrials.gov identifier NCT01636713) was conducted to compare the efficacy and safety of once-daily inhaled UMEC/VI to placebo in 580 Asian COPD patients, and 385 were Chinese. The subjects had post-salbuterol FEV1/FVC ratio<0.70 and FEV1<70% of predicted normal values with no requirement on exacerbation history. The primary end point was trough FEV1 on day 169 with time to first exacerbation as other endpoint. Proportions of on-treatment exacerbation were summarized between UMEC/VI 62.5/25mcg and placebo groups; Cox-proportional hazard model analysis (treatment and smoking status as covariates) was conducted in time to first exacerbation data in Chinese subgroup patients.

Results: On-treatment exacerbations were reported in more subjects receiving placebo (18%, n=129) than UMEC/VI 62.5/25mcg (10%, n=128) in Chinese subjects (Table 1). This analysis does not include the UMEC/VI 125/25mcg arm(n=128) in the same study as it is not launched for treatment of COPD. Analysis of time to first exacerbation showed on average a reduced risk following UMEC/VI 62.5/25mcg treatment by half as compared to placebo (hazard ratio: 0.5, 95% CI (0.3,1.1), p=0.077). The result is similar to that seen with UMEC/VI vs. placebo in previous studies (HR 0.48 RR: 52% p=0.01).

Conclusions: The data demonstrated the trend towards UMEC/VI 62.5/25mcg reducing the risk of first exacerbation compared with placebo in Chinese patients. The study was not powered to evaluate the effect of
Background and Aims: Oxidative stress contributes to COPD exacerbations and mucocutaneous drugs with antioxidants properties like erdosteine can decrease exacerbation rates. The RESTORE study was a prospective, randomized, double-blind, placebo-controlled, enrolling 528 patients (40–80 years) with old GOLD stage II–III. Patients received erdosteine 300 mg bid or placebo added to usual COPD therapy for 12 months. The primary outcome was the number of acute exacerbations during the study; main secondary outcome was the duration of exacerbations. Erdosteine reduced overall exacerbation rate by 19.4% (p=0.01) and lowered mean exacerbation duration by 24.6%, (p=0.023) showing a placebo-like safety profile. In this analysis we sought to identify patients with the highest response to erdosteine treatment.

Methods: Exacerbations were defined as a symptomatic worsening beyond normal day-to-day variations and requiring a change in regular medication and/or health care resources utilization and were collected using patient’s home daily diaries. In this post-hoc analysis, we considered 254 GOLD II patients defined using the GOLD 2011 definition. The frequency of exacerbations per patient per year collected during the 12 months treatment has been analyzed non-parametrically using the Wilcoxon rank sum test.

Results: After 1-year treatment of 254 COPD GOLD II patients (126 patients treated with erdosteine, 128 with placebo), 127 exacerbations have been recorded: 74 exacerbations (57.8%) have been registered in the placebo treated group and 53 exacerbations (42.1%) in the erdosteine group. Compared to placebo erdosteine reduced the exacerbation rate by 47% (OR: 0.530, 95%CI 0.322-0.872, p= 0.017). This result was independent of the patient’s sex, age, BMI, exacerbations during past 12 months or background treatment including ICS use.

Conclusions: In GOLD 2011 stage II patients, compared to placebo erdosteine added to usual COPD treatment significantly reduced the exacerbation rate. This result confirms highlights the potential role of erdosteine in moderately severe COPD.

Environmental and Occupational Health / Epidemiology

FACTORS ASSOCIATED WITH PNEUMOCOCCAL VACCINATION AMONG THE ELDERLY AT ELDERLY CLUBS IN MIYAKONOJO CITY, MIYAZAKI PREFECTURE, JAPAN

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Background and Aims: Pneumonia is the third leading cause of death in Japan. All the elderly aged 65 years or older were recommended to receive pneumococcal vaccine. Besides, subsidy for pneumococcal vaccine among this age group was introduced in 2014. However, present vaccination rate and its associated factors among the elderly have not been reported in Japan to date. This study was conducted to evaluate the vaccination rate and its associated factors among elderly people who regularly visit elderly clubs in Miyakonojo City, Miyazaki Prefecture, Japan.
been well reported. The aims of this study were to clarify present pneumococcal vaccination rate and to investigate factors associated with vaccine uptake among elderly people.

Methods: We conducted a cross-sectional study among the elderly at club events in Miyakonojo City, Miyazaki Prefecture, Japan in April 2017. A self-administered questionnaire was developed specifically for this study according to the PREEDE-PROCCEED model and used to measure the variables. Logistic regression analysis was performed to identify the associated factors with pneumococcal vaccination.

Results: A total of 208 elderly club members participated in. The mean age (± SD) was 77.2 ± 5.3 years. Pneumococcal vaccination rate was 53.2%. Multivariate analysis found that three variables had significant association with pneumococcal vaccination: perception of severity of pneumonia (aOR 1.23 95% CI 1.03 - 1.48, p = 0.026), influenza vaccination in any of previous 3 seasons (aOR 3.94, 95% CI 1.70 - 9.13, p = 0.001), and recommendation from medical personnel (aOR 8.42, 95% CI 3.59 - 19.72, p < 0.001).

Conclusion: Although the vaccination rate has increased compared to previous reports, almost half of the elderly has not received pneumococcal vaccine yet. Our results demonstrated the factors which are important to be more focused on for further increase of pneumococcal vaccine coverage. These findings could be helpful for future vaccination strategy among the elderly.

SMOKING BEHAVIOUR AMONG METRO NORTH HOSPITAL AND HEALTH SERVICES EMPLOYEES

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Background and Aims: Healthcare professionals’ smoking status, knowledge and attitudes may impact smoking cessation delivery. Metro North Hospital and Health Service (MNHHS), Queensland, Australia has ~16,000 employees and a catchment of ~900,000 people. 12% of the general population are daily smokers. We aimed to document smoking prevalence, smoking health knowledge and cessation training/practice amongst MNHHS employees.

Methods: An online survey of 28 items, covering demographics, smoking status, Fagerström Test for Nicotine Dependence (FTND), smoking health and knowledge, cessation training and practice, was advertised to all MNHHS staff through newsletters, email invitations, educational meetings, word of mouth, flyers and posters. Participation ran from 30/05/2017 to 19/06/2017, coinciding with WHO World No Tobacco Day.

Ethics approval: HREC/16/QPCH/138.

Results: Response rate was 8% (n=1288), Table 1. Current smoking prevalence was 10.8% (8.0% clinical group; 13.3% non-clinical group). 8.4% were daily smokers. Median FTND score= 1.4 (range 0 - 3).

12.5% of current or former smokers and 15.3% of never smokers do not routinely check patients’ smoking status. 71.3% of clinical staff provide cessation advice, however, 87% were uncertain of pharmacotherapy available in the Government formulary. 52.2% had received smoking cessation training.

Table 1. Employee responses

<table>
<thead>
<tr>
<th>Employee role</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>736 (58.8%)</td>
</tr>
<tr>
<td>Nursing and Midwifery</td>
<td>397 (30.8%)</td>
</tr>
<tr>
<td>Health Practitioner/Allied Health</td>
<td>277 (21.5%)</td>
</tr>
<tr>
<td>Medical Officer</td>
<td>124 (9.6%)</td>
</tr>
<tr>
<td>Dental Officer</td>
<td>18 (1.4%)</td>
</tr>
<tr>
<td>Non-clinical</td>
<td>495 (40.2%)</td>
</tr>
<tr>
<td>Administrative Officer</td>
<td>353 (27.4%)</td>
</tr>
<tr>
<td>Operational Officer</td>
<td>79 (6.1%)</td>
</tr>
<tr>
<td>Professional Officer</td>
<td>33 (2.6%)</td>
</tr>
<tr>
<td>Technical Officer</td>
<td>5 (0.4%)</td>
</tr>
<tr>
<td>Building, Engineering and Maintenance</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>1288</td>
</tr>
</tbody>
</table>

Conclusions: In line with prior studies, healthcare workers report lower rates of smoking compared to the general population. Current or former smoking status may impact cessation practice. There is significant scope to improve training in the workforce.

VAping knowledge, attitude and practice amongst general public in Malaysia

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Background and Aim: E-cigarette or vaping has gained the attention not only in Malaysian but worldwide, yet data on it is scarce. It’s marketed as smoking cessation device due to its ability to simulate smoking and deliver nicotine but recent data is veering towards its harmful effect to health. This study was conducted to assess the prevalence and understand the knowledge, attitude and practice towards vaping in Selangor.

Methods: This is a cross-sectional questionnaire based study of general population in Selangor. The questionnaire is designed to assess knowledge, attitude and practice towards vaping.

Results: 1129 responded with majority being female (61.5%) and Malay (77.8%). Mean age of respondents were 27.5±9.0 year old. The prevalence of vaping with or without smoking cigarettes was 8.1%. 70.3% uses nicotine cartridge of 6mg. 9.5% of respondents were ex-vapers/smokers. Median age of first start vaping was 23 (IQR 4) with mean of 4.2 ± 12.4 cigarette usage per day. Most rate their vaping addiction as moderate (29.9% as 5/10 and 14.9% as 6/10). 34.4% feel that vaping is less harmful than smoking cigarette while 65.6% do not know whether it is less harmful or not. A proportion responded that vaping is less addictive than cigarette (27.3%), less expensive (17.2%) and is a tool to quit smoking (28.4%). 44.8% have the intention to stop vaping. 46.3% received advice from healthcare professional to quit smoking or vaping but only 20.7% received help by healthcare professional.

Conclusion: Despite the low prevalence of smoking, the rate of addiction to vaping is high and so was the intention to stop vaping. However the awareness on harmful effects of vaping was still low within the general public in Selangor.
OBJECTIVE: To investigate associations between occupational exposure to solvents and metals and fixed airflow obstruction using post-bronchodilator spirometry.

METHODS: From 1,335 participants in the 2002-2008 follow-up of the Tasmanian Longitudinal Health Study (TAHS) cohort who completed lung function testing and lifetime work history calendars. Ever exposure and cumulative-exposure-unit-years were calculated using the ALOHA+Job Exposure Matrix. Fixed AO was defined by post-bronchodilator FEV1/FVC<0.7 and FEV1/FVC<lower limit of normal. Diffusing capacity of the lung for carbon monoxide (DLco) was combined with FEV1/FVC<0.7 to define fixed airflow obstruction plus low DLco. Multivariable linear and logistic regression models were used to estimate associations adjusting for sex, smoking, pack-years, asthma in childhood and adulthood, socioeconomic status in childhood and adulthood and co-exposures to gases/fumes and pesticides. We also investigated the effect modification by sex, smoking and asthma by including an interaction term in the regression models.

RESULTS: Ever exposure to metals was associated with fixed airflow obstruction (RR=1.71, 95% CI 1.03-2.85) and lower level of z-score FEV1/FVC (-0.17, 95% CI -0.33, -0.02). Ever exposure to solvents was not associated with fixed airflow obstruction. However, there was a significant interaction between obesity and air pollution (p=0.09, 0.07 respectively).

CONCLUSIONS: The lung function was lower as long-term exposure to PM10 increased in a COPD cohort. There was no interaction between obesity and air pollution at baseline in this study.

ELEVATED EXPRESSION OF MIR-691, MIR-181A, MIR-146A AND MIR-21 INVOLVED IN REGULATING TH1/TH2 BALANCE WITH ACUTE EXPOSURE OF FINE PARTICULATE MATTER IN MICE

Background and Aim: Airborne fine particulate matter (PM2.5) has been seriously harmful to human health. However, the pulmonary toxicological mechanism induced by PM2.5 remains obscure. Our previous studies have confirmed that PM2.5 hurt the immunological system causing the imbalance of Th1/Th2 lymphocytes. MicroRNAs (miRNAs) are post-transcriptional gene suppressors and potential mediators of environmental effects, which play an important role in the regulation of CD4+ T lymphocytes differentiation.

METHODS: We performed mice experiments to observe changes of cytokines and miRNAs in lung after an intratracheal instillation of PM2.5 for 1, 7 and 14 days, using the Agilent Mouse miRNA Microarray and quantitative real-time polymerase chain reaction (qRT-PCR) detecting the levels of IL-4 and IFN-γ with ELISA.
RESULTS: Suggesting that 10 miRNAs (such as miR-21-340a-691,-181a-155 and -146a) were remarkably upregulated associated with the pathogenesis of PM2.5. IL-4 level was found decreased, nevertheless, IFN-γ level was increased. The ratio was inclined to Th1 shifting, miRNA-691,-181a,-146a,-146b,-21a-3p,-21a-5p and -340 had a positive linear correlation with BLAF. IFN-γ while a negative correlation was observed between microRNA-691,-181a-21a-3p with IL-4 mRNA level.

CONCLUSION: miR-691,-mir-181a,mir-146a and miR-21 play the vital role in regulating immune imbalance triggered by PM2.5, driving a Th1-biased immune response after PM2.5 acute exposure. These findings improve our understanding of the toxicological pathways of PM2.5 exposure.

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COMPARISON OF ASBESTOS FIBER DETECTION METHODS IN BAL FLUID AND LUNG TISSUE OF RAT

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Background and Aims: In Korea, the lung cancer patients can be saved by asbestos damage relief law when the association with asbestos is proved based on Helsinki criteria. However, it is difficult to demonstrate the association between lung cancer and asbestos due to no experience of asbestos analysis in lung tissue or cytology samples in domestic circumstances. In this study, we tried to find the most efficient method to detect the asbestos fibers(AF) and to standardize the detection method in bronchoalveolar lavage fluid (BALF) and lung tissue of rat.

Methods: We injected two types of asbestos, crocidolite and amosite to a total of 80 SD rats. The animals were divided into 4 groups: crocidolite-control group (n=12), amosite-control group (n=12), crocidolite group (n=28) and amosite group (n=28). At two and four weeks after injection, the animals were sacrificed. We observed the BALF slides, using 2 classical methods (Membrane filter, Cytospin) and 2 alternative methods (Thinprep, Surepath) with phase contrast microscope, polarized microscope and electron microscope.

Results: In rat BALF samples, membrane filter method revealed many AF but it is inconvenient for usual pathologist and dangerous for technologist. Although cytospin is a convenient method, the number of AF is lower than in membrane filter method. Thinprep method is similar with cytospin in the number of AF but the cytomorphic is much better. Surphot is more convenient than membrane filter method as well as the number of AFs is higher than cytospin and thinprep methods. In rat lung tissue, we observed AF near terminal or respiratory bronchioles and several giant cells forming granuloma.

Method Asbestos Fiber number Alveolar macrophage morphography Convenience

| Classical Method | Memb. *** | (cell digestion) | - |
| Alternative Method | Cyto. + | + | +++ |
| Method | TP + | + | +++ |
| Method | SP ++ | + | ++ |

AO120

CHILDHOOD ASTHMA DEVELOPMENT IN RELATION WITH PERINATAL AND ENVIRONMENTAL FACTORS

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Abstracts

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Background and Aim: Asthma is the most common chronic disease in children, caused by a combination of genetic predisposition and environmental factors. Perinatal risk factors are also expected to have a significant impact on the development of asthma, but sufficient studies have not yet conducted. We evaluated whether perinatal factors and environmental factors have an independent/synergistic effect on the development of asthma.

Methods: This study was conducted on 3,770 children (mean (range) age, 9.1(5.68-12.16) years; male, 51.9 %) who were enrolled in the "Elementary School Student Cohort (2009 - 2014)" in the Atopy Environmental Health Center, Ulsan University Hospital. The subjects were examined with questionnaires and laboratory tests. Accordingly, subjects were divided into asthma group (n=514) and non-asthma group (n=3256). To identify independent/synergistic risk factors, multivariate and stratification analyses were performed.

Results: Multivariate analyses showed that the oxygen therapy in first week (adjusted odd ratio [aOR], 1.864; 95% CI, 1.156-3.004), environmental tobacco smoking (ETS)(aOR, 1.634; 95% CI, 1.298-2.058), and parental allergic disease (aOR, 1.882; 95% CI, 1.521-2.328) are potent risk factors for the development of asthma. In contrast, breastfeeding had a preventive effect on asthma development (aOR, 0.763; 95% CI, 0.679-0.986).

Conclusion: We found that the oxygen therapy in first week after birth, ETS, and parental allergic disease were very synergistic risk factors for the development of asthma. Further, there were synergistic association between perinatal factors (early life oxygen therapy and breastfeeding) and traffic-related air pollution.

AO121

THE APPLICATION OF SIGE/SIGG4 AND IFN-γ IN INFANTILE ALLERGY MARCH

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Background and Aims: To investigate the expression level and clinical significance of IFN-γ, sigE / sigG4 in process of food allergies into inhalation allergies in infants.

Methods: The levels of IFN-γ, tIgE, egg white sigE, sigG4 and house dust mite sigE in serum of 60 infants (1 ~ 4 years old) were detected by ELISA and ImmunoCAP respectively. According to sigE, infants were divided into food allergy group and inhalation allergic group, at the same time, according to the appearance of clinical symptoms, inhalation allergic group were divided into symptomatic group and asymptomatic group. The T-test was used to analyze the difference and the ROC curve was drawn, the area under the curve was analyzed.

Results: 1)IFN-γ, tIgE, egg white sigE / sigG4 and house dust mite sigE in serum of infants were: 10.2 pg / ml, 364.9Ku / L, 1, 1 and 14.6Ku / L, respectively. The results of food allergy group were: 8.1 pg / ml, 209.3Ku / L, 2.0, 14.6Ku / L, the inhaled allergic group were 14.6 pg / ml, 658.9Ku / L, 0.06, 39.7Ku / L.2) The IFN-γ level of the inhaled allergic group was higher than that food allergic group, but the sigE / sigG4 decreased, which was not statistically significant. tIgE was statistically significant difference between the two groups. 3)The area under the ROC curve of IFN-γ and sigE / sigG4 in the symptomatic group and the asymptomatic group was 0.667 and 0.714 respectively. The area under the ROC curve of the combined IFN-γ, sigE / sigG4 was 0.750, the sensitivity was 62.5% and specificity was 75%.

Conclusions: The levels of IFN-γ were increased and sigE / sigG4 was decreased in allergic march. The combination of IFN-γ, sigE / sigG4 on the basis of the house dust mite sigE could prompt the appearance of inhaled allergy symptoms.

AO122

PEANUT SENSITIVITY AND ALLERGIC RHINITIS AT 6 YEARS OF AGE ARE ASSOCIATED WITH INCREASED SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OPPOSITIONAL DEFANT DISORDER LATER IN LIFE

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Background and Aim: Previous studies have found that allergic disease in children may be associated with anxiety, stress and attention deficit hyperactivity disorder. However, most studies to date are cross-sectional in nature and do not include allergen sensitivity data. In this longitudinal study of children from 6 to 12 years of age, we investigate the temporal relationship between allergic disease, allergen sensitization and symptoms of attention deficit hyperactivity disorder and oppositional defiant disorder.

Methods: In total 97 children were followed from 6 to 12 years of age. Clinical examination and blood samples for total and specific IgE were collected at 6 and at 12 years of age. Symptoms of attention deficit hyperactivity disorder and oppositional defiant disorder at 12 years of age were assessed using the Swanson, Nolan, and Pelham, Version IV Scale Parent Form.

Results: Results of a linear regression model showed that allergic rhinitis at 6 years of age was associated with increased inattention and opposition / defiance scores at 12 years of age (β-coefficient 0.277, p = 0.005 and β-coefficient 0.245, p = 0.025, respectively). In addition, higher levels of specific IgE against peanuts at 6 years of age was associated with higher hyperactivity / impulsivity scores at 12 years of age (β-coefficient 0.060, p < 0.001).

Conclusion: In this longitudinal study we found that allergic rhinitis and peanut allergen sensitivity at 6 years of age were associated with higher scores for attention deficit hyperactivity disorder and oppositional defiant disorder at 12 years of age. Our findings suggest that early onset of allergic disease and food sensitization may increase symptoms of attention deficit hyperactivity disorder and oppositional defiant disorder later in life.
CRITICAL EVALUATION OF SCIENTIFIC CONTENT IN PEDIATRIC RESPIRATORY GUIDELINES IN CHINA

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**Background and Aim:** The pediatric guidelines for respiratory diseases in China have been rapidly proliferated under increasing pressures to provide high quality healthcare with the best possible evidence, but little is known about their quality and validity. The purpose of this study is to critically assess the development process and scientific content of pediatric guidelines for respiratory diseases in China.

**Methods:** We systematically searched four Chinese databases (CBM, WANFANG, VIP and CNKI) to identify pediatric guidelines for respiratory diseases published in a peer-reviewed journal. Four reviewers independently appraised eligible guidelines with Appraisal of Guidelines for Research and Evaluation II (AGREE II), and the overall agreement among reviewers was assessed by intra-class correlation coefficient (ICC). Each eligible guideline was to determine recommendations given and scientific evidence used.

**Results:** A total of 30 Chinese pediatric guidelines were identified which published in 11 medical journals from 2000 to 2016. Of these, 21 (70.0%) guidelines were developed by medical societies or government, and 9 (30.0%) guidelines were focused on Traditional Chinese Medicine (TCM). The majority (23,76.7%) were focused on both diagnosis and treatment. Only 6 (20.0%) guidelines claimed themselves as evidence-based guidelines and 13 (43.3%) as Expert consensus. The scores of the six AGREE domains were low: 45.8% for scope and purpose (range: 18.1 to 73.6%), 16.1% for stakeholder involvement (range: 1.4 to 38.9%), 5.4% for rigor of development (range: 1.0 to 27.1%), 59.1% for clarity and presentation (range: 37.5 to 76.4%), 11.1% for applicability (range: 1.0 to 28.1%), and 4.2% for editorial independence (range: 0 to 64.6%). Only one guidelines (3.3%) were recommended for clinical practice with modifications.

**Conclusion:** The overall quality of pediatric guidelines for respiratory diseases in China was poor. More effort needs to be paid to improve the quality of guidelines especially in rigorous methodology and transparency of development. Further, there are still areas in pediatric respiratory diseases that need more high-quality research.

DEVELOPMENT OF AN IN-VITRO MUCUS MODEL TO EVALUATE THE EFFECT OF MAGNESIUM ON CURRENT MUCOLYTIC THERAPIES FOR CYSTIC FIBROSIS

TREATMENT

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**Background and Aim:** Cystic Fibrosis (CF) is a genetic life limiting disease. In CF patients, respiratory failure accounts for more than 90% of deaths due to build-up of thick mucus that obstructs the airways and leads to inflammation and infection. Dormase alfa (DNase) reduces the viscosity of CF sputum. However, DNase is not always effective and there are a number of factors that may influence this, including local magnesium (Mg) concentration. The aim of this study is to develop an *in-vitro* mucous model that represents CF airway sputum so that we can study how such factors influence DNase effectiveness.

**Methods:** An artificial mucous (AM) model was developed containing DNA, mucin, egg yolk, amino acids, NaCl, KCl, DTPA and actin. As a preliminary study and to set up the AM model, a sputum sample was collected from CF clinic at the Children’s Hospital at Westmead. (Ethics approval LNR/15/SCHN/511). Dynamic elasticity (G’) of the AM and sputum was measured at angular frequency 1 rad/sec using an Advanced Rheometer 2000 (20mm, 0.5˚ aluminium cone and plate). Measurements were made using 2.5μg/ml of DNase with and without the addition of 5mM Mg2+.

**Results:** The AM model was shown to have rheological behaviour similar to sputum collected from a CF patient. DNase reduced dynamic elasticity of AM and sputum by 56% and 40%, respectively. Combining DNase with Mg significantly reduced elasticity of AM and sputum by 99% and 91%, respectively (Figure 1).

**Conclusion:** The AM model presented in this study showed promising results in mimicking real CF sputum. Furthermore, we have shown that Magnesium ion concentration has an impact on DNase’s ability to modify sputum rheology.

ALLERGEN IMMUNOTHERAPY MIGHT REDUCE BASOPHIL RESPONSE IN HOUSE DUST MITE ALLERGIC PATIENTS

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**Background and Aims:** Allergen immunotherapy (AIT) is an effective treatment for IgE-mediated allergic disease, it is unclear whether AIT could reduce allergen effective cell activation. The aim of this study was to evaluate the level of basophil response after AIT treatment and its relationship with clinical outcomes.

**Methods:** This study involved 32 patients with allergic rhinitis and/or asthma, of which, 17 receiving a 104-week course of Dermatophagoides pteronyssinus (Der-p) subcutaneous immunotherapy (SCIT), and 15 receiving only medications. Immunogenicity was assessed by the
levels of Der-p IgG4 and an allergen induced CD63 basophil activation test. The primary clinical end point was the combined symptom and medication score (SMS).

Results: SCIT patients had much significant decreased in SMS at week 104 comparing with medication subjects (p<0.01). Levels of Der-p slgG4 in SCIT patients showed a significant increase at week 104 (p<0.01). A significant decrease in allergen-induced basophil activation at submaximal allergen concentrations was demonstrated at the end of 104 weeks AIT (p<0.05).

Conclusions: AIT might reduce the allergen-induced basophil activation in Der-p allergic rhinitis and/or asthma patients.

A0127

OBESITY, DEFINED BY BODY MASS INDEX OF NO LESS THAN 25 KG/M², IS A RISK FACTOR FOR POOR ASTHMA CONTROL IN EAST-ASIAN FEMALE POPULATIONS

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Background and Aims: Obesity has been identified as a risk factor for poor asthma control. Obesity-related non-eosinophilic asthma has been identified as a phenotype of asthma, which is characterised by late onset, female predominance, and an increased frequency of severe symptoms. Reports on the characteristics of obese asthmatic patients in East-Asian populations are lacking while characteristics of obesity and obesity-related disorders differ between East-Asian and Western patients. This study aimed to investigate the clinical characteristics of obesity-related severe asthma in East-Asian female populations and elucidate the associations between obesity and poor asthma control.

Methods: We conducted a retrospective observational study on female patients with severe asthma who visited Department of Allergy and Respiratory Medicine at Fraternity Memorial Hospital. Patients were classified into two groups based on the definition of obesity provided by Japan Society for the Study of Obesity (Obesity: body mass index (BMI)≥25), and data were compared between the groups.

Results: A total of 283 patients (obesity (OB), n=108 and non-obesity (NOB), n=175) were enrolled. Age, pack-year, daily controller use, and spirometry data showed no significant differences between OB and NOB groups. The frequency of rescue courses of corticosteroid use was higher in the OB group than in the NOB group. Multivariate logistic regression was performed to examine the association between obesity and poor asthma control. The results showed that obesity was an independent risk factor for poor asthma control in East-Asian female populations.

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A0126

Ghrelin Protects Against Airway Eosinophilic Inflammation in Asthma

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Background and Aim: Ghrelin is an endogenous ligand for the growth hormone secretagogue-receptor (GHS-R). While ghrelin is known to have anti-inflammatory effect, the role of ghrelin in allergic inflammation remains unknown. In this study, we showed that ghrelin administration suppressed the features of the asthmatic phenotypes. In addition, we investigated the usefulness of measuring plasma ghrelin levels as a disease marker in patients with asthma.

Methods: C57BL/6 mice and GHS-R deficient (GHSR-KO) mice were sensitized to OVA (day 0, 7, and 14). Following sensitization, C57BL/6 mice were administered 20 nmol/mouse of ghrelin or PBS intraperitoneally (day 16-18) and challenged with aerosols of either PBS containing 4% OVA or PBS alone (day 16-18). We assessed the plasma ghrelin levels, the ghrelin mRNA expression levels in the stomach, the amount of inflammatory cells in the bronchoalveolar lavage fluid (BALF) and airway responsiveness on day 19 of experimental protocol. In addition, we measured the plasma ghrelin levels in 15 healthy controls, 21 patients with well-controlled asthma and 19 patients without well-controlled asthma.

Results: In OVA-challenged C57BL6 mice, the amelioration of eosinophil infiltration in the bronchial mucosa and mitigation of excessive airway hyperresponsiveness were notable in ghrelin-treated mice. The plasma ghrelin levels and the ghrelin mRNA expression levels in the stomach of OVA-challenged mice were lower than those in the PBS-challenged control. OVA challenge enhanced airway obstruction and airway inflammation in GHSR-KO mice compared with C57BL6 mice. The plasma ghrelin levels of the patients without well-controlled asthma were lower than those of healthy controls and well controlled asthma patients.

Conclusion: Our results indicate that endogenous ghrelin may have an important role in protection against airway eosinophilic inflammation and ghrelin signal may be a therapeutic target in asthma.
analysis showed that obesity was independently associated with frequency of rescue courses of corticosteroid use.

**Conclusions:** This study indicated that obesity defined by BMI ≥25 kg/m² has an independent association with poor asthma control in East-Asian female populations. This study also implied that poor asthma control is induced by obesity without restrictive pulmonary dysfunction in East-Asian female population. The present findings provide important information for the management of severe asthma with obesity.

**FREE FATTY ACID RECEPTORS 1 AND 4 ARE NOVEL BRONCHODILATOR TARGETS FOR ASTHMA**

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**Background:** Improved bronchodilators are required when the efficacy of β2-adrenoceptor agonists is limited, including in poorly controlled asthma associated with obesity. Free fatty acid receptors, FFAR1 and FFAR4, have been identified as potential therapeutic targets for metabolic and chronic inflammatory diseases, including obesity-induced diabetes. Since FFAR1 and FFAR4 receptors are highly expressed in the lung, we hypothesised that TUG891 (FFAR4 agonist) and GW9508 (FFAR1/ FFAR4 agonist) may have beneficial effects on airway function.

**Aim:** To confirm airway expression of FFAR1 and FFAR4 receptors and test the bronchodilatory effects of GW9508 and TUG891 in situ using mouse precision cut lung slices (PCLS) containing small airways (100-300 μm diameter).

**Methods:** Using lung sections from naïve BALB/C mice, airway expression of FFARs was examined using immunohistochimistry. PCLS were prepared from separate agarose-filled lungs to visualise changes in airway area under phase contrast microscopy, comparing dilator responses to TUG891, GW9508 and salbutamol following submaximal and maximal MCH-induced contraction.

**Results:** FFAR1 and FFAR4 expression was evident in airway smooth muscle. TUG891 and GW9508 caused concentration-dependent relaxation with greater efficacy but similar nM potency to salbutamol (% relaxation to 10 nM dilator: TUG891 48±9%, salbutamol 26±9%, n=7). Relaxation to TUG891, but not salbutamol, was maintained in maximally contracted airways (% relaxation vs % pre-contraction: TUG891 R2=0.1 n=12, salbutamol R2=0.86 n=11).

**Conclusion:** TUG891 and GW9508 are more efficacious than salbutamol in relaxing small airways of naïve mice. While assessment of FFAR1 and FFAR4 agonists as novel bronchodilators in obesity-associated asthma remains to be conducted, these drugs have the potential to overcome the functional antagonism that limits the effectiveness of β2-adrenoceptor agonists in severe asthma.

**ASSOCIATIONS BETWEEN NUTRIENT-BASED DIETARY PATTERNS AND LUNG FUNCTION IN MIDDLE-AGED AND OLDER AUSTRALIAN ADULTS**

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**Background:** Intakes of foods and nutrients are generally strongly correlated, making it difficult to establish the relationship between individual foods or nutrients and lung function. Several studies have assessed the relationship between food-based dietary patterns and lung function. However, there has been no research assessing this relationship using nutrient-based dietary patterns.

**Aims:** To investigate the relationship between nutrient-based dietary patterns and lung function in middle-aged and older adults.

**Methods:** A population-based sample of men and women aged 45-72 years from inner south-east Melbourne was invited to participate in a cross-sectional study of risk factors for COPD. Participants were assessed by spirometry and questionnaires including a food frequency questionnaire (n=1193). Nutrient intakes were calculated and energy-adjusted nutrient intakes were computed using the residual method. Uncorrelated components were created using principal components analysis (PCA). Components explaining 80% of the variation in the diet were retained. Scores were calculated for each component and used in regression analyses assessing the relationship with lung function measures. Age, gender, height, energy intake, BMI, asthma, COPD, atopy and smoking were considered as confounders.

**Results:** Eight components from the PCA explained 82% of the variation in diet. Component 1, representing a diet high in potassium, magnesium, folate and fibre, was positively associated with FEV1, and FVC (p-values: 0.002 and <0.001 respectively). Component 7, representing a diet high in saturated fat and low in polyunsaturated fat, calcium and phosphorus, was negatively associated with FEV1, FVC and FEV1/FVC (p-values: 0.001, 0.008 and 0.019 respectively).

**Conclusion:** Diets high in potassium, magnesium, folate, fibre, polyunsaturated fat, calcium and phosphorus and low in saturated fat are associated with better lung function. This combination of nutrients corresponds to a diet high in wholegrains, legumes, leafy green vegetables and low-fat dairy products.

**ANALYSIS OF T CELL-INDUCED BRONCHOCONSTRICTION IN MURINE ASTHMA MODEL**

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**Background and Aim:** To investigate a role of helper T (Th) cells in asthma, T cell-transfer model was analyzed for immediate and late phase asthmatic responses after antigen challenge.

**Methods:** Ovalbumin (OVA) specific Th clones were derived from either the regional lymphnodes of Balb/c mice immunized with OVA/CFA or splenocytes of DO11.10 transgenic mice expressing T cell receptor specific for OVA-H-2Kd. Th clones were adoptively transferred into unprimed mice. After intranasal or inhalation challenge with OVA, airway resistance was continuously monitored by either unrestrained whole body plethysmography (BUXCO) or resistance/compliance analyzer under anesthetized condition. Bronchoalveolar lavage and analysis of airway
hyperresponsiveness (AHR) were performed 48 hr after OVA challenge. Supernatants of stimulated Th clones were analyzed for contractile activity using collagen gels embedded with murine primary bronchial smooth muscle cells. Effects of H2R and LTR1 antagonist were analyzed both in vitro and in vivo.

Results: When unprimed mice were transferred with Th clones, T5-1, T6-2, T6-4, and T6-7, Pehn values were significantly increased 6 hr after OVA challenge. In contrast, mice transferred with other Th clones, B7, T6-1, or T6-10 did not show any change. Airflow limitation was confirmed by a direct measurement of airway resistance under anesthetized, restrained, and intubated conditions. The airflow limitation was also efficiently induced by the challenge with T cell epitel peptide, OVA.

Conclusion: Activation of Th cells resulted in an airflow limitation besides eosinophilic inflammation, AHR, and mucous hyperplasia. T cell-derived bronchoconstriction might be a target for treatment-resistant asthma.

ENZYME MARKERS OF NEUTROPHIL SEGMENT OF BRONCHIAL INFLAMMATION AT OSMOTIC AIRWAY

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Background and Aim: Airway hyperresponsiveness in patients with asthma is caused by persistence of inflammation, induced by eosinophilic and neutrophilic granulocytes. The enzymes of myeloperoxidase and neutrophilic elastase are the markers of neutrophilic segment of inflammation. The aim was to study association between the contents of neutrophils in bronchi, the level of the peroxidase and proteolytic activity and development of obstructive asthma. The aim was to study association between the contents of neutrophils in bronchi, the level of the peroxidase and proteolytic activity and development of obstructive asthma.

Methods: FEV1, airway response (ΔFEV1) to 3-minute ultrasound inhalation with distilled water (IDW), the contents of myeloperoxidase (MPO, pixels) in the induced sputum (IS), the level of MPO (ng/ml), neutrophilic elastase (NE, mg/ml) and α1-antitrypsin (AAT, mg/dl) in the blood serum before and after IDW were studied in 36 patients with asthma (mean age 40.6±1.6 years old).

Results: According to the results of cytolological study, 11 patients with low contents of neutrophils in IS (11.5±1.2%) were included in the 1st group, 25 patients with high contents of neutrophils (37.5±3.9%, p=0.0001) in the 2nd group. The level of asthma control was lower in the 2nd group than in the 1st group (17.1±0.98 and 20.0±1.0 points of ACT, respectively, p=0.05), FEV1 was lower (89.6±2.8 and 100.2±3.9%, p=0.04), and the response to IDW was more intensive (ΔFEV1 -6.5±1.5% and -1.8±1.9%, p=0.049). In response to IDW the patients of the 2nd group had a decrease of MPO from 267.5±227.8 (p=0.003), of NE from 411.1±227.8 (p=0.0001), of AAT from 71.8±59.6 (p=0.0001), and the response to IDW was more intensive (ΔFEV1 -6.5±1.5% and -1.8±1.9%, p=0.049). In response to IDW the patients of the 2nd group had a decrease of MPO from 267.5±227.8 (p=0.003), of NE from 411.1±227.8 (p=0.0001), of AAT from 71.8±59.6 (p=0.0001), and the response to IDW was more intensive (ΔFEV1 -6.5±1.5% and -1.8±1.9%, p=0.049). In response to IDW the patients of the 2nd group had a decrease of MPO from 267.5±227.8 (p=0.003), of NE from 411.1±227.8 (p=0.0001), of AAT from 71.8±59.6 (p=0.0001), and the response to IDW was more intensive (ΔFEV1 -6.5±1.5% and -1.8±1.9%, p=0.049).

Conclusion: Activation of neutrophilic component of bronchial inflammation in patients with asthma leads to worsening of the lung function and is concomitant with the decrease of the system level of peroxidase, protease and antiproteolytic activity in response to IDW.

EFFECTS OF THE ADDITION OF TIOTROPIUM VERSUS MONTELUKAST ON AIRWAY INFLAMMATION AND REMODELING IN SYMPTOMATIC ASTHMA

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Background and Aims: Asthma often remains uncontrolled despite treatment with inhaled corticosteroids (ICS), long-acting β2-agonist (LABA), or both, which necessitates an additional treatment. We evaluate the effect of tiotropium, long-acting anticholinergic bronchodilator, versus leukotriene receptor antagonist montelukast on airway inflammation and remodeling in patients with symptomatic asthma receiving ICS and LABA.

Methods: Patients, all of whom were concurrently using ICS plus LABA, were treated for 48 weeks with tiotropium 5 μg once daily (n = 25), montelukast 10 mg once daily (n = 28), or no add-on (n = 30) to maintenance therapy. Airway dimensions were assessed by quantitative computed tomography. Fractional exhaled nitric oxide (FeNO), pulmonary function, and asthma quality of life questionnaire (AQLQ) were measured.

Results: Compared with maintenance therapy, the add-on of tiotropium significantly decreased airway wall area corrected for body surface area (WA/BSA, p < 0.05) and wall thickness (T/BSA, p < 0.05), meanwhile the add-on of montelukast significantly decreased FeNO (p < 0.05), and each add-on treatment improved airflow obstruction (p < 0.05, respectively). In the tiotropium group, the changes in predicted forced expiratory volume in 1 s (FEV1) were significantly correlated with the changes in WA/BSA and T/BSA (r = −0.87, p < 0.001 and r = −0.82, p < 0.001, respectively). In the montelukast group, the changes in FEV1 were significantly correlated with the changes in FeNO (r = −0.71, p < 0.001). There were more improvement in the AQLQ score for the tiotropium and montelukast group than the maintenance-only group.

Conclusions: A triple combination of tiotropium or montelukast and ICS plus LABA may have additive protective effects of airway remodeling and inflammation, and provide improvement of lung function and quality of life in asthma.

THERAPEUTIC EFFECTS OF HISTONE DEACETYLASE ENZYME 8 INHIBITORS (HDAC8I) IN A MURINE ASTHMA MODEL

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Background and Aims: Airway inflammation, airway remodeling and airway hyperresponsiveness are major aspects of asthma pathology. Histone deacetylase inhibitors have a wide range of effects that demonstrate therapeutic effects in animal models of chronic inflammatory diseases. In this study, we investigated the effect of PCI-34051, a selective HDAC8 inhibitor, on the development of chronic allergic airway disease mice with airway inflammation, airway remodeling and airway hyperresponsiveness.

Methods: Wild-type BALB/C mice were sensitized intraperitoneally with ovalbumin (OVA) and aluminum hydroxide gel (on weeks 0, 1, 2) and nebulized 8 weeks. Ovalbumin-exposed mice were treated with PCI-34051 or vehicle control. The expression pattern changes of HDAC8 were assessed by immunohistochemical staining. Western Blot and colorimetric method. Airway inflammation was assessed by bronchoalveolar lavage...
fluid cell counts and HE staining of lung tissue sections. Airway remodeling was assessed by Alcian blue-Periodic acid Schiff staining, Masson trichrome staining and Western Blot. Airway hyperresponsiveness was assessed by plethysmography measurement of airway resistance.

**Results:** Compared with normal mice, HDAC8 was higher expressed in airway epithelial cells, airway inflammatory cells and vascular smooth muscle cells in asthma lung tissue. And the total expression level and enzyme activity increased significantly in asthma lung tissue. Compared with asthma mice, PCI-34051 treatment relieved airway inflammation (P < 0.05), reduced the quantity of goblet cell (P < 0.05), subepithelial collagen deposition (P < 0.05) and attenuated airway resistance (P < 0.05), and its effects were similar with dexamethasone treatment.

**Conclusions:** These results demonstrate that HDAC8 is closely related to asthma pathogenesis, and treatment with PCI-34051 can reduce airway inflammation, airway remodeling and airway hyperresponsiveness, suggesting that blockage of HDAC8 may be a useful treatment for bronchial asthma.

**AO134**

**CLINICAL DIFFERENCE BETWEEN DIRECT AND INDIRECT CAUSES OF ACUTE RESPIRATORY DISTRESS SYNDROME: A RETROSPECTIVE COHORT STUDY OF 216 PATIENTS**

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**Background and Aims:** Acute respiratory distress syndrome (ARDS) is a life-threatening condition, and is associated with a poor prognosis. Although it was reported that ARDS have various clinical phenotypes with different risk and prognostic factor, there have been few reports about them since the Berlin definition of ARDS was published in 2012, and also few reports concerning about clinical features and prognosis of direct causes of ARDS compared with those of indirect ones. We aim to investigate clinical difference between direct and indirect ARDS.

**Methods:** Two hundred and sixteen patients with ARDS who met the Berlin Criteria were enrolled from October 2004 to July 2016 at our institution. We divided the patients into two groups: direct and indirect ARDS group. We evaluated each group for 28-day prognosis, ventilator-free days, and other clinical features.

**Results:** There were 139 patients in the direct ARDS group and 77 in the indirect ARDS group. In the direct ARDS group, serum LDH (median; 308 vs 401, p= .001) and HRCT score suggestive of the extent of fibro-proliferation (Radiology 2006; 238: 321-329) (median; 208.3 vs 261.7, p=.011), and PaO2/FiO2 ratio (median; 99.9 vs 124.7, p=.047) were significantly lower compared with indirect ARDS group. After adjusting for potentially confounding covariates, there was no significant difference in 28-day mortality (HR, 1.252; 95% CI, 0.757-2.071; P = .382) and ventilator-free days between direct and indirect ARDS group. In direct ARDS group, serum LDH and HRCT score were significantly associated with mortality, while low platelet count, low serum albumin, and DIC score were in indirect ARDS group.

**Conclusions:** Although there was no significant difference in prognosis and ventilator weaning, clinical predictors of mortality differ between direct and indirect ARDS.

**Critical Care Medicine**

**AO135**

**EFFICACY OF CONTINUOUS BLOOD PURIFICATION ON PATIENTS WITH SEVERE ACUTE PANCREATITIS ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME**

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**Background and Aims:** Acute respiratory distress syndrome (ARDS) is a frequent complication in patients with severe acute pancreatitis (SAP), which leading to increased mortality. Continuous blood purification (CBP) can remove inflammatory cytokines and maintain the stability of the internal environment in the organism. In this study, we retrospectively analysed the effect of CBP in the treatment of patients with severe acute pancreatitis associated ARDS.

**Methods:** From January 2012 to April 2017, the continuous venous-venous hemofiltration (CVVH) was performed in 23 patients(15 male,8 female and mean age 43.6 years) with severe acute pancreatitis associated ARDS. The therapy of CVVH was performed continuously at least 72 hours. Three of these patients also received plasma exchange(PE) due to hyperlipoidemia. All patients received mechanical respiratory support.

**Results:** Among 23 patients, 22 survived and 1 died. The average duration of mechanical ventilation were 5.1±3.8 days. There were remarkable improvement in mean arterial blood pressure (MAP),heartrate(HR) and oxygenation index in survival group after CBP (P<0.05).The lactic acid and the scores of acute physiology and chronic health evaluation II (APACHE II) also declined in survival group after CBP (P<0.05). Compared to those before CBP, the serum TNF-α, IL-6, and CRP decreased significantly in survival group (P<0.05).

**Conclusions:** Continuous blood purification is effective in the treatment of patients with severe acute pancreatitis associated ARDS. The haemodynamic variables were stable during CBP and no obvious side-effects related to CBP were found.

**AO136**

**VENTILATORY DYSSYNCHRONY IN MECHANICALLY VENTILATED PATIENTS: IS IT A PROBLEM?**

**PETER SOTTILE**

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Despite significant advances in ventilator management, mortality from the acute respiratory distress syndrome (ARDS) remains unacceptably high. Mechanical ventilation with large tidal volume, high pressure ventilation, and repeated alveolar collapse can injure the lung, called ventilator induced lung injury (VILI). Defined as the inappropriate timing and delivery of a breath in response to a patient effort, ventilator dysynchrony (VD) may potentiate VILI despite low tidal volume ventilation.

However, until recently, VD was difficult to monitor and quantify. To better understand the role of VD, we developed an automated machine-learning algorithm that detects three types of VD from continuously measured ventilator pressure and flow waveforms. Using our algorithm, we demonstrated that VD is frequent and that two types of VD commonly deliver large tidal volumes—suggesting a plausible mechanism to cause lung injury. We then showed that the use of NMB, eliminating VD, was associated with decreased biomarkers of pulmonary epithelial and endothelial injury in patients, supporting that VD may indeed propagate VILI. Others have demonstrated that frequent VD, defined as 10% or greater of
breaths with evidence of VD, has been significantly associated with increased ICU duration and worse mortality. The optimal combination of ventilator and non-ventilator interventions to manage VD but avoid over sedation is unknown. Our data suggests that increasing PEEP may be associated with a decrease in flow-limited breaths, but may increase other types of VD. Additionally, we have demonstrated that sedation may reduce some types of VD, and that NMB eliminates all types of VD. However, the use of NMB needs to be balanced against its potential deleterious effects.

Consequently, reducing the frequency of VD may improve the outcomes of patients with or at-risk for ARDS if it can be balanced against the potentially negative side-effects of over sedation.

AO137

EFFICACY AND SAFETY OF ACETAZOLAMIDE FOR HYPERCAPNIC RESPIRATORY FAILURE ASSOCIATED WITH METABOLIC AKALOSIS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A META-ANALYSIS OF RANDOMIZED TRIALS

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Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) patients can develop respiratory acidosis and metabolic alkalosis, the latter causing impaired ventilation. Acetazolamide, a carbonic anhydrase inhibitor, can theoretically stimulate breathing by inducing mild metabolic acidosis. This study aims to determine safety and effectiveness of acetazolamide in reducing the duration of mechanical ventilation, length of Intensive Care Unit (ICU) stay and mortality among COPD patients with hypercapnic respiratory failure.

Methods: The authors searched several databases for randomized controlled trials of COPD patients with hypercapnic respiratory failure comparing acetazolamide versus placebo to reduce the duration of mechanical ventilation, length of intensive care unit stay and mortality, and arterial blood gas parameters. Two independent reviewers extracted data, assessed.

Results: Three randomized placebo-controlled trials were included in the analysis, with a total of 499 patients (246 – acetazolamide; 251 - placebo). All trials have low risk of bias. The use of acetazolamide showed a trend towards decreasing length of mechanical ventilation (mean difference [MD] -22.19 hours; 95% CI -49.87, 5.49; P = 0.12), shorter ICU stay (MD -2.31 days; 95% CI -5.80, 1.17; P = 0.19), but these were not statistically significant. All cause mortality was not significantly decreased (risk ratio [ RR] 0.88; 95% CI 0.53, 1.47; P = 0.63). There was no significant change in pH (MD -0.05; 95% CI -0.12, 0.03; P = 0.21) and decrease in CO2 (MD -0.06 kPa; 95% CI -0.18, 0.06; P = 0.36). There is mild improvement in oxygenation (MD 0.48 kPa; 95% CI 0.15, 0.82; P = 0.004).

Conclusions: Acetazolamide is not shown to improve blood gas parameters apart from a small improvement in oxygenation. Its use in such patients cannot be recommended yet based on currently available data.

Figure 3. Forest plot for duration of mechanical ventilation.

Figure 4. Forest plot for length of ICU stay (days).

Figure 5. Forest plot for all-cause mortality.

Figure 6. Forest plot for mean change in pH.

Figure 7. Forest plot for mean change in PaCO2 (kPa).

Figure 8. Forest plot for mean change in PaO2 (kPa).

AO138

THE ROLE OF CIAP2 IN AVIAN INFLUENZA A (H7N9) INDUCED ACUTE LUNG INJURY THROUGH INDUCING RIPK1/3-DEPENDENT NECROPTOSIS

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Background and Aim: Human infection with avian influenza A (H7N9) virus has been continuously reported since 2013. ARDS/ALI was the leading cause of the high mortality. Cell death of airway epithelia cells participated in ALI/ARDS. Necroptosis is a newly identified type of cell death. ciAP2 is involved in necroptosis as a key upstream regulation factor. We aimed to investigate the role of ciAP2 in ARDS/ALI induced by H7N9 virus through regulating RIPK1/3 necroptosis pathway.

Methods: Lung tissues of 11 patients dying from H7N9 infection and complicated with ARDS between 2013-2016 were obtained as the experimental group. Lung tissues near benign lung nodules were acquired as the control group. Histological changes of the lung tissues were evaluated by H&E staining. Protein levels of ciAP2, RIPK1, RIPK3, p-RIPK3, MLKL and p-MLKL in the lung tissues were detected by Western Blot.

Results:
1. A total of 22 cases of human infection with avian influenza A H7N9 virus has been hospitalized in Wuxi People’s Hospital since 2013 with a 50% mortality. All dead patients were complicated with ARDS.
2. In H&E staining, the experimental group showed broadened alveolar septum, congestion and infiltration of inflammatory cells and disordered airway epithelia.
3. The protein level of ciAP2 in the experimental group was significantly lower than that in control group. However, the experimental group showed higher RIPK1, RIPK3 and p-RIPK3 protein levels than control group, as well as the protein expression level of MLKL and p-MLKL, which is a key downstream protein in necroptosis. (P<0.05).
Conclusion: In human infection with H7N9 virus, ALI/ARDS was an important cause of its fatal prognosis. The low expression of clpA2 inhibited its combination with RIPK1, which caused the combination of RIPK1 and RIPK3. Necroptosis was then induced with the recruitment and activation of MLKL, which destructed the airway epithelium cells followed with ALI/ARDS and triggered the deaths of patients.

Induced Pluripotent Stem Cells Prevent Endothelial Cell Leakage Via TIMP-1 To Reduce FAK/Snail Pathway In Sepsis-Induced Acute Lung Injury

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Background and Objective: We investigated the effect of induced pluripotent stem cells (iPSCs) in moderating pulmonary endothelial leakage in endotoxin-induced acute lung injury (ALI).

Methods: Male C57BL/6 mice at 8 to 12 weeks of age were studied. Murine iPSCs were delivered through the tail veins of mice 4 hours after intratracheal instillation of lipopolysaccharide (LPS). Lung histopathological findings, proteins level and proinflammatory cytokines in peripheral blood and bronchoalveolar lavage fluid (BALF), expression of junctional proteins, and regulatory signaling pathways were analyzed after 24 hours. Human umbilical vein endothelial cells (HUVECs) were cultured as a relevant model as cells expressed major junctional proteins to be responsible for maintaining vascular integrity in vivo.

Results: iPSCs significantly diminished the histopathological changes of ALI mice compared to treatment with control cells. Proteins leakage, IL-6 and MIP-2 levels in BALF were significantly reduced in iPSC-treated ALI mice. The iPSC therapy restored VE-cadherin expression in the lung of ALI mice. iPSC reduced the permeability of HUVECs monolayer increased by LPS or VEGF. In HUVECs, the iPSCs restored the expression of VE-cadherin in response to LPS or VEGF via reducing Snail expression and phosphorylation of focal adhesion kinase (FAK) in Tyr937 (pFAK-Tyr937). We found conditioned medium of iPSCs (iPSC-CM) contained TIMP-1, an antiangiogenic factor. Pharmacological TIMP-1 inhibition significantly reduced the histopathological benefit and the change of VE-cadherin and pFAK-Tyr937 expression from iPSC-CM in ALI mice.

Conclusion: iPSCs attenuate endothelial cell leakage in endotoxin-induced ALI. These effects are mediated, at least in part, by the enhancement of TIMP-1 activity and reduction of FAK/Snail pathway.

Key Words: Induced pluripotent stem cell, endothelium; TIMP-1; acute lung injury

Short Title: iPSCs Reduce Pulmonary Endothelial Leakage

MIR-34B-5P Inhibition Alleviates Inflammatory Response and Apoptosis Via Targeting Progranulin in Acute Lung Injury Induced by Lipopolysaccharide

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Background and Aim: Recent studies have showed that progranulin (PGRN) plays essential roles in inflammation and apoptosis. We previously found down-regulation of PGRN during acute lung injury (ALI). However, the roles of PGRN and its miRNAs regulatory mechanisms has not been well studied in ALI. This study was to investigate the roles of PGRN-targeting miRNAs and whether PGRN involved in during ALI.

Methods: PGRN knockdown/overexpression and wild-type mice via locally instilling recombinant adenovirus containing the mouse PGRN gene and the mouse PGRN shRNA, were subjected to lipopolysaccharide for assessing the roles of PGRN in ALI. The bioinformatics method was used to screen potential miRNAs targeting PGRN in ALI, and determined the exact roles of miR-34b-5p and the mechanism involved in ALI through gain- and loss-of-function analysis in vivo and in vitro. The lung injury scores, apoptosis were then evaluated and analyzed. To explore underlying signaling pathways associated with alteration of miR-34b-5p, major proinflammatory cytokines were measured by quantitative polymerase chain reaction or ELISA and PGRN proteins were examined by Western blotting.

Results: PGRN was gradually increased in ALI (1-12h), and then significantly decreased to the lowest value at 24h. The gain- and loss-of-function analysis showed the protective effects of PGRN may be achieved by suppressing inflammatory mediators production and apoptosis. The results of bioinformatics method demonstrated that miR-34b-5p is apparently up-regulated among the 12 putative miRNAs. The dual-luciferase reporter assay validated that PGRN is the functional target of miR-34b-5p. Inhibition of miR-34b-5p ameliorated ALI and improved survival by reducing production of inflammatory mediators and apoptosis in vitro and in vivo. Furthermore, PGRN is necessary for the protective effects of miR-34b-5p inhibition for ALI.

Conclusion: miR-34b-5p knockdown attenuates ALI by affecting PGRN-regulated inflammatory response and apoptosis

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Pleural Research in Intensive Care (PRince-1) A Prospective Observational Study of Pleural Effusion Management

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Background and Aim: Pleural effusions affect 60% of patients in intensive care units (ICU) but their impacts and treatment are inadequately studied. Effusions are drained without full understanding of risks and benefits. Studies of the effects of fluid drainage on oxygenation and complication rates will improve clinical decision making. Aim. To determine frequency, efficacy and safety of pleural effusion drainage in ICU.

Methods: Prospective, observational, study across 4 ICUs. Screening: daily clinical rounds and chest radiographs reviewed weekly for significant pleural effusion. Inclusion Criteria: patients with - a. pleural effusion of > 2cm (maximum depth) on ultrasound or CT and b. treating physician decides impacting on clinical progress. Choice of drainage or medical management left to treating team. Exclusion: <18 years. Clinical, radiological, physiological and arterial blood gas data recorded at diagnosis of effusion, one hour pre and post-drainage and daily for three days. Outcomes: P:F ratio change from baseline, adverse events and mortality assessed at ICU and hospital discharge.

Results: 1064/2952 (35.7%) ICU admissions had pleural effusion on CXR. 102 (3.5%) deemed to warrant U/S or CT and to have effusions
clinically impacting upon patient. 39 patients (38.2%) underwent drainage - Drainage Group (DG). 63 patients (61.8%) formed the Medical Management Group (MMG). DG: Median (IQR) P:F ratio significantly increased from 185 (109) to 304 (123) and 260 (81) at 24 and 48 hours respectively (p<0.01). MMG: no change from baseline P:F ratio 269 (130) (Figure 1). No significant difference detected in adverse events between groups: DG 7/39 (17.9%), MMG 7/63 (11.1%), p=0.38, nor mortality (28.6% and 28.2%, p=0.89).

Conclusion: Drainage of clinically significant pleural effusions safely improves oxygenation in critically ill patients. Further research to guide effusion management in ICU is required.

Acknowledgement: EF and KH receive support from the WA Department of Health and YCGL from NHMRC.

![Figure 1. P:F ratio significantly increased from baseline at 24 and 48 hours in the drainage group and did not change in medically managed group](image)

Tuberculosis 3

A CLUSTER RANDOMISED CONTROLLED TRIAL OF CONTACT INVESTIGATION FOR THE DETECTION OF TUBERCULOSIS: THE ACT2 TRIAL

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Background and Aims: Active case-finding is a top priority for global tuberculosis (TB) control, but robust evidence for its effectiveness in high-prevalence settings is lacking. The ACT2 Trial evaluated the effectiveness of household contact investigation, compared to standard ‘passive’ measures alone, in Vietnam.

Methods: A cluster randomized controlled trial was performed at District clinics in eight provinces of Vietnam. Districts were allocated to perform household contact investigation plus standard ‘passive case-finding’, or ‘passive case-finding’ alone. In Intervention Districts, household contacts of patients with smear positive TB were invited for clinical assessment and chest radiography at baseline, six, 12 and 24 months. The primary outcome was the cumulative incidence of registered TB among contacts over two years. Secondary outcomes included cumulative incidence of smear-positive confirmed TB and all-cause mortality.

Results: In 70 selected Districts, 25,707 household contacts of 10,964 patients with smear positive pulmonary TB were enrolled. In 34 Districts randomized to Control, 110 of 15,638 contacts were registered as TB cases (703 per 100,000) within 2 years of enrolment. In 36 Districts randomized to the Intervention, 180 of 10,069 contacts were registered as TB cases (1,787 per 100,000). The relative risk (RR) of registering a case of TB in Intervention Districts, compared to Control Districts, was 2.5 (95% CI 2.0 – 3.2) and 6.4 (95% CI 4.5-9.0) for smear-positive confirmed TB. Importantly, all-cause mortality was lower among contacts in intervention Districts (RR 0.6; 95% CI: 0.5 - 0.8).

Conclusion: Household contact investigation was effective for enhancing detection of TB in a high-prevalence setting.

Background and Aim: Healthcare workers (HCW) are group of population that are prone to tuberculosis (TB). One of the tuberculosis infection control measure is the evaluation of HCW, especially those who have contact with TB patient. Interferon gamma release assays (IGRA) is a method for diagnosing latent TB infection (LTBI). The aim of this study is to evaluate the prevalence of LTBI in HCW in Persahabatan Hospital, a high burden TB hospital in Indonesia.

Methods: This cross sectional study was conducted among 99 HCW in Persahabatan Hospital who have contact with TB patient. Sample was recruited by consecutive sampling. The participants were subject to history taking, physical examination, chest X ray and gene xpert to exclude active TB. Interferon gamma release assays (IGRA) was administered to HCW who have contact with TB patient. There was a significant association between IGRA result and the working place (P = 0.001). The odd ratio of LTBI in TB outpatient clinic was 9.8 with CI 95% (2.554 – 37.43).

Conclusion: Prevalence of LTBI in HCW in Persahabatan Hospital by using IGRA was 37.4%. LTBI was affected by the working place.

Tuberculosis disease among healthcare workers: clinical characteristics, drug resistance and treatment outcomes in Chiang Mai University Hospital, Thailand

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Conclusion: Prevalence of LTBI in HCW in Persahabatan Hospital by using IGRA was 37.4%. LTBI was affected by the working place.
Background and Aims: Tuberculosis (TB) disease among healthcare workers (HCWs) highly impacts morbidity and TB transmission in a healthcare setting. We describe the clinical and microbiological characteristics and treatment outcomes of TB in HCWs.

Methods: A retrospective cohort study of TB in HCWs from a registered database during 2003 to 2016 at Chiang Mai University Hospital. Outcomes at the end of the treatment were evaluated.

Results: Seventy-eight cases of HCWs, 56 nurses (71.8%), 12 physicians (15.4%), and 10 paramedics (12.8%), were diagnosed as TB disease. Female: male ratio of 52:48, mean age of 37.0±14.0 years, median work duration of 12.0 years and body mass index of 19.4±2.5 kg/m². Numbers of TB cases, categorized by working place, were 28 (33.9%) in Medical department, 12 (15.4%) in out-patient department/emergency room (OPD/ER) and 11 (14.1%) in Surgical department. Pulmonary TB (PTB) is the most common (89.7%) manifestation of TB in HCWs, followed by extra-pulmonary TB (7.7%) and combined pulmonary and extra-pulmonary TB (2.6%). Although 60.3% were symptomatic, 39.7% had sub-clinical TB. The sputum acid-fast stains were positive in 30 (41.7%) HCWs with PTB. Cultures were positive in 27 (34.7%) cases, 92.6% was M.tuberculosis. Drug sensitivity patterns showed drug-susceptible TB of 76%, resistance to any one 1st-line drug of 19.2%, and multidrug-resistant TB (MDR-TB) of 3.7%. All of the Drug-resistant TB cases had never been treated for TB before. Success rate of treatment was 100% (46.1% cure and 53.9% complete treatment) in evaluable cases. None of them relapsed.

Conclusion: Our results indicate that HCWs are a high risk group for TB disease. Primary MDR-TB can be found in HCWs, which indicates hospital transmission of tuberculosis. Annual active TB screening in HCWs will enable early detection and treatment for improving outcomes. TB control guidelines should be strictly implemented to prevent TB transmission in healthcare setting.

Background and Aims: A private-initiated Programmatic Management for Drug Resistant Tuberculosis (PMDT) facility located in an urban community in Cavite, Philippines has been recognized by the Regional Health Office for its contribution to MDRTB detection and treatment. This study evaluated the treatment management and referral networks of this facility to determine best practices for improving MDRTB diagnostic and treatment outcomes.

Methods: The presumptive MDRTB masterlist, registry, individual records were reviewed for characteristics, treatment outcome of 2015 cohort. The sources of referral were also reviewed from the 2016 records of presumptive MDRTB patients.

Results: In 2015, 160 (84.2%) of the 190 diagnosed MDRTB were enrolled for treatment in this private initiated PMDT facility. The average turnaround time for enrolment was 25.9 days. The reasons for non-enrollment were illness denial, death, preference for other treatment facility. Among the enrolled, 90% were more than 15 y.o., 24% were diabetics, while one was HIV (+). Among those with known treatment outcome after 18 months, 38.6% (41/106) had successful outcome. 53% (53/106) were lost to follow-up, 9.4% (10/106) died, and 1.9% (2/106) failed. Reasons for those who lost to follow-up includes family concerns (35%), financial constraints (7.5%), adverse drug events (6%), co-morbidities (3%), relocation (2.5%), conflict with work/school (2.5%). Fifty-six (35%) had extended treatment beyond 18 months due to frequently missing doses. Review of 2016 reports showed that majority (73%) of referrals came from public facilities. Only 12% and 8% of referrals came from the hospitals and private physicians, respectively.

Conclusions: In spite of good and excellent services offered by the facility, high rate of lost to follow-up were reported. One third of the cases extended the treatment beyond 18 months. Interventions must be done to increase the treatment success rate. Majority of detected DRTB cases were referred from the nearby public health centers.

Respiratory Medicine (2017) 22 (Suppl. 3), 4-87
Methods: We analysed routinely collected data of newly notified MDR-TB patients from national TB surveillance system in Japan, in terms of treatment duration and co-morbidities. Treatment duration was calculated by subtracting the therapy start date from the therapy end date.

Results: Between 2011 and 2012, a total of 147 MDR-TB patients were newly notified to TB surveillance. 85 (57.8%) had completed treatment at the end of 2015. Duration of treatment was calculated for 80 (94.1%) patients. Mean of treatment duration was 724 days. Median of treatment duration by age group 0-29, 30-39, 40-49, 50-59, 60-69, 70+ was 761 days and interquartile range was 563-859 days. Mean of treatment duration by male and female was 737 days and 694 days respectively. Mean of treatment duration by male and female was 737 days and 694 days respectively. There were 36 patients cured/completed treatment, 8 who passed away, 28 had defaulted treatment and 12 patients were transferred out to other center for continuation of treatment. Majority was male patient, 27 (61.4%) and foreigner (Myanmar majority) about 50% out of the patient being treated. Diabetic patient around 40.9% among treated MDR TB cases. Around 36.2% were active and former smoker. All patients were started on conventional MDR TB regimen with injectable drug for period of 20 to 24 months. Treatment success rate was 42.8%. We found significant correlation in advanced radiological changes (p<0.012) poor nutrition in term of low albumin (p<0.021) and Malaysian citizen (p=0.045). Side effects from treatment; hypothyroidism (25%) followed by neurological side effect mainly psychosis (15.9%) and others were renal failure, ototoxicity, rashes, joint pain and gynecomastia. Only 6 patients required change of regime due to side effects.

Conclusion: Our result demonstrated that majority of MDRTB cases were primary and foreign borne patients. Advanced radiological findings, poor nutrition and Malaysian citizen were associated with poor outcome and there is trend noted in older age with poor outcome.

Background and Aim: WHO reports increasing numbers of multi-drug resistant tuberculosis(MDR-TB) cases worldwide over the years. These pose huge public health threats and major obstacles to the clinicians due to their complicated and long treatment duration with high mortality rate as compared to pan susceptible tuberculosis (TB).

Methods: A retrospective study of MDR-TB patients treated between January 2011 and December 2014. The aim is to study the demographic characteristic and describe the outcome of MDRTB treatment.

Results: 84 MDRTB cases were being diagnosed in the period of 4 years in our center. Primary MDR TB being majority diagnosed in our cases around 59.1%. Our MDR TB cases mainly pulmonary in origin (97.7%). There were 36 patients cured/completed treatment, 8 who passed away, 28 had defaulted treatment and 12 patients were transferred out to other center for continuation of treatment. Majority was male patient, 27 (61.4%) and foreigner (Myanmar majority) about 50% out of the patient being treated. Diabetic patient around 40.9% among treated MDR TB cases. Around 36.2% were active and former smoker. All patients were started on conventional MDR TB regimen with injectable drug for period of 20 to 24 months. Treatment success rate was 42.8%. We found significant correlation in advanced radiological changes (p<0.012) poor nutrition in term of low albumin (p<0.021) and Malaysian citizen (p=0.045). Side effects from treatment; hypothyroidism (25%) followed by neurological side effect mainly psychosis (15.9%) and others were renal failure, ototoxicity, rashes, joint pain and gynecomastia. Only 6 patients required change of regime due to side effects.

Conclusion: Our result demonstrated that majority of MDRTB cases were primary and foreign borne patients. Advanced radiological findings, poor nutrition and Malaysian citizen were associated with poor outcome and there is trend noted in older age with poor outcome.
Background and Aims: Patients completing treatment for tuberculosis (TB) in high-prevalence settings face risk of developing recurrent disease. Despite the public health impact of TB recurrence, little is known about how individual demographic and clinical factors might co-act to impact relapse.

Methods: Subjects were 538 cases and 618 controls drawn from a large prospective cohort study of 10,964 smear positive pulmonary TB patients in eight provinces in Vietnam. Data were collected on a number of personal demographic factors such as age, income, education, and tobacco and alcohol consumptions. Clinical factors such as HIV and diabetes diagnoses, whether the patient had drug resistant TB (MDR-TB), and treatment adherence were also recorded. Stepwise logistic regression modelling methods were used to identify an updated model for odds of recurrence.

Results: The final model included MDR-TB (OR = 124.6; 95% CI: 30.7 – 506.4), past history of TB (OR = 2.8; 95% CI: 1.9 – 3.9), incomplete adherence (OR = 2.0; 95% CI: 1.3 – 3.1), alcohol use (OR = 0.63; 95% CI: 0.5 – 0.9), and urban residence (OR = 1.6; 95% CI: 1.2 – 2.1). There were no significant interactions.

Conclusion: Using data from a nested case-control study, we created a multivariate model of risk factors and the odds of recurrent tuberculosis in a resource poor area. Further research should determine whether these factors impact both relapse or re-infection, and which factors can be most reliably addressed in a clinical setting to impact disease recurrence in high burden countries.

Lung Cancer 2

EXAMINATION OF THE RATE OF QUITTING TO SMOKE AMONG SMOKER PATIENTS WHO UNDERWENT LUNG CANCER OPERATION

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1Department of Surgery, Toho University Ohashi Medical Center, Tokyo, Japan

Background and Aims: Smoking is the leading cause of lung cancer. For smokers, surgical hospitalization is likely to be a good motivator to quit smoking.

Methods: Data was collected from respiratory surgery patients between April 2009 to June 2015. They were primary lung cancer (P-group) - 160 cases, metastatic lung cancer (M-group) - 54 cases. Smoking history (smoker/non-smoker or never-smoker, number of cigarettes smoked per day, number of years smoking, Brinkmen Index(BI), Nicotine dependence test (TDS) was enforced in some cases) was checked in each case at before hospitalization or at hospitalization. The main outcome is set in the smoking status 1) at pre-hospitalization, 2) at discharge, 3) at one month after discharge and 4) three months after discharge. Patients who were smoking until just before the operation were specifically given attention to see whether the post-operative non-smoking instructions had become a motivation to quit.

Results: Patient with smoking history was 115 cases in P-group (72%), 26 cases in M-group(48%). BI average was 941 in P-group, 753 in M-group. Patients who smoked until just before operation was 36 cases in P-group (23%), 5 cases in M-group (9%). Non-smoking achievement rate by post-operative instruction at post-operative three months was 78% in P-group, 100% in M-group. However, postoperative re-smoking was seen in 8 cases in P-group.

Conclusions: More than 70% of patients achieved 3-months non-smoking status after undergoing surgery and were given post-operative non-smoking instructions. This suggests that hospitalization for respiratory surgery can become a motivator for smokers to quit the habit.

Figure 1. Recruitment and management flow-chart

UPDATE FROM THE LUNGSEREN WA PROJECT – A FEASIBILITY STUDY OF LOW-DOSE CT LUNG CANCER SCREENING OF HIGH-RISK EVER SMOKERS IN AUSTRALIA

Kuan Pin Lim1, David Manners2, Brendan Adler2, Stephen Melson2, Edward Harris3, Fraser Brims1,4,5, Annette McWilliams3,4,5

1Sir Charles Gardiner Hospital, Nedlands, Australia, 2St. John of God Midland Public Hospital, Midland, Australia, 3Fiona Stanley Hospital, Murdoch, Australia, 4Curtin Medical School, Faculty of Health Sciences, Curtin University, Perth, Australia, 5Institute for Respiratory Health, Nedlands, Australia, and 6University of Western Australia, Perth, Australia

Background and Aims: Important knowledge gaps remain regarding the lung cancer screening with LDCT. To evaluate the feasibility of lung cancer screening in the Australian healthcare setting using the PLCOm2012 model to identify high-risk participants and the Brock nodule malignancy risk-calculator to guide management of detected pulmonary nodules.

Methods: Current or former smokers, aged 55-74 years, were recruited from the community. Eligibility for LDCT screening was defined as PLCOm2012 ≥1.51% over 6 years. Participants underwent interview, spirometry and LDCT chest. The nodule risk score from the Brock University (PanCan) nodule malignancy risk-calculator was used to guide follow-up (Figure 1). Enrolment commenced in March 2015 and we report results after 24-month follow-up.

Results: 104 enquiries were received, of which 53 were eligible for screening and 49 completed baseline screening LDCT. In the eligible group, the median age was 66 (IQR 62-71) years and median PLCOm2012 risk was 3.48% (IQR 2.56-5.70) (Table 1). Nodules were detected in 53.1% (26/49) participants. 46.9% (23/49) participants had spirometric evidence of COPD. Other CT findings included coronary artery calcification in 77.6% (38/49), emphysema in 65.3% (32/49) and interstitial lung disease in 4.1% (2/49) (Table 2). Of the 26 participants with pulmonary nodules, the PanCan risk scores of the highest-risk nodule were >10% in 2 participants (7.7%), 6-10% in 6 (23.1%), 1.5-6% in 5 (19.2%) and <1% in 12 (46.2%) (Table 3). Using this approach, based on risk scores, 65.4% of participants with nodules did not require further investigations within the first year of screening. Lung cancers were identified in 2 screened participants (4.1%) – 1 underwent surgical resection of a Stage 1b adenocarcinoma, and the other participant had an enlarging nodule treated with stereotactic radiotherapy. 1 further participant is due surgery a 53mm3 enlarging, slow-growing nodule.

Conclusions: A targeted, algorithmic approach to lung cancer screening is feasible and identifies early-stage lung cancers.
Table 1. Baseline demographics and eligibility parameters of participants

<table>
<thead>
<tr>
<th></th>
<th>CT-eligible (n=53)</th>
<th>CT-ineligible* (n=26)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (IQR)</td>
<td>66 (62–71)</td>
<td>62 (58–65)</td>
<td>0.146</td>
</tr>
<tr>
<td>Mean Age (±SD)</td>
<td>65.7 (±5.3)</td>
<td>63.1 (±5.0)</td>
<td>0.037</td>
</tr>
<tr>
<td>Gender (Ratio of M:F)</td>
<td>27 M, 26 F (1.04)</td>
<td>16 M, 10 F (1.60)</td>
<td>0.374</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>52 (98.1%)</td>
<td>26 (100%)</td>
<td>–</td>
</tr>
<tr>
<td>Highest Level of Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Less than high school</td>
<td>13 (24.5%)</td>
<td>2 (7.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>- High school</td>
<td>7 (13.2%)</td>
<td>6 (23.1%)</td>
<td>–</td>
</tr>
<tr>
<td>- Post-high school</td>
<td>15 (28.3%)</td>
<td>1 (3.8%)</td>
<td>–</td>
</tr>
<tr>
<td>- Some college</td>
<td>6 (11.3%)</td>
<td>2 (7.7%)</td>
<td>–</td>
</tr>
<tr>
<td>- College graduate</td>
<td>11 (20.8%)</td>
<td>10 (38.5%)</td>
<td>–</td>
</tr>
<tr>
<td>- Post-graduate/ Professional</td>
<td>1 (1.9%)</td>
<td>5 (19.2%)</td>
<td>–</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>25 (51.0%)</td>
<td>5 (19.2%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Mean number of pack years (SD)</td>
<td>51.6 (±15.4)</td>
<td>22.6 (±14.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of lung cancer (%)</td>
<td>13 (24.5%)</td>
<td>2 (7.7%)</td>
<td>0.125</td>
</tr>
<tr>
<td>History of malignancy</td>
<td>10 (18.9%)</td>
<td>1 (3.8%)</td>
<td>0.090</td>
</tr>
<tr>
<td>Self-reported history of COPD/emphysema (%)</td>
<td>17 (32.1%)</td>
<td>3 (11.5%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Median PLCOm2012 score (IQR)</td>
<td>3.48% (2.56–5.70)</td>
<td>0.664% (0.26–1.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eligibility by NLST criteria (%)</td>
<td>43 (81.1%)</td>
<td>2 (7.7%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*: Participants excluded solely based on PLCOm2012 risk score only.

Table 2. Demographics, spirometry and CT-findings in screened participants

<table>
<thead>
<tr>
<th></th>
<th>All, n=49</th>
<th>Nodule positive, n=26</th>
<th>Nodule negative, n=23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (SD)</td>
<td>66.0 (±5.3)</td>
<td>65.5 (±5.3)</td>
<td>66.5 (±5.4)</td>
</tr>
<tr>
<td>Median Age (IQR)</td>
<td>66 (62–71)</td>
<td>64 (62–70.5)</td>
<td>66 (64.5–70.5)</td>
</tr>
<tr>
<td>Gender (Ratio of males: females)</td>
<td>25 M, 24 F (1.04)</td>
<td>14 M, 12 F (1.17)</td>
<td>11 M, 12 F (0.92)</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>23 (46.9%)</td>
<td>12 (46.2%)</td>
<td>11 (47.8%)</td>
</tr>
<tr>
<td>Mean number of pack years (SD)</td>
<td>51.1 (±15.6)</td>
<td>47.2 (±12.0)</td>
<td>55.7 (±18.3)</td>
</tr>
<tr>
<td>Median PLCOm2012 score (IQR)</td>
<td>3.48% (2.43–5.65)</td>
<td>3.34% (2.64–5.07)</td>
<td>3.60% (2.41–7.96)</td>
</tr>
<tr>
<td>Number of nodule-positive scans</td>
<td>26 (53.1%)</td>
<td>–</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Table 3. Parameters of the screen-detected nodules

<table>
<thead>
<tr>
<th>Nodule on Baseline Screening LDCT, n=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean size-long axis in mm (SD)</td>
</tr>
<tr>
<td>Median size-long axis in mm (IQR)</td>
</tr>
<tr>
<td>Location</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Nodule type</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Spiculation present (solid nodules)</td>
</tr>
<tr>
<td>Nodule risk score by PanCan nodule risk calculator (of highest-risk nodule, n=26)</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tbody>
</table>
PROTOCOL FOR THE INTERNATIONAL LUNG SCREEN TRIAL (ILST): A COHORT STUDY TO DEFINE LDCT SCREENING SELECTION CRITERIA AND VALIDATE THE PANCan NODULE MANAGEMENT ALGORITHM

KUAN PIN LIM1,2, FRASER BRIMS1,3, ANNETTE MCWILLIAMS2,4, MARTIN TAMMEMÄGI5, CHRISTINE BERG6, HENRY MARSHALL7, EMILY STONE8, RENEE MANSER9, KAREN CANFELL10,11,12, LUKE CONNELLY13,14,15,16, JOHN YEE17,18, KWUN FONG9, STEPHEN LAM17,19

1Department of Respiratory Medicine, Sir Charles Gairdner Hospital, Nedlands, Australia, 2Department of Respiratory Medicine, Fiona Stanley Hospital, Murdoch, Australia, 3Curtin Medical School, Faculty of Health Sciences, Curtin University, Bentley, Australia, 4University of Western Australia, Crawley, Australia, 5Department of Health Services, Brock University, St. Catharines, Canada, 6Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins Medicine, Baltimore, MD, USA, 7University of Queensland Thoracic Research Centre and Department of Thoracic Medicine, The Prince Charles Hospital, Chermside, Australia, 8Department of Thoracic Medicine, St. Vincent’s Hospital and Kinghorn Cancer Centre, Darlington, Australia, 9Department of Respiratory Medicine, Royal Melbourne Hospital, Parkville, Australia, 10Cancer Research Division, Cancer Council New South Wales, Sydney, Australia, 11Sydney School of Public Health, University of Sydney, Camperdown, Australia, 12Prince of Wales Clinical School, University of New South Wales, Sydney, Australia, 13Australian Centre for Economic Research on Health (ACERH), University of Queensland, Brisbane, Australia, 14Centre for National Research on Disability and Rehabilitation Medicine (CONROD), Brisbane, Australia, 15Faculty of Health and Behavioural Sciences, University of Queensland, St. Lucia, Australia, 16Asian-Pacific Centre of Neuromodulation, Queensland Brain Institute, St. Lucia, Australia, 17The University of British Columbia, Vancouver, Canada, 18Department of Thoracic Surgery, Vancouver General Hospital, Vancouver, Canada, and 19British Columbia Cancer Agency (BCCA), Vancouver, Canada

Background and Aims: The NLST reported a 20% reduction in lung cancer mortality with LDCT screening. The USPSTF recommends annual screening of current/former smokers aged 55-80 years with ≥30 pack year smoking history and smoking cessation ≤15 years ago. There remain important questions surrounding the best screening selection criteria and optimal management of screening-detected pulmonary nodules. For predicting lung cancer in 6 years, the PLCOm2012 risk prediction model has a higher sensitivity and positive predictive value than the NLST criteria on analysis of the PLCO ever-smokers. The PanCan model calculates nodule malignancy probability to stratify nodule management and is recommended by the BTS and ACR for management of screening-detected nodules. The International Lung Screen Trial (ILST) is a multi-centre prospective cohort study with recruitment sites in Canada and Australia. The aims are to: (a) define the optimal selection criteria for LDCT screening, and (b) prospectively evaluate lung nodule management using the PanCan nodule risk calculator.

Methods: We aim to recruit 4,000 high-risk individuals with 5 years follow-up. Eligible participants are current/former smokers, aged 55-80 years, with a PLCOm2012 risk prediction score of ≥ 1.51%/6years or USPSTF criteria for LDCT screening (Figure 1). Participants are offered screening LDCT and subsequent surveillance scans dependent on the PanCan risk score (Table 1). The primary outcome is the proportion of lung cancers detected by either selection criteria. Secondary outcomes include: number needed to screen, cancer detection rate, lung cancer mortality, cancer stage distribution, resection rate, interval cancers, recall rate, invasive procedure rate, benign biopsy/surgery rate, screening-related adverse events and healthcare economic evaluation.

Results: This study is in its recruitment phase. Results will be reported in future conferences and peer-reviewed publications.

Conclusions: The ILST trial will provide a clearer understanding on the optimum selection criteria for LDCT screening for lung cancer and prospective validation of the PanCan model.

ClinicalTrials.gov number: NCT02871856

---

**Table 1**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>LCT findings and PanCan nodule risk</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT1</td>
<td>Normal findings</td>
<td>Nodule risk index &lt;1 Biennial LDCT</td>
<td>Repeat LDCT in 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>.5%, benign calcification, harmatoma or peri-fissural nodule</td>
<td>Consider immediate investigation</td>
</tr>
<tr>
<td>CAT2</td>
<td>Low malignancy risk</td>
<td>Nodule risk index 1.5 to &lt;6%</td>
<td>Annual LDCT</td>
</tr>
<tr>
<td>CAT3</td>
<td>Moderate malignancy risk</td>
<td>Nodule risk index 6 to &lt;10%</td>
<td>Repeat LDCT in 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nodule risk index 10 to &lt;30% or interval growth</td>
<td>Consider immediate investigation</td>
</tr>
<tr>
<td>CAT4</td>
<td>High malignancy risk</td>
<td>Nodule risk index &gt;30%</td>
<td>Immediate investigation</td>
</tr>
<tr>
<td>CAT5</td>
<td>Suspicious for lung cancer</td>
<td>Mass lesion of non-infectious aetiology, mediastinal/hilar lymphadenopathy irrespective of nodule size or endobronchial nodule</td>
<td>Immediate investigation</td>
</tr>
</tbody>
</table>

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PREDICTION MODELING USING ROUTINE CLINICAL PARAMETERS TO STRATIFY SURVIVAL IN MESOTHELIOMA PATIENTS UNDERGOING SURGERY

EDWARD HARRIS1,2, STEVEN KAO3,4, TAKASHI NAKANO5, NOBUYUKI KONDO6, ANNA NOWAK1,7, FRASER BRIMS1,2
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Background: Malignant pleural mesothelioma (MPM) is a rare cancer with a heterogeneous prognosis. The role of surgical intervention on a select population (i.e. with better functional status) is controversial, however, has been practiced in specialist centres. We have previously described and validated a prognostic model using a classification and regression tree (CART) model to analyse the interaction of multiple variables with survival in a broad MPM population.(1)

Aim: To test the performance of our CART prediction model on a population with MPM who had surgical intervention.

Methods: Cases from Australia and Japan with confirmed MPM who underwent surgery were analysed. Clinical variables available at the time of referral were recorded (some retrospectively and some prospectively as part of the IASLC mesothelioma staging project). The model uses combinations of different variables (Table 1) to stratify participants into different risk groups (1-4) and the survival characteristics were compared using the Log Rank test.

Table 1. Risk group characteristics

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>Variables:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>No</td>
<td>No</td>
<td>Yes/missing</td>
<td>Yes/missing</td>
</tr>
<tr>
<td>Haemoglobin g/L</td>
<td>&gt;153</td>
<td>121–153</td>
<td>&gt;153</td>
<td>121–153</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>&gt;43/missing</td>
<td>&gt;43</td>
<td>&lt;43</td>
<td>&lt;43</td>
</tr>
<tr>
<td>Histological Diagnosis</td>
<td>Epi/ND</td>
<td>Epi/Bi/ND</td>
<td>Bi/Sarc</td>
<td>Bi/Sarc</td>
</tr>
<tr>
<td>ECOG Performance Status</td>
<td>0–1/missing</td>
<td>0–1/missing</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Histological Diagnosis</td>
<td>Epi/Bi/ND</td>
<td>Epi/Bi/ND</td>
<td>Sarc</td>
<td>Sarc</td>
</tr>
<tr>
<td>n= per subgroup</td>
<td>18</td>
<td>61</td>
<td>2</td>
<td>140</td>
</tr>
<tr>
<td>Total n=</td>
<td>18</td>
<td>63</td>
<td>140</td>
<td>68</td>
</tr>
</tbody>
</table>

Table 2. Baseline parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total N</th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>289</td>
<td>63 (IQR 57.0-67.8)</td>
</tr>
<tr>
<td>Male</td>
<td>289</td>
<td>240 (83.0)</td>
</tr>
<tr>
<td>Right side</td>
<td>215</td>
<td>119 (55.3)</td>
</tr>
<tr>
<td>Histological diagnosis</td>
<td>289</td>
<td></td>
</tr>
<tr>
<td>Epithelioid</td>
<td>220 (80.9)</td>
<td></td>
</tr>
<tr>
<td>Biphasic</td>
<td>52 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Sarcomatoid</td>
<td>15 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Not defined</td>
<td>2 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>232</td>
<td>85 (36.6)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>171</td>
<td>93 (54.4)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>241</td>
<td>70 (29.0)</td>
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<tr>
<td>ECOG PS</td>
<td>182</td>
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<tr>
<td>0</td>
<td>167 (91.8)</td>
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<td>1</td>
<td>15 (8.2)</td>
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<tr>
<td>Surgical Procedure</td>
<td>289</td>
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<tr>
<td>Partial Pleurectomy</td>
<td>171 (5.9)</td>
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<tr>
<td>Pleurectomy/Decortication</td>
<td>88 (30.4)</td>
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<td>Extended Pleurectomy/ Decortication</td>
<td>20 (6.8)</td>
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<td>Extrapleural pneumonectomy</td>
<td>164 (56.7)</td>
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<tr>
<td>Survival (months)</td>
<td>289</td>
<td>34.6 (IQR 17.5-56.1)</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan Meier plot of mesothelioma survival stratified by risk group.

Respirology (2017) 22 (Suppl. 3), 4–87 Editorial material and organization © 2017 Asian Pacific Society of Respirology. Copyright of individual abstracts remains with the authors
Results: A total of 289 cases were included (205 from Australia and 84 from Japan) who had surgery between 1991-2016. Overall median survival was 34.6 (IQR 17.5-56.1) months; median age 63.0 (IQR 57.0-67.8) years, 240/289 (83.0%) were male. Baseline characteristics are presented in Table 2. There were no clinically meaningful differences between the cohorts; 40 patients were alive at censure. Survival across the risk groups was significantly different (Figure 1; Log Rank test p<0.0001). The group with the longest survival (median 78.1, IQR 28.1-152.4 months) had no weight loss, Hb >153g/L and serum albumin >43g/L at the time of referral to specialist surgical centre.

Conclusions: The combination and interaction of simple, routine, clinical variables available early after diagnosis of MPM is able to stratify survival and discriminate higher and lower risk of death in high performance status patients.

REFERENCE

LUNG CANCER IN THE EASTERN PART OF LIBYA
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1Respiratory Medicine, Benghazi University, Benghazi Medical Centre, Benghazi, Libya, 2General Medicine, Benghazi Medical Centre, Benghazi, Libya, and 3Oncology Department, Benghazi Medical Centre, Benghazi, Libya

Background and Aim: Data about lung cancer are scarce in Libya. This is causing real challenges in healthcare planning, patient care and management. The aim of the study was to establish basic data about diagnosed lung cancer cases in the Eastern part of Libya.

Method: All known cancer patients in the Eastern part of Libya are routinely referred to and managed at the Oncology Department of Benghazi Medical Centre (OD-BMC) with catchment area of 2 millions populations. We retrospectively reviewed the medical files of all cancer patients managed at OD-BMC in the years between 2006 and 2015. The total number of new cancer cases for each year was determined and files of lung cancer cases were reviewed. Demographic data, histological types and staging of lung cancer cases were obtained. Files with incomplete data were excluded from analysis. Lung cancer diagnosis required multidisciplinary team decision.

Results: Over ten years period 7916 cancer cases were managed at OD-BMC. 690 (8.7%) cases had lung cancer. 618 (89%) were males and the mean age was 62.3 years (24-91) years. Smoking history was positive in 85.5% of lung cancer cases. 38% had adenocarcinoma, 20% had squamous cell, 9% had small cell histological subtypes. On average 69 new lung cancer cases were seen every year (table).

Conclusion: Over 10 year’s period lung cancer represented 8.7% of all cancer patients undergoing lung cancer surgery in the Eastern part of Libya. On average; 34 lung cancer cases were newly diagnosed per million populations per year.

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</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer %</td>
<td>4.5</td>
<td>9.8</td>
<td>9</td>
<td>9.4</td>
<td>10</td>
<td>6.4</td>
<td>8.6</td>
<td>9.8</td>
<td>9.4</td>
<td>8.2</td>
</tr>
<tr>
<td>Lung cancer (%)</td>
<td>26 (573)</td>
<td>75 (762)</td>
<td>65 (716)</td>
<td>72 (764)</td>
<td>79 (782)</td>
<td>49 (757)</td>
<td>86 (990)</td>
<td>90 (912)</td>
<td>90 (954)</td>
<td>58 (706)</td>
</tr>
</tbody>
</table>

A RARE CASE OF CONCOMITANT MEDULLARY THYMOMA WITH MULTIDRUG-RESISTANT TUBERCULOSIS
ACHMAD GOZALI1, SITA LAKSMI ANDARINI2, PRIYANTI Z SOEPANDI1, ELISNA SYAHRUDDIN1, BUDHI ANTARKSA1
1Department of Pulmonology and Respiratory Medicine, Universitas Indonesia, Persahabatan Hospital, Jakarta, Indonesia

Background and Aim: Thymoma is a common primary tumor in mediastinum which originates in the thymus. Treatment strategies of thymoma depend on the stage of disease. It consists of a combination of surgery, chemotheraphy and radiotherapy. However, the coexistence of thymoma with MDR TB has never been reported. We present a rare case of medullary thymoma in a patient who is undergoing MDR-TB treatment.

Methods: Case report: Herein we report a case of 49 years old male who was admitted to our hospital in January 2017 for complaining of dyspnea and non productive cough. Chest x-ray showed an unusual shadow right side of the heart. After a extensive work up including chest computed tomography (CT) and core biopsy, a diagnosis of medullary thymoma was made. He also had a history of TB infection and had finished his TB treatment in 2015 for 9 months. GenXpert MTB/RIF test revealed rifampicin resistant so he was diagnosed with MDR-TB. He was treated with radiotherapy for the thymoma along with his MDR-TB therapy. He was planned to do the surgery after the conversion of MTB culture and considered to get chemotherapy afterwards.

Results: Discussion: In this patients, the surgery was planned to be performed after the conversion of MTB so the surgery wound healing could be assumed to be well. However, the chemotherapy needs to be put into a huge consideration given the MDR-TB drugs alone have caused so many side effects.

Conclusion: Management of patients with thymoma also depends on the comorbidity.

COMBINED USE OF A LARYNGEAL MASK AIRWAY DURING EXTUBATION REDUCES THE INCIDENCE OF POSTOPERATIVE PULMONARY FISTULA IN PATIENTS UNDERGOING LUNG CANCER SURGERY
HIKARU WATANABE1, ISAMU WATANABE1, NAOKI KANAUUCHI1
1Department of General Thoracic Surgery, Nihonkai General Hospital, Yamagata, Japan

Background and Aims: Prolonged pulmonary fistula after pulmonary resection requires an increased drainage duration. In pulmonary resection, one of the measures to minimize air leakage and reduce the drainage duration may be laryngeal mask exchange: exchanging the endotracheal tube for a laryngeal mask airway during extubation. To determine whether the use of a laryngeal mask airway during extubation reduces the postoperative drainage duration and the incidence of postoperative air leakage.

Methods: We enrolled 178 patients with primary lung cancer who underwent pulmonary resection at our hospital between 2014 and 2016. The patients were divided into two groups: the extubation with a laryngeal mask airway group (LM group; n = 79) and the usual extubation group (Usual group; n = 99). Postoperative pulmonary fistula was defined as prolonged pulmonary fistula lasting beyond postoperative day 7 and that required additional treatments. The patient background characteristics were adjusted by propensity
Background and Aims: Airway closure plays an important role in a number of respiratory diseases including asthma. Recently the forced oscillation technique (FOT) has been used to identify airway closure by performing a deflation maneuver and examining the resultant reactance (Xrs) lung volume relationship. In this study we tested the hypothesis that there are two independent lung volume markers of airway closure during de-recruitment. The first, at initiation of de-recruitment (DR1) and the second at onset of rapid de-recruitment (DR2). We also hypothesize that these lung volumes correlate with different physiological markers.

Methods: Two subject groups were used in the study, asthmatics (n=20) and controls (n=19). Xrs lung volume curves were generated via FOT and a slow vital capacity maneuver. The two markers of airway closure, DR1 and DR2 were identified on the Xrs lung volume relationship. By method of least squares regression, DR1 and DR2 were compared to other physiological measurements obtained via spirometry, multiple breath nitrogen washout and an asthma questionnaire. Differences in asthmatic and control data were also statistically compared.

Results: Asthmatic and control subjects exhibited different shaped de-recruitment patterns. Asthmatic subjects had higher closing volumes (DR1vol and DR2 vol) (p<0.001), and more negative Xrs (DR1 Xrs and DR2 Xrs) (p<0.01). The rate of de-recruitment of the asthmatic subjects was also significantly slower than the control group (p=0.01). In the control group DR2 was significantly effect by age (r2=0.64). Furthermore subjects with an age greater than 70 can expect rapid de-recruitment during normal tidal breathing. In the asthmatic group DR1 vol was highly correlated (r2=0.35) with symptoms and physiological markers of disease (Scond, Sacin, ACQ6, FEV1 and FER), whereas DR2 vol displayed poor correlation.

Conclusions: This study shows the initiation and rate of lung de-recruitment is altered in asthmatics, while rapid de-recruitment increases with age.

AOL010

FORCED OSCILLATION TECHNIQUE AS A PREDICTOR OF EXERCISE TOLERANCE IN COPD
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1Department of Respiratory Medicine, Shizuoka General Hospital, Shizuoka, Shizuoka, Japan

Background and Aims: Expiratory flow limitation (EFL) during tidal breathing is a major determinant of dynamic hyperinflation and exercise limitation in COPD. The forced oscillation technique (FOT) has been reported to detect EFL. However, the usefulness of the FOT for predicting exercise tolerance in patients with COPD is unknown. In this prospective study, we investigated whether FOT could predict a poor 6-min walking distance (6MWD) (<350 m) in the 6-min walking test (6MWT).

Methods: Subjects included 57 outpatients with COPD (54 males and 3 females; median age, 71 years; smoking history, 50 pack-years; and %FEV1, 61.0%). Modified MRC dyspnea scale (mMRC), COPD Assessment Test (CAT), FOT (MostGraph-01), spirometry, and 6MWT were performed in a stable condition. Colored 3D images of forced oscillatory parameters were obtained by using MostGraph-01. The patients were classified into two groups: good (≥350 m) or poor 6MWD (<350 m) and the predictor of poor 6MWD was assessed.

Results: Between the two groups, there were significant differences in gender, CAT score, mMRC, %FEV1, IC, respiratory resistance (Rrs) and reactance (Xrs). There were significant correlations between 6MWD and the CAT score (rho= −0.451), mMRC (−0.381), %FEV1 (0.382), IC (0.346), Rrs at 5 Hz (R5) (−0.277), RS-R20 (−0.314), Xrs at 5 Hz (0.298), resonant frequency (−0.396), and low reactance area (−0.326). In multivariate regression analysis, a poor 6MWD was independently predicted by CAT score (OR 1.15, 95% CI: 1.01-1.30) and RS (OR 6.01, 95%
CI:1.09-33.30). In receiver operating characteristic curves, the area under the curve was 0.76, 0.78 and 0.85 for CAT score, R5 and CAT score + R5, respectively (Figure 1). Figure 2 shows the typical colored-3D images of FOT parameters in the representative good or poor 6MWD patients.

Conclusions: A forced oscillatory parameter, R5, was a predictor of exercise tolerance in COPD.

AOL011
ASSESSING DIRECT SWITCH TO INDACATEROL/GLYCOPYRRONIUM FROM SALMETEROL/FLUTICASONE IN MODERATE TO SEVERE SYMPTOMATIC COPD PATIENTS: THE FLASH STUDY
PETER FRITH1, SAMIHA ASHMAWI2, SRIKANTH KRISHNAMURTHY3, DINA DIAZ4, ALEV GURGUN5, PEGGY HOURS-ZESIGER6, SASHKA HRISTOSKOVÀ5, VIRGINIA PILIPOVIC2
1Respiratory Medicine, Southern Adelaide Health Service, Repatriation General Hospital, Daw Park, Australia, 2Ain Shams University, Cairo, Egypt, 3Ain Shams University, Cairo, Egypt, 4Sri Bala Medical Centre and Hospital, Coimbatore, India, 5Lung Center of the Philippines, Manila, Philippines, 6Ege University Medical Faculty, Izmir, Turkey, and 7Novartis Pharma AG, Basel, Switzerland

Background and Aims: Several randomised head-to-head studies have shown superior clinical outcomes with indacaterol/glycopyrronium (IND/GLY) versus salmeterol/fluticasone combination (SFC) in patients with moderate-to-severe COPD. The present FLASH study investigated if switching symptomatic COPD patients directly (no washout period) from SFC to IND/GLY is safe and leads to improved lung function.

Methods: FLASH was a 12-week, multicentre, double-blind, double-dummy, parallel-group study. Patients with moderate to severe COPD and daily symptoms, but infrequent exacerbations (<2 within 1 year), who were receiving SFC 50/500 μg twice daily for >3 months, were randomised (1:1) to continue SFC or switch, without a washout, to IND/GLY 110/50 μg once daily. The primary endpoint was pre-dose forced expiratory volume in 1 second (FEV1) at Week-12.

Results: Overall, 502 patients were randomised to receive IND/GLY (n=251) or SFC (n=251). Patients switched to IND/GLY demonstrated significantly higher mean trough FEV1 (treatment difference [Δ]=45 mL; p=0.028) at Week-12. Forced vital capacity (FVC) also significantly improved with IND/GLY (Δ=102 mL; p=0.002) at Week-12. Numerical improvements in transition dyspnoea index (TDI: Δ=0.46; p=0.063) and the proportion of patients with clinically important improvement in TDI (≥1 point; odds ratio=1.27; CI: 0.81–1.97) were observed in patients switched to IND/GLY. Rescue medication use (Δ=-0.04 puffs/day; 95% CI: -0.20–0.13; p=0.662) and CAT scores (Δ=-0.4; 95% CI: -1.3–0.4; p=0.319) were comparable between IND/GLY and SFC after 12 weeks of treatment. Both treatments were well tolerated with similar safety profiles. During the treatment period, the proportion of patients with exacerbations was lower with IND/GLY versus SFC (10.1% versus 13.2%).

Conclusions: FLASH demonstrated that a direct treatment switch from SFC to IND/GLY in symptomatic, infrequently exacerbating patients with moderate to severe COPD resulted in improved lung function with a tolerability profile similar to SFC.

Acknowledgements: This study is sponsored by Novartis Pharma AG, Basel, Switzerland

AOL012
A NOVEL QUANTITATIVE-CT/FEV 1 APPROACH OF PHENOTYPING COPD TO PREDICT MORTALITY
LC LOH1, CHO KHOON ONG1, HYUN JUNG KOO2, SANG MIN LEE1, JAE SEUNG LEE3, YEON MOK OH2, JOON BEOM SEO2, SANG DO LEE2
1Department of Medicine, Penang Medical College, Penang, Malaysia, 2Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Research Institute of Radiology, Seoul, Korea, and 3Department of Pulmonary and Critical Care Medicine, and Clinical Research Center for Chronic Obstructive Airway Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: COPD-associated mortality is examined using a novel approach of phenotyping COPD based on quantitative-Computed
Tomography (QCT) and post-bronchodilator (BD) FEV₁ in a local Malaysian cohort.

Patients and Methods: Prospectively collected data of 112 eligible COPD subjects [mean age, 67 yrs; male, 93%; mean post-BD FEV₁, 46.7%] was available for mortality analysis. Median follow-up time was 1000 days (range, 60-1400). QCT and detailed clinico-demographic data were collected at study entry. Based on emphysema index and post-BD FEV₁, subjects were categorized into “emphysema-dominant” [Emphysema index (EI) ≥ 15%, FEV₁ < 50%], “airway-dominant” [EI < 15%, FEV₁ < 50%] and “mild mixed” [EI < 15%, FEV₁ ≥ 50%] and “severe mixed” [EI ≥ 15%, FEV₁ < 50%] disease phenotypes.

Results: Sixteen patients (14.2%) died of COPD-associated causes. There were 29 (25.89%) mild mixed disease, 23 (20.54%) airway-dominant disease, 15 (13.39%) emphysema-dominant disease and 45 (40.18%) severe mixed disease cases. Mild mixed disease were proportionately more in GOLD Group A while severe mixed disease were proportionately more in both GOLD Group B and D. Kaplan-Meier survival estimates showed increased mortality risk with severe mixed disease (log rank test, p=0.03) but not with GOLD groups (p=0.08). Univariate Cox proportionate hazard analysis showed that age, BMI, long-term oxygen therapy, FEV₁, FVC, CAT score, mMRC, SGRQ, emphysema index, and severe mixed disease (vs. mild mixed disease) are associated with mortality. Multivariate Cox analysis showed that age BMI and CAT score remain independently associated with mortality.

Conclusions: Severe mixed emphysema/airway disease defined by a novel QCT/FEV₁ approach may help predict COPD-associated mortality. However age, BMI and CAT score remain as key mortality risk factors in our cohort.

AOI013
RESPECT-MESO: AN INTERNATIONAL MULTICENTRE NON-BLINDED RANDOMIZED CONTROLLED TRIAL TO ASSESS THE IMPACT OF REGULAR EARLY SPECIALIST PALLIATIVE CARE IN MALIGNANT Pleural MesoTHeliOMA
FRASER BRIMES1,2,3, SAMAL GUNTILAKE4, IAIN LAWRIE5, LAURA MARSHALL6, CAROLE FOGG7, NICK MASKELL8, KAREN FORBES9, NAJIB RAHMAN10, STEPHEN MORRIS8, STEPHEN GERRY11, ANOOP CHAUHAN11
1 Curtin Medical School, Bentley, Australia, 2 Department of Respiratory Medicine, Sir Charles Gairdner Hospital, Nedlands, Australia, 3 Institute for Respiratory Health, Nedlands, Australia, 4 Portsmouth Hospitals NHS Trust, Portsmouth, UK, 5 North Manchester General Hospital, Manchester, UK, 6 University of Oxford, Oxford, UK, 7 National Institute for Health Research Oxford Biomedical Research Centre, Oxford, UK, and 8 University College London, London, UK

Background: Malignant pleural mesothelioma (MPM) has a high symptom burden and early specialist palliative care (SPC) may have a beneficial role for these patients.

Aim: To examine the effect of early SPC in patients with MPM.

Methods: Participants with newly diagnosed MPM (within the last 6 weeks) were randomised to early SPC integrated with standard care, or standard care alone, in a 1:1 ratio. SPC visits were 4 weekly throughout the study period. Quality of life (QoL) and mood were assessed at baseline and every 4 weeks for up to 24 weeks with the EORTC QLQ-C30 questionnaire for QoL and General Health Questionnaire (GHQ-12) for anxiety/depression. The primary outcome was the change in EORTC C30 Global Health Status (GHS) QoL 12 weeks after randomisation.

Results: 174 participants underwent randomisation with 148 (85.1%) completing the primary outcome. The two groups were well matched after randomisation (Table 1). The cohort was elderly (median age 72.6 years) and predominantly male. Epithelioid was the most common MPM subtype in 136 (78.2%) cases, ECOG PS 0 in 66 (37.9%) and 1 in 108 (62.1%) participants. At randomisation, 134 (77.0%) participants reported dyspnoea and 100 (57.4%) had chest pain. At least 1 cycle of chemotherapy was completed in 103 (59.2%) participants. At 24 weeks 30 (17.2%) participants had died. Table 2 presents the primary and secondary outcome data. 68 (78.2%) participants in the intervention arm completed all scheduled monthly SPC visits at 12 weeks, and 46 (52.9%) at 24 weeks. 15 (17.2%) participants in the control arm were referred to SPC within 12 weeks, and 30 (34.5%) by 24 weeks.

Conclusion: Provision of early palliative care for all patients with recently diagnosed MPM is not associated with beneficial changes in quality of life as compared to palliative care review based on symptom burden.

Table 1. Baseline characteristics at randomisation (n=174)

<table>
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<th>Control (n=87)</th>
<th>SPC (n=87)</th>
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<tbody>
<tr>
<td>Median age (IQR)</td>
<td>72.8 (69.0-78.9)</td>
<td>72.1 (66.7-77.7)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>72 (82.8)</td>
<td>67 (77.0)</td>
</tr>
<tr>
<td>ECOG PS 0/1 (%)</td>
<td>32/55 (36.8/63.2)</td>
<td>34/53 (39.1/60.9)</td>
</tr>
<tr>
<td>Epithelioid MPM</td>
<td>68 (78.2)</td>
<td>68 (78.2)</td>
</tr>
<tr>
<td>Plan for chemotherapy</td>
<td>45 (52.3)</td>
<td>47 (54.0)</td>
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</tbody>
</table>

SPC = specialist palliative care; IQR = interquartile range; ECOG PS = European Collaborative Oncology Group performance status; MPM = malignant pleural mesothelioma

Table 2. Primary and secondary outcomes

<table>
<thead>
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<th>SPC</th>
<th>Mean difference*</th>
<th>p=</th>
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<tr>
<td>Mean (SD) GHS QoL 12 weeks</td>
<td>59.5 (SD 21.2)</td>
<td>60.2 (23.6)</td>
<td>1.8 (95% CI -0.4 to 8.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Mean (SD) GHS QoL 24 weeks</td>
<td>63.7 (SD 19.8)</td>
<td>61.3 (20.8)</td>
<td>-2.0 (-8.8 to 4.6)</td>
<td>0.55</td>
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<tr>
<td>Mean (SD) GHQ-12 anxiety / depression scores 12 weeks</td>
<td>2.6 (3.2)</td>
<td>2.2 (3.0)</td>
<td>-0.6 (-1.5 to 0.4)</td>
<td>0.24</td>
</tr>
<tr>
<td>Mean (SD) GHQ-12 anxiety / depression scores 24 weeks</td>
<td>2.1 (2.55)</td>
<td>1.75 (2.5)</td>
<td>-0.4 (-1.2 to 0.4)</td>
<td>0.28</td>
</tr>
<tr>
<td>Median (95% CI) survival (months)</td>
<td>12.6 (10.7-19.7)</td>
<td>11.5 (9.8-15.9)</td>
<td>-</td>
<td>0.51</td>
</tr>
<tr>
<td>Mean (SD) GHS QoL alive after 6 months of randomisation</td>
<td>60.9 (20.9)</td>
<td>64.3 (19.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mean (SD) GHS QoL in those who died within 6 months of randomisation</td>
<td>48.4 (21.4)</td>
<td>38.9 (30.6)</td>
<td>3.9 (-2.8 to 10.7)**</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*adjusted for baseline score; † post hoc analysis. SPC, specialist palliative care; SD, standard deviation; CI, confidence interval; GHS, Global Health Status (from EORTC QLQ-C30; higher score = better QoL); GHQ, General Health Questionnaire (higher score indicates depression/anxiety).
PREVALENCE AND COMORBIDITIES OF OBSTUCTIVE SLEEP APNOEA IN THE BUSSELTON HEALTHY AGEING STUDY (BHAS)

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1Department of Pulmonary Physiology and Sleep Medicine, Sir Charles Gairdner Hospital, Perth, WA, Australia, 2School of Population and Global Health, University of Western Australia, Perth, WA, Australia, and 3Busselton Population Medical Research Institute, Perth, WA, Australia

Background and Aims: Obstructive sleep apnoea (OSA) is common and is associated with significant morbidity and mortality. There are few objective prevalence data in Australia, particularly for women. In Busselton, Western Australia, the prevalence of OSA was estimated in 1990 at 4.7% in men (i.e. respiratory disturbance index >15), and in 2007 (N=793) at 12.4% in men and 5.7% in women (i.e. apnea-hypopnea index (AHI)>15 in participants without known OSA). We assessed the prevalence of OSA in the Busselton Healthy Ageing Study, a comprehensive health study of men and women aged 46-64 years.

Methods: Between 2010 and 2015, all residents on the electoral roll of the Busselton Shire, born between 1946 and 1964, were invited to participate. The participation rate was 75% (N=5,082). Single or dual channel ApneaLink devices for a home sleep study were issued to 3,745 participants (73.7%) and 2,707 (53.3%) collections were suitable for analysis. The prevalence of OSA was defined by the AHI obtained from the ApneaLink automated event scoring algorithm, and its relation to demographic data and co-morbidities was assessed. Moderate and severe OSA were defined as AHI>15 and >30 respectively.

Results: Participants with acceptable ApneaLink data had lower rates of smoking, alcohol consumption and previous reported OSA (Table 1). The prevalence of moderate and severe OSA was 15.2% and 5.2% in men and 8.1% and 2% of women respectively. OSA was associated with increased BMI and alcohol consumption. Sleepiness was associated with OSA severity in men only (Table 2). OSA was associated increased BMI and hypertension in men and women, with current depression in men only, and with diabetes and cancer in women only (Table 3).

Conclusions: The prevalence of OSA in Busselton has increased, and the prevalence in women is higher than reported elsewhere. Sex-based differences in comorbidities are observed.

Table 1. Characteristics of participants with and without acceptable ApneaLink data

<table>
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<tr>
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<th>Men (n=1089)</th>
<th>Women (n=1286)</th>
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<td>Non-ApneaLink</td>
<td>ApneaLink</td>
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</tr>
<tr>
<td>Age, years</td>
<td>58.2 (5.0)</td>
<td>58.1 (5.0)</td>
<td>0.456</td>
</tr>
<tr>
<td>BMI, kg/m2*</td>
<td>28.7 (4.2)</td>
<td>28.3 (4.1)</td>
<td>0.012</td>
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<tr>
<td>Alcohol, glasses per week*</td>
<td>18.4 (16.8)</td>
<td>15.8 (15.11)</td>
<td>0.0001</td>
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<tr>
<td>Epworth Sleepiness Score*</td>
<td>6.0 (3.8)</td>
<td>6.1 (3.8)</td>
<td>0.29</td>
</tr>
<tr>
<td>Current smoker, %*</td>
<td>15.3</td>
<td>8.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Reported OSA, %*</td>
<td>12.8</td>
<td>4.7</td>
<td>&lt;0.0001</td>
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</table>

* data presented as mean (SD)

Table 2. Characteristics of participants with moderate and severe OSA

<table>
<thead>
<tr>
<th></th>
<th>Men (n=1089)</th>
<th>Women (n=1286)</th>
<th>p</th>
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<tr>
<td></td>
<td>AHI &lt;15</td>
<td>15-29.9</td>
<td>≥30</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>958 (79.6)</td>
<td>183 (15.2)</td>
<td>63 (5.2)</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>27.9 (3.7)</td>
<td>29.7 (4.4)</td>
<td>31.3 (5.3)</td>
</tr>
<tr>
<td>Alcohol, glasses per week</td>
<td>15.1 (14.5)</td>
<td>17.4 (16.2)</td>
<td>21.8 (19.3)</td>
</tr>
<tr>
<td>ESS</td>
<td>6.0 (3.8)</td>
<td>6.6 (4.1)</td>
<td>7.2 (4.0)</td>
</tr>
</tbody>
</table>

* data presented as mean (SD)

Table 3. Prevalence of comorbidities in participants with and without OSA

<table>
<thead>
<tr>
<th></th>
<th>Men (n=1089)</th>
<th>Women (n=1286)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AHI &lt;15</td>
<td>AHI ≥15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>958 (79.57)</td>
<td>246 (20.43)</td>
<td>1352 (90.85)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>39.14</td>
<td>57.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>6.06</td>
<td>9.35</td>
<td>0.0664</td>
</tr>
<tr>
<td>Current Depression</td>
<td>13.26</td>
<td>20.33</td>
<td>0.0052</td>
</tr>
<tr>
<td>Cancer</td>
<td>13.88</td>
<td>14.63</td>
<td>0.7623</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.33</td>
<td>7.76</td>
<td>0.148</td>
</tr>
<tr>
<td>Sleepy driving</td>
<td>18.29</td>
<td>14.05</td>
<td>0.1206</td>
</tr>
</tbody>
</table>

*History of hypertension or elevated blood pressure on assessment. †Questionnaire (DASS)
Lung Cancer 3

AO158

COMMON AND UNCOMMON EGFR MUTATIONS ANALYSIS IN CYTOLOGY AND PLASMA SAMPLES OF TREATMENT-NAIVE LUNG CANCER PATIENTS

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Background and Aim: Although cytological samples are routine sources of EGFR mutation testing, we would like to assess the feasibility of cell-free DNA (cfDNA) as an alternative DNA source using routine genotyping procedures.

Methods: Pairs of cytology and plasma samples were collected from 116 treatment-naive patients. DNA from both plasma and cytology samples was isolated and analyzed using combination of PCR High Resolution Melting (HRM), Restriction Fragment Length Polymorphism (RFLP), and Sanger Sequencing.

Results: EGFR mutation data were obtained in all 116 (100%) cfDNA plasma samples and 110/116 (94.82%) of cytology samples. EGFR mutations were detected in 46/110 (41.8%) plasma and in 69/110 (62.7%) cytology samples. The sensitivity and specificity to detect common EGFR mutations (insertions/ deletions of exon 19, substitution L858R) from plasma were 43.33% and 82.86%, respectively. On the other hands, the rates were slightly lower to detect uncommon mutations (30.77% and 82.86%). Overall survival (OS) in patients having uncommon EGFR mutations (insertions/ deletions of exon 19, substitution L858R) from plasma were 43.33% and 82.86%, respectively. On the other hands, the rates were slightly lower to detect uncommon mutations (30.77% and 82.86%). Overall survival (OS) in patients having uncommon EGFR mutations (excluding baseline T790M) was shorter than patients with common mutations and found more frequently in smokers. These results show that KRAS mutation is related to smoking history, especially transversion mutation. Further studies are required to determine prognostic effects of kras mutation in this cohort.

Conclusion: ctDNA in plasma may be useful to detect common EGFR mutations using combined PCR HRM, RFLP, and Sanger Sequencing.

AO159

KRAS MUTATION IN EGFR WILD TYPE INDONESIAN LUNG CANCER PATIENT

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Background and Aim: Mutation in epidermal growth factor receptor (EGFR) has been established as predictive factor for EGFR-tyrosine kinase inhibitor treatment in NSCLC patients. Several studies also suggesting that KRAS mutation can be used to predict poor response to EGFR-tyrosine kinase inhibitor therapy. KRAS transversion mutation is the most common type of KRAS mutation and found more frequently in smokers. These results show that KRAS mutation is related to smoking history, especially transversion mutation. Further studies are required to determine prognostic effects of kras mutation in this cohort.

Methods: Sixty-one of lung cancer patient's specimens were collected. These samples were previously tested for EGFR mutations. Eighteen samples (30%) were positive for common EGFR mutation (L858R and exon 19 insertion/deletion). Forty-three patients without EGFR mutation were further analysed for KRAS exon 2 mutations. KRAS mutations were detected using DNA sequencing, high resolution melting (HRM) analysis and restriction fragment length polymorphism (RFLP).

Results: KRAS mutation was detected in 7 samples of EGFR wild type cases (N=53, 13%). Transversion mutations were found in 6 cases with G12C being the most frequent mutations (3/6), while 1 case was transition mutations. KRAS mutations were higher in smokers (24%) than non-smokers (4%, p=0.043). Moreover, KRAS transversion mutation frequency is higher in patients with smoking history.

Conclusion: Transversion was the most common type of KRAS mutation and found more frequently in smokers. These results show that KRAS mutation is related to smoking history, especially transversion mutation. Further studies are required to determine prognostic effects of kras mutation in this cohort.

AO160

RISK IN HIGH-RISK POPULATIONS: MOVING CT SCREENING BEYOND THE SEARCH FOR A POTENTIAL LUNG CANCER

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Background and Aims: Low dose CT screening of high risk current and former smokers results in a reduction in mortality, but does not allow us to distinguish between the many benign nodules vs. a lung cancer. CT scanning is also the first “test” for most lung cancer patients but offers little in the way of guidance around therapy. However, modern quantitative analysis methods are evolving to allow us to leverage a number of features available on the CT scan for diagnosis, staging, and treatment planning.

Methods: CT based characteristics of the nodule, lung, vasculature, and body composition from large datasets have been used to predict risk of cancer and cancer-related death.

Results: Features of the lung surrounding a nodule, such as regional low attenuation areas less than -950 (LAAs) >950, are associated with lung cancer size and aggressiveness. Moving beyond mere attenuation, measurement of morphological emphysema demonstrates that moderate centrilobular emphysema is a risk factor for lung cancer. Extra-pulmonary features are also associated with lung cancer outcomes.

Conclusions: Pulmonary and extra-pulmonary features identified on a CT scan can be potentially used to enhance lung cancer risk stratification and treatment planning.

AO161

IMPORTANCE OF THE PREOPERATIVE NEUTROPHIL/LYMPHOCYTE RATIO AND PROGNOSTIC NUTRITIONAL INDEX FOR PATHOLOGICAL-STAGE I LUNG CANCER PATIENTS

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Background and Aims: Indices of nutritional state and systematic inflammation have been considered useful in determining risk factors for recurrence and prognosis. This study aimed to assess the recurrent and
prognostic factors for pathological-stage I lung cancer, especially preoperative nutritional condition, as estimated by the prognostic nutritional index (PNI), and systemic inflammation, as estimated by the neutrophil/lymphocyte ratio (NLR).

**Methods:** From July 2008 to December 2014, 259 patients with pathological-stage I lung cancer who had undergone curative operations were enrolled. These included 136 men and 123 women, with a median age of 74 years (range 44–88 years). The operative procedures were lobectomy in 190 (73%) and sublobar resection in 69 (27%). The histological types were adenocarcinoma in 218 (84%) and non-adenocarcinoma in 41 (16%). PNI was scored based on the laboratory data of albumin and lymphocyte counts. NLR was the neutrophil/lymphocyte ratio. Using receiver-operating characteristics curve analysis, we established cutoff values for the NLR and the PNI. We retrospectively analysed the clinicopathological risk factors with respect to NLR and PNI, as well as the overall and recurrence-free survival.

**Results:** The overall 5-year survival rate was 83.4%, and the recurrence-free 5-year survival rate was 84.9%. The associations of NLR and PNI showed an adverse correlation with 20% contribution degree. Multivariate analysis with Cox’s proportional hazards model revealed that high NLR (HR 3.33; p < 0.01) and lymphatic and/or vascular invasion (LVI) (HR 2.31; p = 0.02) were independent negative predictors of recurrence-free survival and that low PNI (HR 2.73; p = 0.018) and LVI (HR 3.43; p < 0.01) were independent predictors of mortality.

**Conclusion:** High NLR and LVI are independent factors related to recurrence. Low PNI and LVI are independent prognostic factors. Thus, NLR and PNI might be useful preoperative indicators in patients undergoing surgery for pathological-stage I lung cancer.

**Serum CEA and CYFRA Responses as Prognostic Factors in Advanced Non-Small Cell Lung Cancer Patients**

**Methods:** We retrospectively included chemotherapy-naive advanced NSCLC patients with increased values of serum CEA or CYFRA from April 2010 through December 2015. The association between tumor marker changes one month or four months after the initiation of chemotherapy and overall survival was analyzed.

**Results:** We identified 111 CEA-positive and 62 CYFRA-positive NSCLC patients. One month and four months after chemotherapy initiation, significant decrease (>25% of pretreatment values) of CEA levels was observed in 85 (77.3%) and 81 (82.7%) patients, respectively while that of CYFRA levels was observed in 59 (83.1%) and 40 (71.4%) patients. Univariate analyses showed that serum CEA response after four months and serum CYFRA response after one month and four months were significantly associated with overall survival (p = 0.019, p = 0.001, p < 0.001, respectively). In multivariate analyses, in addition to EGFR mutation status, serum CEA and CYFRA responses after four months were significantly associated with overall survival (p = 0.023, p = 0.031, p < 0.005, respectively).

**Conclusions:** In advanced NSCLC patients, the changes of serum CEA and CYFRA after chemotherapy were predictive for overall survival.

**PD-L1 TPS Analysis in Real-world Clinical Practice: Evaluation of Specimens Obtained by Respiratory Endoscopic Biopsy**

**Methods:** We evaluated patients with advanced NSCLC whose expression of PD-L1 was pathologically evaluated before systemic first-line chemotherapies at the National Cancer Center Hospital, Tokyo, Japan, between February and April 2017. We assessed PD-L1 expression by IHC using the clone 22C3 pharmDx kit, clinical and molecular characteristics, type of specimens and technical success rate.

**Results:** A total of 40 patients who underwent a respiratory endoscopy were included in this study. The procedures performed consisted of transbronchial biopsy (TBB) (n = 25), endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) (n = 15) and pleuroscopic biopsy (n = 2). Both TBB and EBUS-TBNA were performed for diagnosis and staging in two patients. The diagnostic yield of small transbronchial biopsy samples for malignant cells was 90.0% (22/25 [88.0%] for TBB, 14/15 [93.3%] for EBUS-TBNA). Among the patients with positive diagnostic results, almost all the specimens were adequate for PD-L1 TPS analysis (97.2% [35/36]). One specimen from EBUS-TBNA was inadequate for the evaluation of PD-L1 expression because of the small number of malignant cells.

**Conclusions:** Respiratory endoscopic biopsy is a feasible procedure for the PD-L1 TPS analysis.
Pulmonary Circulation

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KOTANI1, REINA HARA 1, HARUKA YAMAKI 1, HIROSHI SHIMA 1, KUMASAKA3, TAMIKO TAKEMURA3, SOICHIRO IKUSHIMA1, KATAYAMA1, MOTONARI FUKUI1, HAYASHI1, HISANORI AMIMOTO 1, YUSUKE SHIRAISHI 1, AYA AO164

THE EFFICACY AND SAFETY OF CARBOPLATIN AND WEEKLY PACLITAXEL COMBINATION THERAPY FOR PREVIOUSLY TREATED SMALL CELL LUNG CANCER PATIENTS WITH INTERSTITIAL LUNG DISEASE

RYO ITOTANI1, SATOSHI MARUMO1, MICHIHIO UYAMA1, YUSUKE HAYASHI1, HISANORI AMIMOTO1, YUSUKE SHIRAISHI1, AYA KOTANI1, REINA HARA1, HARUKA YAMAKI1, HIROSHI SHIMA1, MASASHI SHIRATA1, TAKAMASA KITAJIMA1, DAIKI INOUE1, YUKO KATAYAMA1, MOTOHARU FUKUI1

Background and Aims: Chemotherapy is a standard treatment strategy in patients with small cell lung cancer (SCLC). However, there are few regimens which are effective and safe for SCLC patients with interstitial lung disease (ILD). In the present study, we investigate the efficacy and safety of carboplatin (CBDCA) and weekly paclitaxel (PTX) combination therapy for previously treated SCLC patients with ILD.

Methods: A retrospective chart review was performed on SCLC patients with ILD who received CBDCA + weekly PTX regimen after more than one cytotoxic chemotherapy regimen at The Tazuke Kofukai Medical Research Institute Kitano Hospital between Jan 2011 and Dec 2016. We assessed progression free survival (PFS), overall survival (OS), and adverse events, especially exacerbation of ILD.

Results: The characteristics of 21 SCLC patients with ILD were as follows; age of 70 ± 5.6 years-old, 18 male and 3 female, all of them were current or former smoker (57.6 ± 8.5 pack-year), Eastern Cooperative Oncology Group-performance status (ECOG-PS): 0-1/2-4 15/6, median number of past chemotherapy regimen was 2 (2 – 6), computed tomography-pattern of ILD: usual interstitial pneumonia (UIP) pattern/non-UIP pattern 8/13. The response rate (RR) was 28.6 %, and disease control rate (DCR) was 61.9%. Median PFS was 3.5 months (95% confidence interval [CI] 2.7 – 4.3). Median OS was 7.1 months (95% CI 3.2 – 11.0). ILD was exacerbated in 4 cases (19%) after administration of CBDCA + weekly PTX. All of them had UIP pattern ILD and 2 cases of them experienced Grade 5 ILD.

Conclusions: In previously treated SCLC patients with ILD who had received more than one cytotoxic chemotherapy regimen, CBDCA + weekly PTX was effective regimen with 28.6% of RR and 61.9% of DCR. However, 19% patients experienced exacerbation of ILD. Further examinations were required.

Pulmonary Circulation

AO165

TWO CASES OF PULMONARY HYPERTENSION ASSOCIATED WITH CHRONIC MYELOPROLIFERATIVE DISORDERS

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1Department of Respiratory Medicine, Japanese Red Cross Medical Center, Tokyo, Japan, 2Department of Hematology, Japanese Red Cross Medical Center, Tokyo, Japan, and 3Department of Pathology, Japanese Red Cross Medical Center, Tokyo, Japan

Background and Aim: Pulmonary hypertension (PH) is a monumental complication associated with chronic myeloproliferative disorders (CMPDs) and is included in group 5 of the most recent clinical classification; however its etiology remains unclear and only a limited number of cases of PH have been reported in literature.

Methods: We report two cases of CMPDs associated with PH.

Results: The first patient was a 72-year-old woman with polycythemia vera (PV) who was treated with hydroxyurea for 21 years. She presented with a cough and subsequent chest computed tomography (CT) revealed mosaic perfusion. Estimated pulmonary arterial pressure (esPAP) was 70 mmHg using transthoracic echocardiography, mean pulmonary arterial pressure (mPAP) via right heart catheterization was 43 mmHg, and pulmonary wedge aspiration cytology revealed the presence of megakaryocytes. Other causes were not detected and she was diagnosed with PH associated with PV. She was treated with hydroxyurea, sildenafil, ambrisentan and radiation therapy, however she died due to pulmonary hypertension. The second patient was a 66-year-old woman with essential thrombocytocynia (ET) diagnosed at the age of 39. After treatment with hydroxyurea for 4 years, she complained of exertional dyspnea and a chest CT revealed ground glass attenuation. esPAP was 59 mmHg and mPAP was 37 mmHg. There was no evidence of pulmonary embolism by enhanced chest CT, however multiple defects in both lungs were documented by lung perfusion scintigraphy. She was diagnosed with chronic thromboembolic pulmonary hypertension associated with ET and treated with hydroxyurea and warfarin which led to improvements in esPAP.

Conclusion: Few reports exist on the subject of circulating megakaryocytes and PH associated with CMPDs. Pulmonary capillary obstruction by megakaryocytes and secondary microthrombosis may contribute to pulmonary vascular disease with CMPDs. Therefore, in addition to thrombi, megakaryocytes and hematopoietic stem cells should also be assessed in diagnosing PH associated with CMPDs.

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Conclusions: This study demonstrates differential effects of inflammatory mediators on vascular contractile responses in PCLS. The application of this technique as demonstrated here, and in the context of models of pulmonary hypertension, has the potential to provide insights into mechanisms underlying increased vasoreactivity and to identify novel targets for therapeutic intervention targeting small intrapulmonary arteries.

DYNAMIC CHANGES OF MACROPHAGE M1/M2 POLARIZATION IN MONOCROTALINE-INDUCED PULMONARY ARTERIAL HYPERTENSION
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Background and Aims: Macrophages are key orchestrators of the inflammatory and repair responses in lung tissue, and have been demonstrated to be vital in the pathogenesis of pulmonary arterial hypertension (PAH). However, the specific macrophage polarization status (M1/M2) in different stages of PAH and its underlying function on pulmonary arterial smooth muscle cell (PA-SMC) still unclear.

Methods: A rat model of monocrotaline (MCT) induced PAH was established, and were executed on day 3, 7, 14, 21, 28. Hemodynamic analysis was conducted at each time point, and right ventricular hypertrophy index was measured. Lung tissue macrophage M1 and M2 phenotypes were detected via immunofluorescence, western blot and quantitative RT-PCR, while alveolar macrophage phenotypes by flow cytometry. In vitro, M2 macrophages were obtained using RAW264.7 cells via IL-4 treatment. PA-SMC from PAH rat were cultured in macrophage conditioned medium or in a co-culture system, then proliferation and migration of PA-SMC were tested.

Results: In lung tissue, confocal microscopic images showed that CD68+ NOS2+ M1 macrophage significantly increased on day 3 after MCT injection, remained high until day 7, and dramatically decreased from day 14. Meanwhile, CD68+ CD206+ M2 macrophage in PAH rat accumulated from day 7 and increased progressively to day 28. Furthermore, alveolar macrophage phenotypes analyzed by flow cytometry showed the similar trends: M1 macrophage phenotype increased in the initial stage and M2 macrophage in the progressive stage. The ratio of M2/M1 increased gradually from day 3 (0.43±0.32) to day 28 (5.90±1.54), and had a positive correlation with right ventricular hypertrophy. The expression of M1 and M2 polarization markers detected by western blot and quantitative RT-PCR were consistent with the results. Further in vitro studies revealed that M2 macrophage could significantly promote the proliferation and migration of PA-SMC.

Conclusions: These data demonstrate a dynamic change of macrophage M1/M2 polarization in the development process of experimental PAH. M2 macrophages predominate in the progression of PAH, and may associate with pulmonary vascular remodeling.

BIO-DISTRIBUTION OF EPCS IN DISEASE AND THE POTENTIAL ROLE OF EXOMES IN CELL THERAPY FOR PULMONARY VASCULAR DISEASES
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Background and Aims: Background: Pulmonary arterial hypertension (PAH) is a rare but devastating lung disease with survival of 55% at 3 years. Reduced expression of the bone morphogenetic protein receptor type-2 (BMPR2) is causally linked to PAH. We have shown that EPCs transduced to over-express BMPR2 then transplanted into rats with PAH reduces pulmonary pressures and vascular remodelling. We aimed to examine both the bio-distribution of EPCs in the disease context and the role of exosomes (Exo) trafficking BMPR2 from the injected augmented EPCs to the pulmonary endothelium.

Methods: Bio-distribution: EPCs were isolated cultured, characterised and transduced with AdTrackLuc. These were injected (IV) into rats with MCT induced PAH and control at 1x10^6 cells/rat, imaged on a BioPhotonic Imager (Lumina IVIS) at 1, 6 & 24 hrs. Organs were extracted and analysed further for luciferase activity.

Exo: EPCs were isolated and cultured and transduced with AdBMPR2 for 24h, serum starved for 48h and the supernatant removed for centrifugal isolation of Exos. These BMPR2-Exo’s were used to treat secondary EPCs for 48h, these EPCs were lysed and analysed for BMPR2 expression via western blot.

Results: Bio-distribution studies: Imaged animals (n=4/group) showed strong positive luminescence (2.47x10^8 photons/sec) at one hour in the lungs with minimal expression elsewhere. Expression was increased and longer lasting in the lungs of MCT (Figure 1) vs control, however, the lung expression was largely lost by 24 hours in both groups. Exos derived from BMPR2 transduced EPCs had a 3.4-fold increase in BMPR2 expression. EPC lysates treated with BMPR2-Exo’s had a significant 34.5-fold increase in BMPR2 expression compared to irrelevant virus-Exos and a 16.8 fold increase compared to media only-Exos. (Figure 2)

Conclusions: The therapeutic impact of EPC treatment is not due to retention of the cells themselves in the lungs and may be due to Exo released by the cells.
Background: Patients in clinical trials are highly selected and may not reflect the heterogeneity of real-life PAH patients. Furthermore, recent trials have excluded patients with risk factors or haemodynamic findings suggestive of co-existing left heart disease (LHD). It is unclear whether such excluded PAH (excl-PAH) patient's respond less well to therapy or display different natural history.

Aims: To characterise treatment response and outcomes of idiopathic PAH patients who may fail enrolment into clinical trials.

Method: Using the PHSANZ registry, patients with physician-diagnosed idiopathic PAH were classified as excl-PAH according to the exclusion criteria in the AMBITION study. Excluded patients had ≥3 risk factors for LHD (hypertension, coronary artery disease, diabetes mellitus and obesity) or the following haemodynamic findings (PAWP<15mmHg or PAWP=13-15mmHg with PVR<500 dynes.sec/cm5 or PVR<300 dynes.sec/cm5). Treatment response was assessed by change in 6MWD and improvement in functional class (FC) at 12-months.

Results: From 337 idiopathic PAH patients, 40.1% were classified as excl-PAH (15.1% and 30.0% patients displaying ≥3 LHD risk factors or fulfilling haemodynamic exclusion criteria, respectively). Compared with non-excluded patients, excl-PAH patients were older (66±12 vs. 52±18 years) and had shorter 6MWD (271±118 vs. 328±121m). Excl-PAH patients also had lower mean pulmonary artery pressure (40±14 vs. 50±14 mmHg), higher PAWP (13±3 vs. 10±3mmHg) and higher cardiac index (2.8±0.9 vs. 2.2±0.6L/min/m2). Patients in the excl-PAH group were less likely to be initiated on upfront combination therapy (10% vs. 22%). Treatment responses were similar in non-excluded PAH and excl-PAH patients in terms of change in 6MWD (61±9 vs. 55±79m, respectively), and FC improvement (29.7 vs. 28.9%, respectively). Almost identical survivals were observed for the two groups (median follow-up 48 months).

Conclusion: Patients excluded from clinical trials appear to respond similarly to PAH therapy. Despite major differences in baseline characteristics, non-excluded and excl-PAH patients have similar survival.

OUTCOMES OF IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION IN THE ERA OF COMBINATION THERAPY: A REPORT FROM THE PHSANZ REGISTRY

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1Royal Prince Alfred Hospital, Sydney, Australia, 2St Vincent’s Hospital, Sydney, Australia, 3The University of Notre Dame, Sydney, Australia, 4Fiona Stanley Hospital, Perth, Australia, 5Green Lane Hospital, Auckland, New Zealand, 6The Wesley Hospital, Brisbane, Australia, 7The Prince Charles Hospital, Brisbane, Australia, and 8The Alfred Hospital, Melbourne, Australia

Background: Epidemiology and treatment strategies continue to evolve in pulmonary arterial hypertension (PAH). We sought to define the characteristics and survival of adult patients with idiopathic, heritable and drug-induced PAH in the current management era.

Methods: Consecutive newly diagnosed cases of idiopathic, heritable and drug-induced PAH between Jan 2012 and August 2016 were prospectively enrolled in the Pulmonary Hypertension Society of Australia and New Zealand (PHSANZ) Registry.

Results: A total of 220 patients (mean age 57.2±18.7 years, female 69.5%) were included with a median follow-up of 26 months (IQR 17–39). Co-morbidities such as obesity (34.1%), systemic hypertension (30.5%), coronary artery disease (16.4%) and diabetes mellitus (19.5%) were common. Initial combination therapy was used 54 patients (triple; n=4, dual; n=50). Estimated survivals at 1-yr, 2-yr and 3-yr were 96%, 87% and 79% Multivariate analysis showed that male sex and lower six-minute distance were independent predictors of worse survival, whereas higher BMI was associated with improved survival. Co-morbidities other than obesity did not impact on survival. Initial dual oral combination therapy was associated with a positive trend towards better survival compared with initial oral monotherapy (adjusted HR 0.29; 95% CI 0.07–1.20, p = 0.086).

Conclusions: Although survival has improved with contemporary management, PAH is still a disease associated with significant early mortality. Male gender and poorer exercise capacity are predictive of mortality whereas obesity exerts a protective effect. A strategy of initial combination therapy may have a positive impact on survival.
Conclusions: This study suggests that sBNP plays a compensatory role in right ventricular dysfunction in elderly patients undergoing lobectomy.

AO172

NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO AS PREDICTIVE MARKERS FOR DEEP VEIN THROMBOSIS

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Background and Aims: The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are known indicators of systemic inflammation. Thrombotic disorders are pro-inflammatory in nature. NLR and PLR have not yet been established as predictive markers of deep vein thrombosis (DVT). The objective is to determine the ability of elevated NLR and PLR to predict DVT.

Methods: We conducted a retrospective chart review of patients who presented with lower extremity swelling at St. John Hospital and Medical Center from 1/2010 to 12/2014. Patients with a diagnosis of DVT confirmed via ultrasound Doppler (DVT group) were compared to patients with a negative Doppler (Control group). The NLR and PLR were calculated based on a complete blood count (CBC) done on the same day of the Doppler study. Values of NLR ≥ 3.4 were considered positive; values of PLR ≥ 260 were considered positive. For comparison, D-dimer was also assessed with values ≥ 500ng/ml considered positive. We assessed the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of NLR, PLR, positive on both NLR and PLR and D-Dimer.

Results: We reviewed 708 charts; 51 charts met the inclusion criteria for the DVT group and 51 charts were randomly selected for the controls. There was no difference in mean age between the DVT and the Control group (60.5 ± 20.4 years vs. 60.4 ± 18.7 years, respectively). There were also no differences between groups by sex or race. The table shows the sensitivity, specificity, PPV and NPV of each test.

Conclusions: Both NLR and PLR are better predictors of the presence or absence of DVT compared to D-Dimer. NLR can be useful to rule-out DVT when it is negative; whereas PLR can be useful in ruling-in DVT when it is positive. Furthermore, a positive NLR and positive PLR yielded the best prognostic value for predicting DVT. NLR and PLR ratios offer a new powerful, affordable, simple and readily available tool in the hands of clinicians to help them in the diagnosis of DVT.

COPD 4

THE PREVALENCE OF REDUCED TLCO AND THE EMPHYSEMA INDEX IN SMOKERS WITH NORMAL SPIROMETRY

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Background and Aims: The prevalence of Chronic Obstructive Pulmonary Disease (COPD) has been extensively studied, however little evidence exists for the usefulness of Transfer Factor for carbon monoxide (TLCO) in the diagnosis and classification of COPD. The guidelines for the Global Initiative for Chronic Obstructive Lung Disease (GOLD) currently utilise spirometry predominately to aid a physician-diagnosis of COPD. Since only a relatively small proportion of smokers develop COPD, we aim to assess how TLCO can serve as a useful early biomarker for the detection of lung disease in younger smokers with normal spirometry.

Methods: We performed a cross-sectional analysis of subjects who have had both spirometry and TLCO measured at the Respiratory Laboratory at Monash Lung & Sleep, Monash Health. Subjects included male and females aged 40 to 60 years with normal spirometry and at least 10 pack-years smoking history. As a substudy, CT scanning was used to assess the emphysema index in this group.

Results: Five hundred and seven subjects aged between 40 and 60 with normal spirometry and significant smoking histories were identified. Of this cohort, 241 subjects (47.5% of the group) had a TLCO below their lower limit of normal (using ATS criteria). A sub-study of 48 subjects who had a low TLCO and also had a CT scan showed a high incidence of emphysema (on CT scanning) in this cohort.

Conclusion: A low transfer factor for carbon monoxide (TLCO) is prevalent amongst younger smokers with normal spirometry. This low TLCO may be an important early indicator of potential lung damage in COPD.

AO174

SPIROMETRIC INDICES DO NOT DETECT MISMATCH BETWEEN VENTILATION AND PERFUSION IN COPD

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Background: Gas exchanging capacity is better predictor of mortality in COPD than spirometric lung function. It suggests declining expiratory lung function (obstruction and hyperinflation) and gas exchanging capacity (airway obstruction and parenchymal damage) do not progress in synchrony. We aimed to compare progress of lung function decline in moderate to severe COPD by measuring both spirometry and ventilation/perfusion mismatch.

Methods: Thirty patients with stable COPD (47-83 years, GOLD stages II-IV, post-bronchodilatation FEV1 23-74 % predicted) were followed-up for 12 months. Ventilatory capacity (FEV1 % predicted), forced vital capacity (FVC % predicted) and airway obstruction (FEV1/FVC %) were measured (ATS/ERS standard). In ventilation and perfusion tomography (V/P SPECT, EANM guidelines) total preserved lung function (TPLF%) falling due to reduction of ventilation and/or emphysema was calculated as percentage of total lung volume. Ventilation defect (including small airway disease) was quantified by penetration of Technegas™ to periphery (V grade). Parenchymal damage was defined as an area of mismatched or reversed mismatched V/P defects (%).

Results: Two patients died from cardiovascular events. In remaining patients FVC fell from 89% to 72% predicted (CI95% -11 to -22%, p<0.0001), FEV1 was stable (+1%, CI95% -3% to 5%) and FEV1/FVC elevated (+5%, CI95% 1-9%, P<0.01). Both progress of small airway disease (V grade n=0.67, p=0.0003) and emphysema (E% +10%, CI95% 4-16%, p=0.0002; n=0.72 and p=0.0001) contributed to a fall of matched ventilation and perfusion (TPLF%) from 33% to 24%, CI95% -5 to -13%, p=0.0005). The reduction of FVC was not associated with a fall of TPLF% (n=0.10, p=0.62).

Conclusions: V/P SPECT evidenced significant 10% reduction of lung function over 12 months in moderate to severe COPD. This increase...
in V/P mismatch suggested reduced gas exchanging capacity which was
unsynchronized to impaired spirometric lung function.

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AO175
MUSCLE ECHO INTENSITY CORRELATES WITH PHYSICAL ACTIVITY IN PATIENTS WITH STABLE COPD
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Background and Aims: Previous research revealed that muscle quality in patients with COPD is lower than that in healthy individuals and is associated with physical activity (PA) level. Moreover, certain studies reported that muscle quality assessed using magnetic resonance imaging or computed tomography correlates with muscle echo intensity (EI) assessed using ultrasonography. Therefore, we hypothesized that muscle EI might be associated with PA level in patients with COPD.

Methods: Twelve outpatients with stable COPD (age, 71 ± 6 years; FEV1, 57.3 ± 31.5% predicted) consented to participate in this study. We measured the muscle cross-sectional area (CSA) and EI of the rectus femoris (RFCSA and RF EI, respectively) using B-mode ultrasonography. With the patient in the supine position, the transducer was placed perpendicularly to the long axis of the thigh on its superior aspect, two-thirds of the distance from the anterior superior iliac spine to the superior patellar border. RFCSA and RF EI were measured on frozen images using an electronic caliper and 8-bit gray-scale analysis with Image J, respectively. The objective PA level was determined by counting daily steps with an activity monitor. Spearman rank-order correlation coefficient (r s) was used to assess the relationship between parameter values.

Results: The parameter values were as follows: RFCSA, 3.9 ± 1.0 cm²; RF EI, 100.9 ± 11.7 arb. units; and daily steps, 4740.3 ± 2484.3 steps/day. RFCSA and RF EI significantly correlated with daily steps (rs = 0.816, P = 0.001; rs = -0.657, P = 0.020, respectively).

Conclusions: Our study revealed a close relationship between muscle ultrasonography data and the PA level. To follow up muscle condition, not only muscle CSA but also muscle EI assessed using ultrasonography, which is real-time and non-invasive, may be considered. Future research is needed to investigate the relationship between changes in muscle EI and PA.

AO176
STUDY OF SARCOPENIA IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE
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Background and Aims: Patients with chronic obstructive pulmonary disease (COPD) have 1) decreased muscle mass, 2) decreased muscle strength, or 3) deteriorated physical abilities, and are likely to develop the so-called sarcopenic state. However, only few previous reports have been published on the association between COPD stage and sarcopenia.

Methods: In a study conducted with 36 male patients with COPD who were receiving outpatient care at our hospital (age: 78.4 ± 5.1 years; stage I: 13 patients, stage II: 13 patients, stage III: 5 patients, stage IV: 5 patients), total-body skeletal muscle mass, muscle strength (grip strength and knee extensor strength), and gait speed were measured by using dual-energy X-ray absorptiometry (DXA) upon approval by the institutional review board (IRB) and reception of the patients' written consent.

Results: A significant positive correlation (p = 0.029) was found between total-body skeletal muscle mass (measured using DXA) and % FEV1.0 (against the predicted value). Total-body skeletal muscle mass decreased with the progression of the COPD stages. The mean value of 5.64 ± 0.84 kg/m² at stage IV showed a significant decrease from 6.98 ± 0.85 kg/m² at stage I (p = 0.008). Gait speed decreased with the progression of the COPD stages. Muscle strength, including grip strength and knee extension strength, tended to decrease. The prevalence of sarcopenia was 30.8% in the patients with stage I COPD, 46.2% in those with stage II COPD, and 100.0% in those with stage III and IV COPD.

Conclusions: The progression of the COPD stages was accompanied by significantly progressive decreases in total-body skeletal muscle mass, muscle strength, and physical ability. Along with osteoporosis, sarcopenia is closely associated to COPD as a systemic comorbidity. It requires aggressive therapeutic intervention and needs to be further studied.
0.022 (0.028 to 0.082) favoured the home-based group. The probabilities that the home-based programme was cost-effective at a $0 threshold for willingness-to-pay were 74% in the cost-effectiveness analysis and 73% in the cost-utility analysis.

**Conclusion:** In the 12 months following pulmonary rehabilitation, healthcare provider costs and outcomes were not significantly different between home and centre-based groups. These economic analyses support wider clinical implementation of this new model of pulmonary rehabilitation.

**AO178**

**INCREASING LIGHT PHYSICAL ACTIVITY AND DECREASING SEDENTARY TIME IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A PRELIMINARY STUDY**

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**Background and Aim:** Current physical activity (PA) guidelines focus on moderate-to-vigorous physical activity (MVPA) that is too strenuous and not feasible for long term maintenance in many people with COPD. Growing evidence suggests that substantial health benefits are associated with increases in the volume of light physical activity (LPA). We developed the Active-for-Life with COPD (Active-Life) intervention to increase total PA with an emphasis on increasing the time spent in LPA and decreasing sedentary time by approximately 60 minutes/day.

**Methods:** Active-Life is a 10wk intervention. Key components include (a) exercise with functional circuit training and walking, (b) behavioural strategies based on self-efficacy and self-regulation and (c) education that explains the potential health benefits of increasing LPA and decreasing sedentary time. We pilot tested Active-Life in 10 people with moderate to severe COPD. Outcomes were measured at baseline, end of the intervention and 2 months after completion of the intervention. PA was measured for 7 consecutive days with ActiPAL (sitting/lying, standing and stepping time 24 hours/day) and ActiGraph GT3X accelerometers (time spent in LPA and sitting/lying during waking hours).

**Results:** ActiPAL data - time spent in PA increased by 60 (SD=78) min/day at the end of the intervention and 80% of gains were maintained at 2-month follow-up (P = 0.029). Time spent in sedentary behaviour decreased by 55 (SD=77.1) min/day and 86% of gains were retained at 2-month follow-up. ActiGraph GT3X accelerometers (time spent in LPA and MVPA during waking hours).

**Conclusion:** Preliminary evidence suggests that the Active-Life intervention has the potential to increase PA and decrease sedentary behaviour. Further testing is needed to determine if these results hold up in a larger randomized controlled trial.

**AO197**

**QUANTITATIVE EVALUATION OF A NOVEL SELF-MANAGEMENT EDUCATION PROGRAM FOR COPD IN THE CONTEXT OF MULTI-MORBIDITY**

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**Background and Aims:** COPD often occurs in the presence of co-morbidities which impact presentation of symptoms, disease progression and resulting mortality. Patients with COPD usually have little understanding about implications of the condition and its management, especially in primary care. The Activating Primary Care COPD Patients with Multi-morbidity (APCOM) pilot study, conducted in Sydney general practice, aimed to empower patients in terms of their COPD self-efficacy in the face of their existing co-morbidities.

**Methods:** The study included patients aged between 40 and 84 years with a recorded spirometry diagnosis of COPD and at least one other co-morbidity. A self-management education program for COPD in the context of multi-morbidity, developed by the researchers based on the Health Belief Model, was tailored and delivered to the patients by trained practice nurses in three one-to-one sessions. Impact of the program was assessed by the Patient Activation Measure (PAM 13), COPD Knowledge Questionnaire (COPD-Q), COPD Assessment Test (CAT), Multimorbidity Illness Perceptions Scale (MULTIPleS), Morisky Medication Adherence Scale (MMAS-8) and accuracy of inhaler technique.

**Results:** Among 50 patients at baseline (25 males and 25 females, mean age: 69.22), 44 completed six months’ follow-up. Pre and post-test comparison of their data showed significant improvement in patient activation from 57.69 to 64.85 (p<0.001), COPD knowledge from 7.27 to 9.02 (p<0.001) and clinical impact of COPD from 20 to 17.55 (p=0.012). Perception of their multi-morbidity and medication adherence were slightly enhanced from 25.58 to 26.02 (p=0.822) and 1.88 to 1.5 (p=0.139) respectively. Number of patients who performed their inhaler technique accurately increased from 5 at baseline to 20 at post-test (p=0.001).

**Conclusions:** The study was successful in improving the patient’s COPD self-efficacy. The findings form an evidence base for upscaling the program to be tested in a larger trial to further assess its impact in day-to-day general practice.

**AO105**

**DO AUSTRALIAN COMMUNITY PHARMACISTS HAVE A ROLE IN COPD CASE FINDING?**

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**Background and Aim:** COPD case-finding by community pharmacists could identify a substantial number of people with undiagnosed COPD but little is known about the feasibility and effectiveness of pharmacy-based COPD screening in Australia. To assess the role of Australian community pharmacists in screening for COPD, utilizing a combination of a risk assessment questionnaire and micro-spirometry.

**Methods:** A 6-month screening service was conducted in 21 community pharmacies in NSW, Australia. Trained pharmacists invited their undiagnosed patients aged ≥35 years with a history of smoking and/or respiratory symptoms to participate. High risk patients were identified by means of a COPD risk assessment questionnaire (ISQ); based on COPD guidelines and underwent lung function testing using the Piko6® device. Pharmacists referred patients with an FEV1/FEV6 ratio <0.75 to their GP for further assessment and diagnosis. Participating pharmacists completed feedback questionnaires at baseline and study end.

**Results:** The ISQ indicated that 91 of 167 (54%) patients were at high risk for COPD. Of the 157 patients who completed lung function testing, 61 (39%) had an FEV1/FEV6 ratio < 0.75 and were referred to their GP. Patients reporting high levels of symptoms on the ISQ were at a significantly higher risk of an FEV1/FEV6 ratio < 0.75. Fifteen (10%)...
patients were diagnosed with COPD by their GP and 8 (5%) were diagnosed with other medical conditions; 20 of these 23 patients (87%) were initiated on treatment. Pharmacists perceived the service as useful and feasible.

Conclusions: A brief community pharmacy-based COPD case finding service is feasible and may lead to the identification and diagnosis of a substantial number of people with COPD. This might be an important strategy for reducing the burden of COPD, through timely diagnosis.

Acknowledgements: Pharmacy Guild of Australia, Lung Foundation Australia, Prof. Christine Jenkins, Dr Brett Toelle and all participating pharmacists.

Abbreviations: COPD – Chronic Obstructive Pulmonary Disease FEV1 – Forced expiratory volume in 1 second FEV2 – Forced expiratory volume in 6 seconds

Asthma 3

IDENTIFYING A NOVEL THERAPEUTIC STRATEGY FOR ASTHMA: TARGETING AIRWAY EPITHELIAL CELL RESTITUTION

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Background: The increase in asthma in the western world has not been mirrored in rural areas of the Third world where parasitic worms (helminths) are endemic, leading to the suggestion that these pathogens may protect humans from developing asthma. By analysing the excretory/secretory products of the human liver fluke Fasciola hepatica, we have discovered a novel peptide (termed FhHDM-1) with immune modulatory activity (Robinson MW PLoS Pathogens, 2011; Robinson MW FASEB J, 2012). We hypothesised that FhHDM-1 will protect against the development of allergic asthma in mouse models.

Aim: To determine whether FhHDM-1 protects against airway inflammation in a mouse model of allergic asthma.

Methods: Female C57BL/6 mice (n=8) were sensitized with house dust mite allergen (100µg) or vehicle control (PBS) on day 0 and challenged with allergen (5µg) or PBS on days 14, 15, 16, 17 via the intranasal route. FhHDM-1 (25µg) was administered intravenously 30 min prior to each allergen exposure during the challenge phase (days 14–17). Mice were euthanized 24 h after the final allergen challenge and bronchoalveolar lavage fluid was collected for analysis of cellular infiltration and cytokine and chemokine release.

Results: FhHDM-1 significantly reduced the number of total BALF cells (23.2 ± 2.6 vs 45.1 ± 1.2 x 10⁶ cells/mL, p<0.01), eosinophils (7.39 ± 1.5 vs 2.59 ± 0.5 x 10⁶ cells/mL, p<0.01), neutrophils (2.6 ± 0.57 vs 0.49 ± 0.13 x 10⁶ cells/mL, p<0.01) and lymphocytes (0.96 ± 0.22 vs 0.41 ± 0.11 x 10⁶ cells/mL, p<0.05) in house dust mite treated mice. Reduced cellular infiltration was associated with a significant reduction in BALF levels of several cytokines and chemokines, including GMCSF, IL6, IL8, KC, TNFa and MCP1.

Conclusion: Peptides from parasitic worms are potential novel therapeutic treatments for the management of eosinophilic and neutrophilic inflammation in people with asthma.
THE ROLE OF MITOCHONDRIAL FUSION IN THE PATHOGENESIS OF SEVERE ASTHMA WITH FUNGAL SENSITIZATION

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Background and Aims: Under persistent stressful condition, the balance between fission and fusion of mitochondria is out of control. However, there is little information on mitochondrial dynamics and mitophagy in the pathogenesis of bronchial asthma. In this study, we aimed to evaluate the morphologic changes of mitochondria in cells from lung tissues of a murine model of fungus-induced bronchial asthma.

Methods: Transmission electron microscopic (TEM) analysis was used to measure the mitochondrial dynamics in lung of fungal allergen inhaled mice.

Results: The mice sensitized and challenged with Aspergillus fumigatus (Af-exposed mice) showed the typical features of bronchial asthma. Interestingly, these asthmatic features were refractory to the treatment with oral dexamethasone, whereas they were improved significantly by the administration of mitochondrial reactive oxygen species (ROS) inhibitor, NecroX-7. In addition, TEM analysis revealed that in lung cells from Af-exposed mice, the mitochondria were dramatically elongated and fused each other compared to the finding in cells from control mice. The levels of mitofusin (Mfn)-1 and Mfn-2, mitochondrial fusion proteins, were significantly increased in BAL cells, primary cultured tracheal epithelial cells, and lung tissues of Af-exposed mice. The increases in Mfn-1 and Mfn-2 levels and morphological changes did not respond to oral dexamethasone, but NecroX-7 decreased the expression of mitofusins and restored the morphology of mitochondria. We also found that in vivo administration of siRNA targeting Mfn-2 modestly improved the asthmatic manifestations and mitochondrial dynamics in Af-exposed mice. We also found that the levels of the mitochondrial fission related protein and mitophagy related indicators were increased in Af-exposed mice.

Conclusions: These findings indicate that the mitochondrial hyperfusion can be induced by fungal allergen stimulation in lung cells and it may be one of the molecular mechanisms for the pathogenesis of steroid-resistant allergic airway inflammation.

METHODS:

We utilized two in vivo models induced by exposure to Aspergillus fumigatus (Af) and Alternaria alternata (Aa) as well as Af-exposed in vitro experimental system. We also checked expression of NLRP3 protein in lung tissues from allergic bronchopulmonary aspergillosis (ABPA) patients.

RESULTS:

Assembly/activation of NLRP3 inflammasome was remarkably increased in the lung of Af-sensitized/challenged mice. Elevation of NLRP3 inflammasome assembly/activation was also observed in Af-stimulated epithelial cells. Similarly, pulmonary expression of NLRP3 in patients with ABPA was increased compared to that in healthy subjects. Importantly, neutralization of NLRP3 inflammasome-derived IL-1β alleviated various pathophysiologic features of Af-induced allergic inflammation. Furthermore, blockade of PI3Kδ is improved Af-induced allergic inflammation through modulation of NLRP3 inflammasome assembly/activation, especially in epithelial cells. NLRP3 inflammasome was also implicated in Aa-induced eosinophilic allergic inflammation, which was improved by blockade of PI3Kδ.

CONCLUSIONS: These findings demonstrate that fungi-induced assembly/activation of NLRP3 inflammasome in airway epithelium may be modulated by PI3Kδ isoform. Inhibition of PI3Kδ may have potential for treating fungi-induced severe allergic lung inflammation in humans.

HOUSE DUST MITE DIRECTLY INDUCES FREE RADICAL PRODUCTION AND DNA DAMAGE, AND WEAKENS ANTIOXIDANT DEFENSE IN HUMAN BRONCHIAL EPITHELIAL CELLS

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Background and Aims: Exposure to environmental allergens is a major risk factor for asthma development. Allergens possess proteolytic activity that is capable of disrupting airway epithelium. Although there is increasing evidence pointing to asthma as an epithelial disease, the underlying mechanism that drives asthma has not been fully elucidated. Here, we investigated the direct DNA damage potential of allergen on human bronchial epithelial cells and elucidated the mechanisms mediating the damage.

METHODS: Human bronchial epithelial BEAS-2B cells were directly exposed to house dust mite (HDM) and were assayed for free radical production using CellROX and MitoTracker, DNA damage using CometChip and γH2AX immunoblotting, antioxidant defense using Nrf2 nuclear translocation and RT-PCR, and cell death using Annexin V/PI staining.

RESULTS: Direct exposure of BEAS-2B cells to HDM resulted in enhanced DNA damage as measured by the CometChip and the staining of DNA double-strand breaks (DSB) marker, γH2AX. HDM stimulated cellular reactive oxygen species (ROS) production, increased mitochondrial oxidative stress and promoted nitrosative stress. Expression of Nrf2-dependent antioxidant genes was reduced immediately after HDM exposure, suggesting that HDM altered antioxidant responses. HDM exposure also reduced cell proliferation and induced cell death. Importantly, HDM-induced DNA damage can be prevented by antioxidants glutathione and catalase, suggesting that HDM-induced ROS can be neutralized by antioxidants. Mechanistic studies revealed that HDM-induced cellular injury is NADPH oxidase (NOX)-dependent, and apocynin, an NOX inhibitor, protected cells from DSBs induced by HDM.

CONCLUSIONS: Direct exposure of bronchial epithelial cells to HDM leads to the production of ROS that damage DNA and induce cytotoxicity.
Antioxidants and NOX inhibitor can prevent HDM-induced DNA damage, revealing a novel role for antioxidants and NOX inhibitor in mitigating allergic airway disease.

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**Efferocytosis of Apoptotic Granulocytes by Monocyte-Derived Macrophages in Adults with Asthma**

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**Background and Aims:** Efferocytosis is the process whereby dead host cells and debris are ingested by phagocytic cells such as macrophages, and it is essential to maintain tissue integrity. Efferocytosis has been reported to be decreased in some people with asthma, particularly those characterised by high airway neutrophil infiltration. The aim of this study was to compare monocyte-derived macrophage (MDM) efferocytosis of granulocytes in adults with asthma and healthy controls.

**Methods:** Eligible non-smoking adults with asthma (n=13, mean age 57) and healthy controls (n=8, mean age 31) underwent a clinical assessment, venepuncture and sputum induction. The participants with asthma had a doctor’s diagnosis with evidence of variable airway obstruction and 12 (92%) were taking inhaled corticosteroids (ICS). Mononuclear cells were isolated from blood by discontinuous density gradient centrifugation and RBC lysis. Granulocytes were purified by magnetic cell isolation and cultured with monocytes at a ratio 1:5. Efferocytosis (median (q1, q3)) was higher in the cohort with asthma (35 (16, 45)%) compared with the healthy controls (13 (0, 33)%), but did not reach significance (Spearman r=-0.341, p=0.278) or lung function (Spearman r=0.105, p=0.006) but not with BMI (Spearman r=0.291, p=0.214), ICS dose (Spearman r=-0.341, p=0.278) or lung function (Spearman r=-0.105, p=0.734). Efferocytosis was negatively correlated with both sputum lymphocyte number (Spearman ρ=-0.692, p=0.009) and proportion (Spearman ρ=-0.659, p=0.014).

**Conclusions:** MDMs from patients with asthma had a similar efferocytic capacity compared with healthy controls, suggesting that their blood macrophages are functioning normally. However, the presence of lymphocytes may be counteracting efferocytosis through a mechanism that remains to be elucidated.

**TWEAK and TGF-β Induced Chemokine Production in Human Bronchial Epithelial Cells during Epithelial Mesenchymal Transition**

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**Background and Aims:** Chronic inflammation of the airways and subsequent airway remodeling play a key role in pathogenesis of asthma. Tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK), a cytokine of the TNF ligand superfamily, regulates cellular proliferation, angiogenesis, inflammation, and apoptosis. In previous reports, TWEAK has pro-inflammatory effects for various cells including epithelial cells, endothelial cells, and other mesenchymal cell types. Moreover, we previously reported that TWEAK enhances TGF-β-induced epithelial mesenchymal transition (EMT) in bronchial epithelial cells. The aim of this study was to investigate the chemokine production in bronchial epithelial cells treated with TWEAK and TGF-β.

**Methods:** Quantitative real-time reverse transcription-PCR (qRT-PCR) and Enzyme-linked immunosorbent assay (ELISA) were used to define productions of chemokine in Human bronchial epithelial cell line, BEAS-2B cells.

**Results:** Firstly, we found that TWEAK induced mRNA expression and protein levels of RANTES (regulated on activation normal T cell expressed and secreted), MCP-1 (monocyte chemotactant protein-1), and IL-8 (Interleukin-8) in bronchial epithelial cells. Moreover, co-treatment with TWEAK and TGF-β induced EMT and enhanced TWEAK-induced the mRNA expressions of RANTES. Furthermore, TWEAK-induced the mRNA expressions of RANTES, MCP-1, and IL-8 were inhibited by inhibitors of nuclear factor (NF)-κB pathway.

**Conclusions:** These findings suggest that TWEAK could induce the production of RANTES, MCP-1, and IL-8 via NF-κB pathway and could induce the production of RANTES in human bronchial epithelial cells during EMT. We conclude that TWEAK may contribute to chronic airway inflammation and remodeling.

**Identification of Novel Genetic Regulations of Asthmatic Airway Epithelium, Using Next-Generation Sequencing Data and Bioinformatics Approaches**

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**Background and Aim:** Airway epithelial cells play important roles in airway remodeling. Understanding gene regulations in airway epithelium may provide new insights into pathogenesis and treatment of asthma. This study aimed to combine gene expression (GE) microarray, next generation sequencing (NGS), and multiple bioinformatics tools to explore genetic regulations associated with airway epithelial homeostasis.
Methods: We obtained primary normal human bronchial epithelial cells and asthmatic bronchial epithelial cells from Lonza. We used GE microarray and NGS to analyze the expression profiles of mRNAs and microRNAs, respectively. We used miRmap to predict putative targets of microRNAs, and the DAVID database to analyze potential biological function of the differentially expressed genes. We selected a representative microarray (accession number, GSE43696) from the GEO database to validate the dysregulated genes identified from cells study.

Results: From the analysis of expression profiles of mRNAs and microRNAs in normal and asthmatic bronchial epithelial cells, we identified 9 genes with potential microRNAs-mRNA interactions. Of these 9 dysregulated genes, downregulation of MEF2C and MDGA1 were validated in the representative microarray (GSE43696) from GEO database. Our findings suggested that upregulated mir-203a might repress MEF2C, a transcription factor, leading to decreased cellular proliferation. In addition, upregulated mir-3065-3p may repress MDGA1, a cell membrane anchor protein, resulting suppression of cell-cell adhesion. We also found that KCNJ2, a potassium channel, was downregulated in severe asthma and may promote epithelial cell apoptosis.

Conclusion: Our study shows that aberrant regulations of mir-203a to MEF2C and mir-3065-3p to MDGA1, as well as downregulation of KCNJ2, play important roles in airway epithelial homeostasis in asthma. These findings provide new perspectives on the development of diagnostic or therapeutic strategies targeting bronchial epithelium for asthma. The approach in this study also provides a new aspect of studying the pathogenesis of asthma.

Interstitial Lung Disease 2

CLINICOPATHOLOGICAL CHARACTERISTICS OF PULMONARY-LIMITED VASCULITIS

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Background: Lung lesion is a very common and important clinical feature in antinuclear cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV). In MPA, diffuse alveolar hemorrhage and interstitial pneumonia (IP) are the most frequent manifestations.

Aim: The aim of this study is to assess the clinical characteristics and outcomes of patients with pulmonary-limited vasculitis (PLV) defined as MPO-ANCA positive IP without other organ involvements.

Patients and Methods: Forty one patients with MPO-ANCA positive IP admitted to our hospital between January 2004 and December 2014 were enrolled. Of 41 patients with MPO-ANCA positive IP, 28 were diagnosed as systemic MPA associated with IP (MPA-IP) and 13 were diagnosed as PLV. The chest HRCT findings in both groups demonstrate a high frequency of UIP, fibrotic-NSIP and combined pulmonary fibrosis and emphysema (CPFE) pattern with honeycombing, traction bronchiectasis, ground-glass opacity and emphysema. In most of these cases, the histologic pattern of UIP has been classified as UIP and/or fibrotic-NSIP. In addition, a high incidence of histological findings such as extensive interstitial fibrosis, lymphoid hyperplasia, and bronchiolitis, are characteristics observed in IP associated with collagen vascular diseases, which are not observed in idiopathic IP. The prognosis of PLV was as worse as MPA-IP (median survival time; not reached vs. 73.0 months).

Conclusions: Clinicians should be aware of MPA as an underlying feature of IP in order to avoid overlooking and misdiagnosing this condition as idiopathic IP.

AO189

INCREASED CONCENTRATION OF B CELL ACTIVATING FACTORS IN THE PATIENTS WITH AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Background and Aim: The elevation of B cell activating factor belonging to the tumor necrosis factor family (BAFF) and a proliferation-inducing ligand (APRIL) in serum is reported in some autoimmune diseases. We confirmed the increased concentration of BAFF and APRIL in the patients with autoimmune pulmonary alveolar proteinosis (APAP). We hypothesized that BAFF and APRIL in BALF also increase and reflects pathological condition of APAP.

Methods: Fifty patients with APAP, 30 healthy controls, and 13 lung disease controls were enrolled in this study. B cell activating factors (BAFF and APRIL) level in serum and BALF were measured by ELISA using commercially available kit (R&D systems and eBiscience). We compared the data with clinical measures and disease severity score (DSS).

Results: We found significant elevation of BAFF and APRIL levels in the patients with APAP compared to healthy control (p<0.05, respectively) in serum. And we also found significant elevation BAFF and APRIL levels in BALF (p<0.0001, respectively) compared to disease controls. BAFF level showed correlations with KL-6, surfactant protein (SP)-D, and SP-A (p<0.05, respectively) in serum and BALF. However, APRIL level in serum and BAFF did not show correlations with these serum biomarkers for APAP. BAFF level in BALF significantly correlated with DSS, however, APRIL level in BALF did not correlate with DSS.

Conclusion: We hypothesis that activation of B cell by BAFF and APRIL might be involved in pathogenesis of APAP.

Serum levels of anti-GM-CSF autoantibody reflected disease severity of autoimmune pulmonary alveolar proteinosis followed up for long-term

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Background: Autoimmune pulmonary alveolar proteinosis (APAP) is a rare lung disease characterized by accumulation of proteinous material due to dysfunction of alveolar macrophages and neutrophils caused by neutralizing anti-granulocyte/macrophage colony-stimulating factor (GM-CSF) autoantibody. Although the autoantibody is supposedly pathogenic for APAP, it is well known that serum levels of the autoantibody are not correlated with disease severity at the diagnosis.

Aims: We examined the relationship between autoantibody levels and clinical parameters in APAP patients followed up for long-term.

Methods: We enrolled 58 patients with APAP observed for more than 3 years in our institute and 38 out of all the cases for 5 years. We
EVALUATION FOR THE THERAPEUTIC RESPONSE BY USING A QUANTITATIVE COMPUTED TOMOGRAPHIC METHOD IN PULMONARY ALVEOLAR PROTEINOSIS

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Background: It has been known that ground glass opacity (GGO) and crazy-paving appearance are frequent high resolution computed tomography (HRCT) findings of pulmonary alveolar proteinosis (PAP). We usually use the visual radiographic method to evaluate HRCT findings, because a useful quantitative CT evaluation has not been established.

Aims: The aim of this study is to evaluate the lung attenuation of GGO by using a quantitative CT method in PAP.

Methods: Follow-up HRCT data in one case of PAP were enrolled in this study. We evaluated the lung attenuation of GGO by the image analyses software (SYNAPSE VINCENT, Fuji Film, Japan) and investigated the extent of GGO, which presented as CT indices. Bilateral lungs were divided into six zones and each zone was analyzed separately. CT indices were obtained from lung parenchymal on each zone before and after treatment with whole lung lavage (WLL). Six zones (upper, middle, lower) of CT indices were evaluated based on the following focused range of HU (all: -1024 to +400HU, higher: -800 to -400HU, and lower: -400 to +200HU).

Results: The ratio of CT indices “higher range to all range” in total six zones decreased after WLL (56.7% to 41.4%, p<0.05). CT indices of both higher range and lower range showed a significant decrease (55.3% to 33.4%, 25.8% to 8.8%, retrospectively) after WLL. The therapeutic response was dramatic especially in the left upper zone. Of note, the change of these CT indices reflected visual semi-quantitative evaluation and was corresponded to the improvement of arterial blood gas analysis.

Conclusions: This new quantitative CT method for GGO might be useful to evaluate the therapeutic response in PAP if the special reference to the range of -800 to -400 HU.

THE DIAGNOSIS OF IDIOPATHIC INTERSTITIAL PNEUMONIAS IN A REAL WORLD: NATIONWIDE SURVEILLANCE IN JAPAN

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Background and Aims: Recent new/updated classification of idiopathic interstitial pneumonias (IIPs), and the guideline of idiopathic pulmonary fibrosis (IPF) stated the requirement of surgical lung biopsy and clinical radiological, and pathological discussion or multidisciplinary discussion (MDD) for the diagnosis of IIPs and IPF, especially for the diagnosis of patients with possible UIP and inconsistent of UIP pattern. In this study, in order to know how the pulmonary physicians (community hospitals and academic hospitals/referral centers) diagnose IIPs and IPF in the real world.

Methods: In 2017, the questionnaires about the diagnosis of IIPs and IPF focusing to surgical lung biopsy and MDD were sent via internet to the doctors in Japan who are seeing patients with IIPs and IPF. Questionnaires (diagnosis of IIPs, IPF, focusing to surgical lung biopsy (SLB) and MDD) were sent to 55 Japanese institutes. 39 institute responded (71% responded) including 26 academic or ILD referral centers, and 13 community hospitals.

Results: Although SLB remains the gold standard for tissue diagnosis, considerable number of patients who need SLB have not receive SLB and MDD in a real clinical setting, especially in a community hospital. However most of the patients were diagnosed and managed within the limitation. 100% of doctors are measuring serum biomarkers (KL-6, SP-D, SP-A), and 60-100% of doctors perform BAL, and 20-80% of doctors perform TBLB. Only one institute are performing Trans bronchial cryo biopsy. Patients were managed by the combined method with HRCT, BAL/TBFLB, and serum biomarkers might be helpful for differential diagnosis.

Conclusions: Development of non-invasive, safe, and simple classification and diagnosis of IPF avoiding SLB is strongly required. We thanks to all doctors in Japan who replies this questionnaires.
**Aims:** To clarify the clinical features and long-term disease courses in UCIP patients who underwent a complete diagnostic evaluation including surgical lung biopsy, and to compare those with idiopathic pulmonary fibrosis (IPF) and idiopathic nonspecific interstitial pneumonia (iNSIP) patients.

**Methods:** There were 90 IIPs patients with surgical lung biopsy between January 2010 and December 2011 in our institution. We classified those into UCIP, IPF, iNSIP or other IIPs on the basis of 2013 ATS/ERS classification statement, and UCIP were subdivided into two groups of with or without histopathological usual interstitial pneumonia (UIP) pattern. Clinical characteristics and prognosis were retrospectively compared by reviewing medical records for five years after surgical lung biopsy.

**Results:** Clinical characteristics at the biopsy of the 23 patients with UCIP, the 31 patients with IPF and the 23 patients with iNSIP are shown in Table 1. The survival curves of the three groups are shown in Figure 1. Survival prognosis of UCIP was in between IPF and iNSIP. FVC change of UCIP patients was also better than that of IPF, and worse than of iNSIP. UCIP patients with pathological UIP pattern had a poorer survival rate as compared with no UIP pattern (Figure 2).

**Conclusions:** UCIP with multidisciplinary evaluation including a surgical lung biopsy showed a better prognosis than IPF. Among UCIP, patients with pathological UIP pattern had a poor prognosis.

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**Table 1. Characteristics of UCIP, IPF and iNSIP at the biopsy period**

<table>
<thead>
<tr>
<th></th>
<th>UCIP</th>
<th>IPF</th>
<th>iNSIP</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients n</td>
<td>23</td>
<td>31</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Median Age (years)</td>
<td>68</td>
<td>66</td>
<td>63</td>
<td>0.149</td>
</tr>
<tr>
<td>Sex: male (n)</td>
<td>12 (52%)</td>
<td>22 (71%)</td>
<td>13 (57%)</td>
<td>0.326</td>
</tr>
<tr>
<td>Smoking history (n)</td>
<td>15 (65%)</td>
<td>21 (68%)</td>
<td>14 (61%)</td>
<td>0.735</td>
</tr>
<tr>
<td>FVC</td>
<td>2.62L</td>
<td>2.63L</td>
<td>2.38L</td>
<td>0.491</td>
</tr>
<tr>
<td>%FVC</td>
<td>86.8%</td>
<td>83.7%</td>
<td>72.8%</td>
<td>0.046*</td>
</tr>
<tr>
<td>%DLCO</td>
<td>80.0%</td>
<td>83.0%</td>
<td>66.4%</td>
<td>0.017*</td>
</tr>
<tr>
<td>KL-6</td>
<td>1346 U/ml</td>
<td>1346 U/ml</td>
<td>1572 U/ml</td>
<td>0.041*</td>
</tr>
<tr>
<td>Distance of 6MWT</td>
<td>364m</td>
<td>415m</td>
<td>363m</td>
<td>0.198</td>
</tr>
</tbody>
</table>

*p.value<0.05
MUC4 VARIABLE NUMBER TANDEM REPEAT POLYMORPHISMS AND SEVERE LUNG INJURY

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Background and Aims: Mucin glycoproteins are critically important in airway epithelial biology and innate immunity. Most mucins have the highly glycosylated tandem repeat (TR) domain which shows variation in repeat number. It was recently reported that variable number tandem repeats (VNTR) polymorphisms of MUC1 and MUC5AC are associated with severity of cystic fibrosis lung disease. MUC1 and MUC4 are two major transmembrane mucins in lung, and molecular structure of MUC4 is similar to that of MUC1. However, MUC4 had not been investigated well about its function and pathological role in lung disease. We studied the role of MUC4 in sever lung injury, such as acute lung injury by drug or acute exacerbation of interstitial pneumonia whose pathological finding is diffuse alveolar damage.

Methods: We gathered 6 patients with acute injury by drug or acute exacerbation of interstitial pneumonia, and 41 controls of healthy Japanese. We analysed the MUC4 VNTR polymorphisms by Southern blot.

Results: Southern blot analysis of 47 samples revealed 6 distinct alleles of MUC4. The largest allele was about 18kb, and the most frequent. In patient group, the largest allele was observed more frequent than in healthy control group, but allele distribution was not significantly different between two groups by Mann-Whitney Rank Sum Test (p=0.065)

Conclusions: Our data revealed patients with severe lung injury might have the specific allele which was showed by Southern blot, but could not reveal the distribution of MUC4 alleles was not different significantly between two groups.
ABSTRACT

Asthma 1

ESTABLISHMENT OF AN EOSINOPHILIC BRONCHITIS MOUSE MODEL
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Background and Aim: This study aimed to establish an eosinophilic bronchitis (EB) mouse model responsive to hormone therapy with increased coughing and airway eosinophilic inflammation and no airway hyperreactivity (AHR).

Methods: Twenty-eight mice were divided into normal saline (NS), asthma (AS), EB, and dexamethasone (DXM) groups. The AS group was stimulated using nasal drops of 200 μg/μl ovalbumin (OVA), and the EB and DXM groups were stimulated using 10 μg/μl OVA. Next, the DXM and NS groups received intraperitoneal injections of 5 mg/kg of DXM and NS, respectively. Cough sensitivities were evaluated after model establishment. After 6 h of cough stimulation, airway reactivity was measured, and percentages of eosinophils (Eos%) in bronchoalveolar lavage fluid (BALF) and pathological changes to lungs tissues were observed.

Results: The number of coughs in the AS, EB, and DXM groups increased significantly compared to that in the NS group (p<0.01). After DXM treatment, the number of coughs significantly decreased compared to that in the AS and EB groups (p<0.05). After methacholine (Mch) stimulation at 12.5 mg/ml and 25 mg/ml, the lung resistance (RL) of the AS group was significantly higher than that in the NS, EB, and DXM groups (p<0.05). The BALF and pathological results showed that the AS and EB groups had obvious airway eosinophilic inflammation, and DXM could attenuate airway inflammatory infiltration in EB mice.

Conclusion: Establishing a mouse EB model with all 4 features is possible using 10 μg OVA nasal drops.

RESULTS: Rapamycin significantly reduced airway hyperresponsiveness to aerosolized methacholine at 6.25 mg/ml, and inhibited IL-4 level in BALF as well as markedly decreased inflammatory infiltration in lung tissues. Notably, rapamycin significantly inhibited mTORC1 activity, whereas had limited effects on mTORC2, as assessed by phosphorylation of their substrates phosphorylated S6 protein and phosphorylated Akt, respectively. However, Treg cells in BALF were significantly reduced after rapamycin treatment.

Conclusions: Antiasthmatic effects of rapamycin during remission time are at least partially through mTORC1 signaling pathway, and it may be worth to use rapamycin for asthma patient in remission to control asthma attack.

JIAN-PI-YI-QI FORMULAE ATTENUATE AIRWAY INFLAMMATION IN A CHRONIC MOUSE MODEL OF ASTHMA VIA SUPPRESSION OF mTORC1 PATHWAY
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Background and Aims: Jian-Pi-Yi-Qi formulae (JPYQF) is frequently used in remission stage in patients with asthma in traditional Chinese medicine (TCM). It aims to remove retained phlegm, a core pathogenic factor in asthma, via methods of nourishing spleen and enriching Qi in TCM. However, the mechanisms through which JPYQF exerts its antiasthmatic effects remain unclear. This study was aimed to the antiasthmatic effects and mechanisms of JPYQF in a chronic mouse model of asthma.

Methods: A chronic mouse model of asthma was established by sensitization and repeated challenge with ovalbumin (OVA), followed with oral administration of JPYQF, and then mouse were re-challenged by OVA. The characteristic features of allergic asthma, including airway hyperreactivity, histopathology, and cytokines (IL-4, -5, -13, -17 and INF-γ) in bronchoalveolar lavage fluid (BALF) were examined. Phosphorylated proteins expression of mTORC1 (P-S6 S235/236, P-4E-BP1 S65, P-p70S6K T389) and mTORC2 (P-mTOR S2481, P-Akt S473) pathway in lung tissue were assessed.

Results: The oral administration of JPYQF markedly suppressed airway hyperresponsiveness to aerosolized methacholine and reduced IL-4, IL-5 and IL-13 levels and increased INF-γ levels in the BALF. Histological studies showed that JPYQF significantly decreased inflammatory infiltration in the lung tissues. Furthermore, JPYQF effectively inhibited the mTORC1 activity (as evidenced by reduced substrates S6 S235/236 and 4E-BP1 S65 phosphorylation), whereas had limited effects on mTORC2 (as assessed by phosphorylated mTOR S2481 and Akt).

Conclusions: JPYQF is effective to attenuate chronic airway inflammation in asthma, the mechanism by which is at least partially via inhibiting mTORC1 signaling pathway.

EFFECT OF HISTONE DEACETYLASE ENZYME 8 INHIBITOR(HDAC8I) ON SOCS3 EXPRESSION IN AN ACUTE MURINE ASTHMA MODEL
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Results: Histone deacetylase 8 inhibitor (HDAC8I) inhibits airway inflammation in acute asthmatic mice, by down-regulating SOCS3 gene expression in airway tissues.
**Abstracts**

**Background and Aims:** Asthma is a chronic obstructive disease, the pathogenesis is related to the imbalance of Th1 / Th2 cytokines. Histone deacetylase inhibitors have a wide range of effects that demonstrate therapeutic effects in animal models of asthma. Previously, in OVA induced mouse model of asthma we found high expression of SOCS3, and SOCS3 plays an important role in the immune response by regulating cytokine responses and Th1 / Th2 imbalance. In this study, we investigated the effect of specific histone deacetylase 8 (HDAC8) inhibitor on SOCS3 protein expression in acute Murine Asthma Model.

**Methods:** Wild-type BALB/C mice were sensitized intraperitoneally three times with ovalbumin (OVA) and aluminum hydroxide gel (on weeks 0, 1, 2) and nebulized 1 week. Ovalbumin-exposed mice were treated with PCI-34051 or vehicle control. Airway inflammation was assessed by bronchoalveolar lavage fluid cell counts and HE staining of lung tissue sections. Airway hyperresponsiveness was assessed by plethysmography measurement of airway resistance. The balance of Th1/Th2 was assessed by Western Blot. The expression of SOCS3 was assessed by Western Blot.

**Results:** Administration of PCI-34051 and Budesonide reduced the eosinophilic inflammation and airway hyperresponsiveness in acute asthma mice, and there was no significant difference, PCI-34051 can increase levels of serum IFN-γ, reduce levels of IL-4, and then regulate the balance of Th1 / Th2. The expression of SOCS3 protein was significantly inhibited by PCI-34051.

**Conclusions:** PCI-34051 can reduce the expression of SOCS3 in acute Murine Asthma Model, and then regulate the balance of Th1 / Th2.

**THERAPEUTIC EFFECTS OF HDAC8 SPECIFIC INHIBITOR PCI-34051 IN ACUTE ASTHMATIC MICE AND ITS EFFECT ON GALECTIN-3**

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**Background and Aims:** Airway inflammation and airway hyperresponsiveness are major aspects of asthma pathology. Present studies have confirmed that broad-spectrum histone deacetylase inhibitors can effectively relieve airway inflammation, airway remodeling and airway hyperresponsiveness in Chronic asthma mice. In this study, we investigated the effect of PCI-34051, a selective HDAC8 inhibitor, on the development of acute allergic airway disease mice with airway inflammation, and airway hyperresponsiveness. And its effect on galectin-3.

**Methods:** Wild-type BALB/C mice were sensitized intraperitoneally three times with ovalbumin (OVA) and aluminum hydroxide gel (on weeks 0, 1, 2) and nebulized 1 week. Ovalbumin-exposed mice were treated with PCI-34051 or vehicle control. Airway inflammation was assessed by bronchoalveolar lavage fluid cell counts and HE staining of lung tissue sections. Airway hyperresponsiveness was assessed by plethysmography measurement of airway resistance. The expression of Galectin-3 was assessed by Immunohistochemistry and Western Blot.

**Results:** Administration of PCI-34051 and Budesonide reduced the eosinophilic inflammation and airway hyperresponsiveness in acute asthma mice, and there was no significant difference. The immunohistochemical studies revealed that Galectin-3 was mainly expressed in bronchial epithelial cells and surrounding inflammatory cells. And the expression of galectin-3 protein was significantly inhibited by PCI-34051.

**Conclusions:** These results demonstrate that treatment with HDAC8 inhibitors can reduce airway inflammation and airway hyperresponsiveness in acute Murine Asthma Model, and it can inhibit the expression of Galectin-3.

**COMPARATIVE STUDY OF ACUTE AND CHRONIC MURINE ASTHMA MODEL IN THE PATHOGENESIS OF ASTHMA**

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**Background and Aims:** Asthma is a chronic respiratory heterogeneous disease, in which long-term repeated attacks induced airway remodeling and hyperresponsiveness. With these backgrounds in mind, we attempted to explore the different characteristics of airway inflammation, airway remodeling, and airway hyperresponsiveness in different phase of asthma, and clarify the pathological changes during the pathogenesis of asthma.

**Methods:** Wild-type BALB/C mice were sensitized intraperitoneally three times with ovalbumin (on weeks 0, 1, 2) and nebulized 1 week (early phase) or 8 weeks (prolonged phase). Untreated mice were used for normal control. Airway inflammation was assessed by bronchoalveolar lavage fluid cell counts, inflammatory cytokines secretion and HE staining. Airway remodeling was assessed by Alcian blue-Periodic acid Schiff staining and Masson trichrome staining. Airway hyperresponsiveness was assessed by plethysmography measurement of airway resistance.

**Results:** We confirmed that airway hyperresponsiveness in early phase and prolonged phase were significantly increased when stimulated with acetylcholine. Interestingly, airway hyperresponsiveness in prolonged phase was significantly increased compared with early phase when stimulated with normal saline. The inflammatory changes were more remarkable in early phase, characterized by increasing numbers of total cells and eosinophils, levels of IL-4, IL-5 and IFN-γ, and aggregation of inflammatory cells in the lung tissue. However, remodeling changes such as the secretion of TGF-β1 and VEGF in the BALF, airway smooth muscle thickening, collagen deposition and subepithelial fibrosis were more significant in prolonged phase.

**Conclusions:** In early phase, asthma mainly manifests inflammatory changes, which is the key factor leading airway hyperresponsiveness, but mild remodeling changes have been presented during this phase. In prolonged phase, although the inflammatory changes are continued, but the main factors that impact airway hyperresponsiveness are the organic changes.

**EFFECTS OF ASTRAGALOSIDE IV ON TH2 RESPONSE IN ALLERGIC ASTHMA IN VIVO AND VITRO**

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**Background and Aims:** Astragaloside IV (AS-IV), a main constituent of Astragalus membranaceus, has been confirmed to have a broad range of pharmacological properties in asthma, including immunomodulatory, anti-inflammatory, and anti-fibrosis properties. Nevertheless, the mechanisms through which AS-IV exerts its antiasthmatic effects have not been fully elucidated. This study was aimed to investigate the effects of AS-IV on Th2 responses in allergic asthma in vivo and vitro.

**Methods:** In vivo study, A mouse model of asthma was established by sensitization and challenged with ovalbumin (OVA). The characteristic features of allergic asthma, including airway hyperreactivity, histopathology, and cytokines (IL-4, -5, -13, -17 and INF-γ) in bronchoalveolar lavage fluid (BALF) were examined. In vitro study, Th2 cytokine production was evaluated in the culture supernatant of D10.G4.1 (D10 cells) followed by the determination of cell viability, meanwhile Th2 transcription factor GATA-3 expression in D10 cells was also determined.
Results: The oral administration of AS-IV markedly suppressed airway hyperresponsiveness to aerosolized methacholine and reduced IL-4, IL-5 and IL-17 levels and increased INF-γ levels in the BALF. Histological studies showed that AS-IV significantly decreased inflammatory infiltration in the lung tissues. In vitro study, AS-IV significantly suppressed Th2 cytokines of IL-4 and IL-13 by ConA-stimulated D10 cells without inhibitory effect on cell viability. Furthermore, GATA-3 protein expression was also markedly reduced by AS-IV.

Conclusions: The antiasthmatic effects AS-IV was associated with the immunomodulatory properties on Th2 response in vivo and vitro.

CHITIN INDUCED AIRWAY INFLAMMATION AND PRODUCTION OF PROSTAGLANDIN E2

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Background: Chitin, a polymer made up of repeating units of N-acetyl-d-glucosamine, is a ubiquitous polysaccharide found in the walls of fungi and the exoskeleton of arthropods such as crabs, shrimp, and insects. As it does not have a mammalian counterpart, chitin could be important inhalant antigen for bronchial asthma. Chitin stimulates innate immune cells and regulates adaptive allergic immune responses. Previous studies have shown that as pathogen-associated molecular patterns (PAMPs), chitin activates Toll-like receptor 2 (TLR2) and TLR3, leading to the production of pro-inflammatory cytokines and chemokines.

Methods: Mice were intranasally injected chitin on consecutive 3 days. After 24 hours from last injection, bronchoalveolar lavage (BAL) fluids were collected. The mice were treated with indomethacin as cyclooxygenase (COX) inhibitor or vehicle during intranasal administration of chitin.

Results: The murine model of chitin-induced airway inflammation showed that the inflammatory cell infiltration into BAL fluids, the concentrations of PG_E2 in BAL fluids, and airway hyperresponsiveness were significantly increased as compared to control mice. The mRNA expression of COX-2 and microsomal PG_E2 synthase 2, and the secretion of PG_E2 was significantly increased in alveolar macrophages after the stimulation with chitin. Moreover, COX inhibitor increased eosinophils and neutrophils in BAL fluids and decreased the secretion of PG_E2 in BAL fluids in the murine model of chitin-induced airway inflammation.

Conclusions: These results suggested that chitin induced the airway inflammation in mice and the production of PG_E2 in alveolar macrophages. PG_E2 might protect against the chitin-induced airway inflammation. The functions of PG_E2 in the chitin-induced airway inflammation still further investigation.

NINTEDANIB AMELIORATED AIRWAY REMODELING BY INHIBITING ANGIOGENESIS OF BRONCHIAL VESSELS

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Background and Aim: Nintedanib is a multi-tyrosine kinase receptor inhibitor recently approved for treatment of idiopathic pulmonary fibrosis. Although angiogenesis is a key process involved in airway structural changes in patients with bronchial asthma, the effect of nintedanib targeting the angiogenesis pathway on airway remodeling has not been evaluated.

Methods: We used a 3-month ovalbumin (OVA) challenge mouse model of airway remodeling. Nintedanib was orally administrated during the challenge period, and the effects were examined the typical pathophysiological features of asthma. Also, we measured the number of blood vessels around the airway and α-smooth muscle actin area was evaluated around vessels. The expression of growth factor receptors was analyzed in mice lung tissues.

Results: The OVA challenged group showed a significant increase in typical features of asthma including airway inflammation and remodeling compared to those in the control group. It was sufficiently suppressed by nintedanib compared to that by OVA. Moreover, the number of blood vessels and ASM area around vessels was significantly decreased by nintedanib. Also, nintedanib effectively suppressed the phosphorylation of vascular endothelial growth factor receptor 2 (VEGFR2), fibroblast growth factor receptor 3 (FGFR3) and platelet-derived growth factor receptor β (PDGFRβ)

Conclusion: Nintedanib effectively ameliorated airway remodeling in an OVA-induced chronic asthma model. These results suggest that nintedanib could be a new treatment agent targeting airway remodeling in patients with severe asthma.

SEROLOGY RESPONSES TO TRIMETHOPRIM-SULFA MEDICATION IN PATIENTS WITH ASTHMA

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Background and Aim: Asthma is a heterogeneous disease with different phenotypes including Th2-high phenotype. Previous study identified tenascin-C (TNC), extracellular matrix proteins, as one of the Th2 cytokines-induced genes in human bronchial epithelial cells. TNC accumulated in airway basement membrane of the patients with asthma and the deposition of TNC is showed as a histopathological subepithelial marker for disease activity in asthma. The objective of this study is to investigate whether serum TN-C levels in patients with asthma was associated with asthma severity and clinical asthma outcomes.

Methods: We recruited 126 adult patients with mild to severe asthma. Peripheral venous blood samples were collected and serum was frozen immediately after centrifugation. The concentration of TNC was measured in simultaneously thawed serum using the enzyme-linked immunosorbent assay.
Abstracts

Results: In the patients with severe asthma, the serum TNC levels were significantly higher as compared with patients with mild to moderate asthma, and were correlated with the daily dose of inhaled corticosteroids, GINA treatment steps, peripheral blood neutrophil counts, and serum IgE levels, but not with airflow limitation. In the patients with a total IgE level of more than 100 IU per milliliter, the serum TNC levels were correlated with serum IgE levels, but not with air.

Conclusions: The serum TNC levels in the patients with asthma were associated with disease severity and were correlated with airflow limitation in IgE-high subgroup. Further studies are needed to investigate whether the serum TNC is a novel serum biomarker candidate in the patients with asthma.

AP011

SERUM MASPIN AS A BIOMARKER FOR AIRWAY OBSTRUCTION IN ASTHMA

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Background and Aim: Maspin (MAmmary Serine Protease Inhibitor) is one of serine protease inhibitor family, which is largely expressed on bronchial epithelial cells. In vitro studies demonstrated that maspin was increased in accordance with the pressure applied to the human bronchial epithelial cells, the maspin level was increased in asthmatics. We planned to find the expression of maspin associated with lung function and other markers in asthmatics.

Methods: Serum maspin levels were measured by ELISA in asthma patients (n=365) who visited the asthma center in Asan Medical Center from May 2005 to December 2014, and healthy controls (n=87) who visited the Health Examination Center in the same hospital. Maspin levels were compared between the two groups, and we subsequently tried to find out if the maspin level correlated with clinical variables within the asthma group.

Results: The serum concentrations of maspin were significant higher in asthmatics than healthy control group (36.76 vs 18.01 ng/ml, P-value < 0.001). The maspin levels in serum were 42.55± 36.57 ng/ml in the group of patients with FEV1 less than 60%, 40.88 ± 50.12 ng/ml in the 60-80% group and 37.86 ± 32.65 ng/ml in the ≥ 80% group. We found a negative correlation between maspin and initial FEV1 (P-value < 0.001). We also found these trends on longitudinal FEV1/FVC ratio. (P-value 0.037).

Conclusion: In this study, maspin concentration was increased in asthmatics, and it showed negative correlation with lung function. These data suggest maspin could be a potential biomarker that reflect airway obstruction. Further replication analysis is necessary to validate the association found in this study.

AP012

ASSOCIATION BETWEEN LIPID PROFILE AND RISK OF ASTHMA: A META-ANALYSIS AND SYSTEMIC REVIEW

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Background and Aims: To explore the association of asthma with serum levels of high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol, and triglyceride.

Methods: PubMed, Cochrane, and Embase databases were systematically searched through November 2015 using the following search terms: dyslipidemia, HDL, LDL, triglyceride, cholesterol, and asthma. Eligible studies included randomized controlled trials (RCTs), retrospective, cohort, and cross-sectional studies. Sensitivity analysis and publication bias were performed.

Results: Twenty studies were included in the analysis with a total 32,604 patients (3,458 in the asthma group and 29,146 in the control group). The pooled analysis found that the mean difference between groups was significantly higher in the asthma group for levels of LDL (6.026 mg/dL, 95% CI= -2.696 to 9.366, P<0.001) and total cholesterol (8.161 mg/dL, 95% CI= -3.006 to 13.316, P=0.002) compared with the control group. No association was observed between asthma and control groups for levels of HDL (mean difference, -0.728, 95%CI= -3.146 to 1.691, P=0.555) or triglycerides (mean difference, 1.436, 95%CI=-2.768 to 5.640, P=0.503).

Conclusions: Levels of LDL and total cholesterol may impact the presence of asthma.
Background and Aims: Fractional exhaled nitric oxide (FeNO) is a potentially useful biomarker for the assessment of airway inflammation. It assists both in diagnosis and treatment in those with undiagnosed and established asthma. We analyzed the usefulness of FeNO measurement with portable analyzer in persistent cough (defined as lasting for 3 weeks or more) patients in Hong Kong in a specialist clinic.

Methods: Consecutive subjects who had been referred to our clinic for persistent cough from April 1st, 2015 to May 28th, 2017 were included. FeNO cut off is defined as 25ppb for adult patients and 20ppb for paediatric patients. Retrospective analysis for patients diagnosed asthma and non-asthma with high FeNO level (>25ppb) and low FeNO were studied. Asthma was diagnosed based on clinical history, lung function test and guidelines suggested by GINA.

Results: 294 patients were included in the study with 558 FeNO tests performed. (Age range 10-72, mean age=46.0; male gender=152 (52%); Smoker=35 (7.1%). 199 patients were diagnosed asthma, while 95 patients diagnosed non-asthma. Asthma patients with high FeNO (AH=106) with a mean FeNO=62ppb, while asthma patients with low FeNO (AL=93) with a mean FeNO=14ppb and non-asthma patient with mean FeNO=16ppb. Asthma patient with high FeNO tends to have more childhood asthma (22%) and allergic rhinitis (29%) comparing with non-asthma patients, with 5% and 16%, respectively.

Conclusions: Normal FeNO could not rule out asthma while higher FeNO patients tends to have higher risk of childhood asthma and allergic rhinitis. Measurement of FeNO can be useful in the management of persistent cough or dyspnoeic patients in clinical practice.

THE IMPACT OF EXHALED NITRIC OXIDE MEASUREMENTS IN THE SPECIALIST OUTPATIENT SETTING

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Background and Aim: Exhaled nitric oxide (FeNO) is a marker for airways inflammation, which can be measured easily with portable devices in the outpatient setting. FeNO measurements may help guide clinicians in the titration of inhaled steroids in asthma and other inflammatory lung conditions. It has been shown that tailoring medications according to FeNO level decreases the frequency of asthma exacerbations and that using a FeNO driven strategy can have a cost-effective advantage. This study will analyse FeNO measurements in the specialist outpatient setting for several endpoints including the impact of real-time FeNO level on clinical decision-making (change/no change), the frequency with which FeNO level led to a change in management with respect to corticosteroids, and the reason that FeNO was undertaken (aid with diagnosis, management, attain baseline or assess compliance).

Methods: Ethics approval was obtained from the St Vincent’s Hospital Human Research Ethics Committee prior to commencement of the project. Patients with asthma and airways inflammation were prospectively identified by the treating physician and their data was recorded prior to the FeNO level being taken. Data was retrospectively analysed. Baseline characteristics of patients, current therapy, changes in therapy, spirometry (pre and post bronchodilator), reason for FeNO measurement and FeNO levels were reviewed. FeNO was measured using the NIOX VERO handheld device.

Results: 129 patients had FeNO levels recorded, with 194 patient encounters in total, and 59% of patients had a primary diagnosis of asthma. In 49% of encounters, FeNO altered clinical management decisions. Clinical decisions were altered the most in encounters where FeNO levels were 50-75, (normal range <25).

Discussion/Conclusion: FeNO levels were simple to measure in the realtime clinical setting. This analysis explores the impact of FeNO levels on clinical decision making in the specialist outpatient setting, with respect to corticosteroid management.

SYMPTOMS CONTRIBUTING TO THE DIAGNOSIS OF ASTHMA IN SUBACUTE OR CHRONIC COUGH PATIENTS WITH LOW LEVELS OF FRACTIONAL EXHALED NITRIC OXIDE

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Background and Aims: Cough is one of the most common symptoms at outpatient department, and asthma is one of the most common causes of cough. Fractional exhaled nitric oxide (FeNO) is known to be useful for diagnosis of asthma. However, it is often difficult to diagnose asthma in patients with low levels of FeNO. In the present study, we evaluated our original questionnaire, and identified symptoms which may be clues to diagnose asthma in patients with cough.

Methods: We retrospectively analyzed the medical records of patients who attended our outpatient department with the chief complaint of subacute or chronic cough and answered to our original questionnaire from April 2014 to May 2017. We investigated optimal cut-off level of FeNO to identify asthma using receiver operating characteristic (ROC) curve analysis. Then, we identified the factors contributing to the final diagnosis of asthma in patients with low levels of FeNO using chi-square test and logistic regression analysis.

Results: In total, 434 patients were included into the final analysis: median age of 54 years old, 247 female (57%), 246 patients with chronic cough (57%). 169 patients (39%) were diagnosed as bronchial asthma or cough variant asthma. In 219 patients, we measured FeNO before treatment. The ROC curve analysis for FeNO revealed the optimal cut-off values at 23 ppb. While there were 95 patients with high FeNO (>23ppb), and 73 patients of them were diagnosed as asthma (76.8%), there were 124 patients with low FeNO (24 patients with asthma). In the latter patients, three question items: wheeze, past history of asthma, and seasonal cough were identified to predict asthma.

Conclusions: We identified that wheeze, past history of asthma, and seasonal cough were the items of questionnaire contributing to the final diagnosis of asthma in subacute or chronic cough patients with low levels of FeNO.

OXIDANT/ANTIOXIDANT STATUS IN PATIENTS WITH BRONCHIAL ASTHMA

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Background and Aim: Bronchial asthma (BA) is a chronic inflammatory airway disease which is characterized by airflow obstruction and airway hyperresponsiveness. Oxidative stress have been indicated an...
important role of airway inflammation in asthmatic patients. The aims of this study is measuring oxidant/antioxidant status and to assess its correlation with laboratory data, airway obstruction and asthmatic symptoms.

**Methods:** We recruited patients with BA from November 2016 through March 2017. We measured serum reactive oxidative metabolites (ROM) levels and biological antioxidant potential (BAP) levels as an oxidant/antioxidant status. We assessed asthmatic symptom using asthma control test (ACT).

**Results:** Forty-nine patients (25 women) were included in this study. Twenty-five patients were non-smokers. The median age was 65 years (22 to 87 years). Serum ROM levels were correlated with ESR, CRP and serum amyloid A (rs = 0.611, P < 0.001, rs = 0.436, P = 0.002, rs = 0.368, P = 0.012, respectively). Serum ROM levels were negatively correlated with ACT, %FVC and %FEV1 (rs = -0.310, P = 0.030, rs = -0.430, P = 0.002, rs = 0.342, P = 0.016, respectively). Serum BAP levels were not correlated with ACT or other parameters.

**Conclusion:** Serum ROM levels were associated with systemic inflammation, and correlated with airflow obstruction and ACT. Assessment of oxidant status may be useful for understanding condition of BA.

**METEORIN AS A BIOMARKER TO PREDICT ASTHMA SEVERITY**

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**Background:** There are intense research efforts in biomarkers to predict disease severity and treatment response in asthmatics. Meteorin-like (Metrnl) is a hormone that regulates immune-adipose interactions and inflammatory cytokines. Until now, there has been no study about a relationship between Metrnl levels and asthma.

**Aims:** Metrnl is hypothesized as a marker related with airway inflammation in asthmatics. It is planned to find out the relationship between Metrnl levels with the lung functions or other clinical parameters.

**Methods:** Metrnl levels in serum were measured by ELISA in asthmatics (n=379) who visited the asthma center in a tertiary referral hospital from May 2005 to December 2014, and healthy controls (n=92) who visited the Health Examination Center in the same hospital. Metrnl levels were compared between these groups and also further evaluated whether the Metrnl levels showed a correlation with the lung functions and with other clinical variables within the asthma groups. The group with high Metrnl levels was defined as patients whose Metrnl level was over 1.06ng/ml in asthmatics. In addition, clinical characteristics of the ‘high meteoin’ phenotype were investigated.

**Results:** The concentrations of Metrnl were significantly higher in asthmatics than in the controls, showing a negative correlation with the lung functions. With multiple regression analysis, Metrnl level showed a negative correlation with blood eosinophil counts and a positive correlation with the age to start asthma medication. The subjects in the group with high Metrnl levels were older, heavier smokers, had lower FEV1 % predicted. They also showed more leukocytosis and were older at the onset of symptoms, diagnosis and treatment of asthma.

**Conclusions:** This study showed that serum Metrnl is higher in asthmatics and had a negative correlation with the lung functions. Thus, Metrnl shows the potential to be a promising new biomarker in asthma.

**THE ROLE OF A2-MACROGLOBULIN IN THE FORMATION OF COLD AIRWAY HYPERRESPONSIVENESS IN ASTHMA PATIENTS**

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**Background and Aim:** α2-macroglobulin (α2MG) is a plasma protein with antiproteinase activity which is also used as a biomarker of plasma exudation in airways. The aim of the study was the assessment of association between the level of α2MG in induced sputum and development of cold airway hyperresponsiveness (CAHR) in asthma patients.

**Methods:** 28 patients with mild persistent asthma were investigated for their asthma control status according to the Asthma Control Test (ACT), lung function (FEV1), and airway reactivity (ΔFEV1, ΔFEF25-75) to 3-min isocapnic cold (-20°C) air hyperventilation (CAH). ΔFEV1 of 10% or more from baseline after CAH was considered as CAHR. The level of α2MG was analyzed in induced sputum (IS) with α2-macroglobulin ELISA Kit (Immundiagnostik AG, Germany).

**Results:** According to the bronchial challenge test, the patients were divided into group I with CAHR (n=18, ΔFEV1=-15.1±8.0%) and group II without CAHR (n=10, ΔFEV1=-3.4±1.4%). Baseline FEV1 was not significantly different between groups I and II (84.1±4.0 vs. 93.5±6.1%, respectively, p=0.19). The patients of group I had lower values as compared to group II for ACT (15.3±1.2 vs. 19.3±1.4 points, p=0.044) and α2MG (2.9±0.47 vs. 4.8±0.79 μg/ml, p=0.048). The correlation between the level of α2MG in IS and the drop of FEF25-75 in response to CAH (r=0.64, p=0.025) was found out.

**Conclusion:** The low level of α2MG in IS may be associated with development of CAHR and uncontrolled status in asthma patients.
ASSOCIATION BETWEEN THE GLCCI1 VARIANT AND RESPONSE TO INHALED CORTICOSTEROIDS IN SOUTH VIETNAMESE ASTHMATICS

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Background: Inhaled corticosteroid (ICS) is the mainstay of asthma treatment. Unfortunately, about 10%–15% of patients still have poor asthma control despite receiving optimal therapy. A significant association between the GLCCI1 variant rs37972 and response to ICS in white asthmatics was reported by Tantisira et al.

Aims: to determine whether variant rs37972 related to ICS efficacy in south Vietnamese asthmatics.

Methods: We enrolled 92 adult patients and assessed their asthma control as well as spirometry testing over the first 12 months starting ICS therapy at 4 time points: at starting ICS treatment, after 3 months, 6 months and 12 months. Genotyping for rs37972 was done with direct sequencing method using DNA extracted from whole blood samples.

Results: The frequency of the risk allele (T allele) was 48%. The rate of asthma control in patients who had CC genotype was higher than TT genotyped patients after 12 months continuously treated with ICS. This genotype-dependent difference was only evident among patients unexposed to occupational asthmagens (92.3% vs 41.7%, p=0.011). Similarly, the CC genotype had the improvement of FEV1 better than the CT and TT genotype after ICS therapy not only 3 months (p=0.05) but also 6 months (p=0.006).

Conclusions: This primary study in the assessment of GLCCI1 variant suggested an association between SNP rs37972 and ICS response in south Vietnamese asthmatics.
### Conclusions:
Flow cytometric analysis of induced sputum could be a useful method to evaluate airway inflammation.

### Background and Aim:
In November 2016, Melbourne experienced the world's most devastating episode of epidemic thunderstorm asthma (ETSA). In excess of 3460 patients presented to emergency departments (EDs) across Melbourne, with 35 ICU admissions and 9 deaths. This study did not include presentations to primary care settings. The aim of this study was to characterise known asthmatics presenting to the ED’s of Melbourne’s two largest health services.

### Methods:
ED respiratory presentations at Eastern and Monash Health (east and southeast Melbourne) over 48 hours (during and immediately following thunderstorm activity) were reviewed. Patients were included if ED records indicated acute asthma. A standardised telephone questionnaire was developed and patients were contacted within one month following the event to assess prevalence of asthma diagnosis; asthma control (adapted asthma control test [ACT]); inhaled preventer usage and asthma action plan ownership and implementation.

### Results:
599 of 779 patients with ETSA completed the questionnaire (76.9% response); 55% (n=330) were male with mean age of 30.6 years (±18.8). Overall, 42% (n=250) had ever been diagnosed with asthma, with 57% (n=184) of these having ‘current asthma’ symptoms in the last 12 months. Of those with current asthma, 53% (n=97) had suboptimal control (ACT<20) and 40% (n=73) had utilised urgent healthcare services for asthma in the last 12 months. Within this group 32% (n=59) used a preventer regularly prior to the event and 42% (n=82) had asthma action plans of which 66% (n=55) implemented their plan.

### Conclusion:
In diagnosed asthmatics affected by ETSA, over half had symptoms in the last 12 months but only a minority used appropriate preventers. Overall asthma control was suboptimal and use of action plans was limited. These findings highlight poor chronic asthma management and treatment adherence and suggest that targeted strategies in at-risk asthma populations, particularly during high-risk periods, may reduce the impact of thunderstorm asthma.

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### Table 1. Demographics and Spirometry, Case (haze 2015) vs Control (no haze 2016)

<table>
<thead>
<tr>
<th>Categories</th>
<th>Case (haze 2015)</th>
<th>Control (no haze 2016)</th>
<th>p-value</th>
<th>NS (not significant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>46.08</td>
<td>47.34</td>
<td>0.665 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>16-93</td>
<td>5-94</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>33.33</td>
<td>33.82</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Mean FEV1 asthmatics (%)</td>
<td>91.9</td>
<td>91.8</td>
<td>0.974 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Mean FVC asthmatics (%)</td>
<td>102.6</td>
<td>99.9</td>
<td>0.404 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Mean FEV1 ratio asthmatics (%)</td>
<td>76.3</td>
<td>79.1</td>
<td>0.0979 NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

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### Table 2. Comparison of Asthma Exacerbations, Hospitalisations and Treatment, Case vs Control

<table>
<thead>
<tr>
<th>% of total</th>
<th>Case (haze 2015)</th>
<th>Control (no haze 2016)</th>
<th>p-value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>74</td>
<td>125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma patients</td>
<td>51 (68.9%)</td>
<td>64 (51%)</td>
<td>0.007</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>4 (5.4%)</td>
<td>1 (0.8%)</td>
<td>0.022</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Asthma exacerbation</td>
<td>21 (28.4%)</td>
<td>19 (15.2%)</td>
<td>0.013</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Nebulisation</td>
<td>4 (5.41%)</td>
<td>5 (4%)</td>
<td>0.323 NS</td>
<td></td>
</tr>
<tr>
<td>Oral steroids</td>
<td>5 (6.8%)</td>
<td>8 (6.4%)</td>
<td>0.460 NS</td>
<td></td>
</tr>
</tbody>
</table>

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### References
D’Amato, Clin Exp Allergy. 2016; 46:390-6
Schatz M, J Allergy Clin Immunol 2006; 117:549-56

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### Abstracts

**AP023**

**Asthma Diagnosis, Control, Preventer Use and Action Plan Usage in Patients with Epidemic Thunderstorm Asthma**

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**Background and Aim:** In November 2016, Melbourne experienced the world’s most devastating episode of epidemic thunderstorm asthma (ETSA). In excess of 3460 patients presented to emergency departments (EDs) across Melbourne, with 35 ICU admissions and 9 deaths. This study did not include presentations to primary care settings. The aim of this study was to characterise known asthmatics presenting to the ED’s of Melbourne’s two largest health services.

**Methods:** ED respiratory presentations at Eastern and Monash Health (east and southeast Melbourne) over 48 hours (during and immediately following thunderstorm activity) were reviewed. Patients were included if ED records indicated acute asthma. A standardised telephone questionnaire was developed and patients were contacted within one month following the event to assess prevalence of asthma diagnosis; asthma control (adapted asthma control test [ACT]); inhaled preventer usage and asthma action plan ownership and implementation.

**Results:** 599 of 779 patients with ETSA completed the questionnaire (76.9% response); 55% (n=330) were male with mean age of 30.6 years (±18.8). Overall, 42% (n=250) had ever been diagnosed with asthma, with 57% (n=184) of these having ‘current asthma’ symptoms in the last 12 months. Of those with current asthma, 53% (n=97) had suboptimal control (ACT<20) and 40% (n=73) had utilised urgent healthcare services for asthma in the last 12 months. Within this group 32% (n=59) used a preventer regularly prior to the event and 42% (n=82) had asthma action plans of which 66% (n=55) implemented their plan.

**Conclusion:** In diagnosed asthmatics affected by ETSA, over half had symptoms in the last 12 months but only a minority used appropriate preventers. Overall asthma control was suboptimal and use of action plans was limited. These findings highlight poor chronic asthma management and treatment adherence and suggest that targeted strategies in at-risk asthma populations, particularly during high-risk periods, may reduce the impact of thunderstorm asthma.

**References**
D’Amato, Clin Exp Allergy. 2016; 46:390-6
Schatz M, J Allergy Clin Immunol 2006; 117:549-56

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**AP024**

**The Effect of Forest Fires in 2015 on Patients with Asthma in a Respiratory Clinic in Singapore and Comparison with a Control Group in 2016**

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**Background:** Singapore experienced increased air pollution (‘haze’) for two months in 2015 arising from regional forest fires. We describe the effect of this on respiratory disease, particularly asthma. Previous studies (Respirology 2000 Jun;5(2):175-82) demonstrated minimal effect, with no increase in hospitalisations.

**Aim:** To describe the effect of forest fires on patients with respiratory disease, specifically asthmatics who visited a respiratory clinic during 2015 for 2 months during ‘the haze’, by documenting number of hospitalisations, asthma exacerbations, ACT (asthma control test) score changes, spirometry and medication adjustments; to compare these effects with a ‘control’ group (no haze) in 2016.

**Method:** Data was collected prospectively from patients over two months during the ‘haze’ in 2015 (‘case’): diagnoses, asthma exacerbations, ACT scores (if asthmatic). This group was then compared with a ‘control’ group (‘no haze’) in the same months, 2016.

**Results:**
Conclusion: Forest fires significantly impacted the health of patients with respiratory disease, particularly asthmatics, as demonstrated by an increase in hospitalisations and asthma exacerbations.

AP025

ASSESSMENT OF KNOWLEDGE OF APPROPRIATE USE OF METERED DOSE INHALER AND DRY POWDER INHALER AMONG PHARMACY STUDENTS USING SIMULATED PATIENT APPROACH: A CLINICAL PHARMACIST-LED INTERVENTION

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Background and Aims: The main cornerstone of asthma therapy is the inhaled medications. As the pharmacist-wannabes, the undergraduate pharmacy students must have adequate knowledge and training to counsel the asthma and COPD patients on the correct way of using the inhalation devices. This study evaluated the impact of clinical pharmacist-led intervention on the level of knowledge of the appropriate use of metered dose inhaler (MDI) and dry powder inhaler (DPI) among final year pharmacy students.

Methods: Post-ethical approval and written consents, 49 final year undergraduate pharmacy students were recruited from MAHSA University, Malaysia. The knowledge of appropriate use of MDI and DPI was assessed on a self-designed questionnaire. A simulated patient approach utilizing five adequately trained pharmacy students was used to assess the knowledge of enrolled students. A clinical pharmacist-led workshop was conducted in a clinical simulation ward to provide hands-on skills training regarding the correct use of inhalers. At the end of two hour training session, students’ knowledge was re-assessed using the same pre-intervention questionnaire and simulated patients. The extracted data were analysed using paired t-test through SPSS version 23 to assess the impact of intervention.

Results: The results of paired t-test showed that there is a significant improvement in the mean knowledge score (±SD) of appropriate use of MDI (pre-intervention score=7.22, ±1.25; post-intervention score=8.64, ±0.52; t = -8.861 (47), p < .001) and DPI (pre-intervention score=5.95, ±1.66; post-intervention score=7.87, ±0.33; t = -8.120 (47), p < .001).

Conclusions: The findings of the present study encouraged the introduction of clinical pharmacist-led training programs for future healthcare providers. Despite the overall improvement in the knowledge score after the intervention, periodic trainings on MDI and DPI techniques among pharmacy students is essential. Such trainings may help in future to maximize the treatment outcomes in the patients living with asthma and COPD.

AP026

CHANGING ICS/LABA THERAPY FROM DPI TO PMDI: AN OBSERVATIONAL STUDY ON ASTHMA COST OUTCOMES IN SOUTH KOREA

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Background and Aims: Pressurised metered-dose inhalers (pMDI) have been associated with improved asthma outcomes for inhaled corticosteroid (ICS)/long-acting β₂-agonist (LABA) therapy compared to delivery via dry powder inhalers (DPI). Changing from a DPI to a pMDI for ICS/LABA treatment in patients with asthma may therefore alter cost outcomes. This study assessed the health economic effect of changing inhaler from a DPI to a pMDI for ICS/LABA treatment in real-life Korean practice.

Methods: This retrospective, matched cohort study used data extracted from the Health Insurance Review and Assessment Service database. One-year cost outcomes were compared for South Korean patients with asthma who changed to fixed-dose combination (FDC) ICS/LABA pMDI from DPI versus patients who continued with ICS/LABA DPI. Patients aged 12-80 years, with ≥2 pMDI and no DPI prescriptions were matched 1:3 to those prescribed ≥2 DPI over a one year period. Exact matching was performed on baseline demographic and asthma severity measures in the year prior to therapy change. Cost outcomes, in terms of asthma-related treatment and asthma control, were described. P values were computed by Wilcoxon signed rank test with continuity correction. This study was co-funded by Mundipharma.

Results: Total treatment and hospital attendance costs over the outcome year were similar between patients that changed to pMDI therapy (n=642) compared to those remaining on a DPI (n=1926) (2073305 KRW vs 1,927,458 KRW respectively, p = 0.451). Patients that changed to a pMDI incurred lower costs for FDC ICS/LABA (p=0.027), oral (p=0.014) and inhaled (p<0.001) short-acting β₂ agonist and oral LABA (p=0.002) treatment and higher costs for leukotriene receptor antagonist treatment (p<0.001) compared to those that continued with DPI therapy.

Conclusions: Changing to a pMDI for ICS/LABA therapy in patients with asthma is associated with similar costs as remaining on a DPI.

1Price et al. (2011), Respiratory Medicine, 105(10):1457-1466
Abstracts

**Efficacy of Air Purifier Therapy in Allergic Asthma**

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**Background and Aims:** This research aims to evaluate its intervention by employing air purifier and efficacy of air purifier therapy in allergic asthma.

**Methods:** 38 subjects who were under eighteen diagnosed with allergic asthma clinically were enrolled in this research. It was divided as treated group (19 subjects, 10 yrs old) and control group (19 subjects, 10 yrs old). The treated group was processed in HEPA air purifier for six months consecutively and the control group did not utilize. Researcher collected PM data (PM2.5, PM10) and dust samples (bedding and static point) from subjects' bedroom before and after using air purifier monthly.

**Results:** The concentration of treated group air purifier for sixth month, FENO concentration of HEPA air purifier was 68.3%, 71.0% individually which demonstrated a significantly decreasing tendency. However, the concentration of house dust mite allergen in bedding, static point was 68.3%, 71.0% individually which demonstrated a significantly decreasing tendency. Treatment with air purifier had no statistical significance within the control group.

**Conclusions:** Digital pMDIs offers Simplified, Accurate & Reliable Tracking of Pseudoadherence in Real world outpatient settings.

**Clinical Allergy & Immunology**

**The attenuation of IL-1beta response in MAC-LD is due to both decreases of NLRP3 inflammasome and TLR2 activation**

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**Background and Aims:** Lung disease (LD) due to nontuberculous mycobacteria (NTM) becomes an important clinical concern. Among the NTM-LD in Taiwan, Mycobacterium avium complex (MAC) and M. abscessus (MAB) are the most frequent pathogenic species. Because MAC and MAB exist in the environment ubiquitously and the host immunity defect may play an important role but lack investigations. Macrophages are the first-line defense while mycobacterial bacilli enter through airway, and inflammasome pathway play an important role to mycobacterial lung infection. However, the inflammasome responses are rarely investigated in MAC-LD.

**Methods:** We enrolled MAC-LD and controls and isolated their peripheral blood mononuclear cells (PBMC) and monocytes which subsequently differentiated to macrophages. We performed MAC stimulation to PBMCs and monocyte derived macrophage and compared the response of IL-1 beta secretion and the related inflammasome and toll like receptor (TLR) activation.

**Results:** In PBMC stimulation assay, the IL-1beta response, either secreted level or intracellular form, was lower in patients with MAC-LD than that in the control group. In human blood monocyte-derived macrophages, MAC bacilli could activate IL-1beta production, which was also lower in MAC-LD group compared with the controls. The RNA expression of IL-1beta and NLRP3 was lower in patient group but AIM2 and ASC were similar between the two groups. In the transcription pathway for IL-beta production, the expression of TLR2 RNA to MAC stimulation was lower in patients group.

**Conclusions:** Mac bacilli could induce inflammasome activation by IL-1beta response, which was lower in patients than did the controls. The NLRP3 inflammasome and TLR2 expression were both lower in patient group and might be responsible for the IL-1 beta attenuation.

**Key words:** inflammasome, activation pathway, transcription pathway, macrophage, Mycobacterium avium complex

**The radiological classifications of allergic bronchopulmonary aspergillosis closely related with clinical manifestations**

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**Background and Aims:** Allergic bronchopulmonary aspergillosis (ABPA) is a respiratory disease whose morbidity has been underestimated. The relationship between the radiological classifications of ABPA and its clinical manifestations remains unclear.

**Methods:** We assigned 165 ABPA patients into seropositive (ABPA-S) or central bronchiectasis (ABPA-CB) or other radiologic findings

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(ABPA-CB-ORF) groups based on high-resolution computed tomography (HRCT) chest imaging from 2002. The ABPA-CB group was further divided into two subgroups according to the presence of high-attenuation mucus (ABPA-CB-HAM), and ABPA-CB-nonHAM. Analysis was performed with patients’ spirometry results, immune indices, and prognoses.

Results: Compared with the ABPA-CB group, the ABPA-S group presented a lower eosinophil count (p<0.001). Subgroup analysis showed that the ABPA-CB-ORF group had a lowest eosinophil count and poorest pulmonary function. The ABPA-CB-HAM group had a higher eosinophil count (p<0.001) and more serious small airway ventilatory dysfunction than the ABPA-CB (non-HAM and non-ORF) group. The 2 years’ follow-up showed that the relapse rates of ABPA-CB and ABPA-CB-HAM groups were 49.5% and 65.6%, respectively, both higher than the ABPA-S group.

Conclusions: Radiological classifications of ABPA are related with its clinical manifestations and disease severity. Based on this classifications of ABPA, clinicians can promote a diversity of personalized treatment in clinic.

THE RELATIONSHIPS BETWEEN ATOPY AND METABOLIC CONDITIONS IN THE ELDERLY: RETINOL BINDING PROTEIN-4 HAS A ROLE?
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Background and Aims: Recent evidence suggests the links between allergic and metabolic disorders. However, the metabolic associations have rarely been examined in older adults. We evaluated the metabolic associations of allergic conditions in the elderly (≥65 years), using a comprehensive database of a community-population cohort study.

Methods: We analyzed the database of the Korean Longitudinal Study on Health and Aging (KLoSHA) cohort study conducted during 2005-2006. Allergic symptoms were assessed using structured questionnaires. Atopy was defined by inhalant allergen skin prick test. Metabolic conditions were assessed by anthropometric indices and serum biomarkers such as fasting glucose, lipid, adiponectin, or retinol-binding protein-4 (RBP-4).

Results: Among 854 elderly subjects, 17.2% had atopy. Atopy was associated with high RBP-4 levels (p=0.003). When RBP-4 percentiles were categorized as under 15% (<34.57 μg/ml), 15%-85% (34.57 – 81.39 μg/ml), and over 85% (>81.39 μg/ml), the prevalence of atopy and current rhinitis increased with percentiles of RBP-4 levels (p=0.019, and 0.007, respectively). log RBP-4 was associated with atopy (odds ratio [OR]: 4.10, 95% confidence interval [95% CI]: 1.43 – 11.75, p = 0.009) and current rhinitis (OR: 2.73, 95% CI: 1.22 – 6.10, p = 0.014), but not with current wheeze. (OR: 1.17, 95% CI: 0.29 – 4.65, p = 0.824). Log RBP-4/adiponectin, a marker for metabolic syndrome, was significantly associated with atopy (OR: 1.86, 95% CI: 1.13 – 3.07, P = 0.015).

Conclusions: RBP-4, a recently identified adipokine that acts on muscle and/or liver affecting insulin sensitivy, was associated with atopy in the elderly.

COMPARISON OF IMMUNOCAP AND IMMULITE 2000 IN DIAGNOSTIC PERFORMANCES
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Background and Aim: Identification of clinically meaningful specific immunoglobulin E (sIgE) is important for diagnosis and management of allergic diseases. Various types of in vitro sIgE detection methods are available worldwide. Depending on the number of antigens that can be tested at one time, there are two representative Methods singleplex and multiplex methods. Singleplex sIgE detection is mainly provided by Thermofisher (ImmunoCAP) and Siemens (Immulite). The aim of the study was to compare diagnostic performances of two singleplex sIgE detection assays.

Methods: Sera from 209 Korean allergic disease patients were used for comparing ImmunoCAP and Immulite assays with respect to the following allergens: inhalant allergens (Dermatophagoides farinae, cat and dog dander, oak, rye grass, mugwort, Alternaria, German cockroach) and food allergens (egg white, milk, wheat, peanut, soybean, and shrimp). Qualitative, semi-quantitative and quantitative comparisons were performed using statistical analysis.

Results: Data from 902 paired comparison tests included for comparisons. In qualitative comparisons, positivity and negativity agreement was ranged from 75% (wheat, shrimp) to 96% (Alternaria). Class consistency (class 0-6) was well matched. Spearman’s rank correlation coefficients of all the allergens were over 0.7 except shrimp. In quantitative comparisons, all allergens showed >0.7 intra-class correlation coefficients excluding shrimp.

Conclusion: The ImmunoCAP and Immulite systems showed significantly similar performances. However, the clinicians should consider fundamental methodological differences between both assays for clinical decision making.

THE EFFECT OF MEPOLIZUMAB TREATMENT IN PATIENTS WITH SEVERE ASTHMA
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Background and Aims: Mepolizumab, a humanized monoclonal antibody against interleukin 5, selectively inhibits eosinophilic inflammation and decreases the number of eosinophils in both blood and sputum, resulting in a reduction of acute exacerbations and improvement in quality of life in severe persistent asthma. The aim of this study is to evaluate the effect of mepolizumab in patients with severe persistent asthma and to investigate a predictive biomarker of response to mepolizumab treatment.
Abstracts

Methods: 23 patients aged 30-75 with severe persistent asthma were treated with mepolizumab in our hospital from Jun 2016 through April 2017. 17 patients were eligible for the efficacy analyses. We evaluated Asthma Control Test (ACT) score, pulmonary function tests including forced oscillation technique (FOT), the fractional exhaled nitric oxide (FeNO) level and the number of acute exacerbation at baseline and 3 months.

Results: After 3 months of mepolizumab treatment, 11 (64.7%) of 17 patients improved ACT scores or achieved Total control. Peripheral eosinophil counts and the number of acute exacerbation improved significantly at 3 months. On the other hand, pulmonary function test, FOT and FeNO level did not improve significantly. We also analyzed the baseline characteristics of patients between responder and non-responder. No significant differences were found between two groups.

Conclusions: Mepolizumab improved ACT scores in 64.7% of patients at 3 months and reduced the number of acute exacerbations. Further studies are needed to investigate a predictive biomarker of response to mepolizumab treatment.

COPD 1

AP034

PREVALENCE OF CO MORBIDITIES AMONG COPD PATIENTS IN CENTRAL SRI LANKA- A DESCRIPTIVE STUDY

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Background and Aims: COPD is a heterogeneous disease with many systemic features. Presence of co morbidities contribute to the morbidity and mortality in all stages of the disease and has important consequences for disease assessment and management.

Methods: To describe the co morbidities among a cohort of COPD population in central Sri Lanka. A descriptive cross sectional study. Diagnosed patients with COPD were staged according to GOLD criteria. Demographic data and known co morbidities were recorded using an interviewer administered questionnaire supplemented by medical records. Data were analyzed using Microsoft Excel.

Results: A total of 101 male patients mean age 67yr, mean FEV1 42.7%. There were 18 (17.82%), 41(40.59%), 41(40.59%), 01(0.99%) patients between 50-59, 60-69, 70-79, 80-89 yrs age groups respectively and 23 (22.7%),52 (51.4%), 21 (20.7%), 5 (4.9%) with very severe, severe, moderate and mild COPD respectively. Out of 101 patients 43 (39%) had one or more co morbidities. The co morbidities were DM 13 (13%), Hypertension 25 (25%), Dyslipidemia 4 (4%), IHD 11 (11%), CVAO, Cancer 2 (2%), and Bronchiectasis 59 (59%).

Conclusion: Nearly fifty percent of the patients in this group has one or more co morbidities, bronchiectasis being the highest and lung cancer being the least. The high percentage of bronchiectasis may be due to the presence of chronic, multiple infections in a tropical country.

AP035

THE PREVALENCE OF GASTRO-OESOPHAGEAL REFLUX DISEASE IN A COHORT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN SRI LANKA: A PRELIMINARY EVALUATION

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Background and Aim: Clinical experience suggests that the prevalence of gastro-oesophageal reflux disease (GORD) is high in Sri Lankan patients with obstructive lung disease. The prevalence of GORD symptoms in asthmatics is reported to be 59.2%. The prevalence of GORD symptoms in chronic obstructive pulmonary disease (COPD) patients in Sri Lanka has not been assessed. To evaluate the prevalence of GORD symptoms in a cohort of COPD patients in Sri Lanka.

Methods: A validated GORD screening questionnaire was used to interview 64 COPD patients (75% male, mean age (SD) 66 (13.9) years) and 56 controls (68% male, mean age (SD) 66 (8.5) years). Asthma was excluded using post-bronchodilator spirometry. Controls were comparable individuals with no respiratory symptoms. The questionnaire assessed the frequency and severity of 7 GORD symptoms and 5 reflux-associated respiratory symptoms (RARS). The patients were categorized GORD patients if the composite GORD score was > 12.5. Height, weight, smoking history and spirometry were also recorded.

Results: The mean (SD) GORD symptom score of COPD patients was significantly higher than controls; (27.9 (9.24) versus 11.6 (4.82), P<0.001). Sixty (93.8%) of COPD patients experienced at least one RARS compared to 3 (5.4%) of controls. The prevalence of GORD symptoms in COPD patients was 93.8% (95% CI, 87.6%-99.8%) versus 30.4% in controls (95% CI, 17.9% - 42.7%). Heartburn, abdominal fullness and belching were the most common GORD symptoms. Shortness of breath and chest tightness were the most common RARS.

Conclusion: GORD symptoms and RARS were more prevalent in a cohort of Sri Lankan adult COPD patients compared to asthmatics and healthy volunteers.

AP036

PRELIMINARY STUDY OF REFLUX ESOPHAGITIS AMONG STABLE COPD AT PERSAHABATAN HOSPITAL JAKARTA, INDONESIA

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Background and Aim: Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal condition in the general population and has emerged as a comorbidity of COPD. The aim of this preliminary study was to investigate the prevalence and risk factors for Reflux Esophagitis (RE) among stable COPD patients.

Methods: Subjects were stable COPD patients who meet the inclusion criteria and agreed to sign informed consent to underwent gastro esophageal endoscopy examination. Subjects were recruited consecutively from the outpatient of Asthma and COPD clinic at Persahabatan hospital Jakarta started from May 2017. COPD was defined as having a ratio of forced expiratory volume in 1 second to forced vital capacity < 0.7 in postbronchodilator spirometry in accordance to GOLD criteria. The diagnosis of RE was based on the mucosal break on the esophageal lining through endoscopic examination. Exclusion criteria were COPD exacerbation and known esophageal disease.

Results: In this ongoing study 9 patients were enrolled. Mean (± SD) age was 64.90 ± 8.18 year, 57.1 % subjects with severe Brinkman Index. The prevalence of RE in COPD was 60% (6/10).
Conclusion: The prevalence of RE in this preliminary study was higher than that previously reported in general population in Jakarta. We still can’t correlate which risk factors was associated with RE due to the small samples in this ongoing study.

METABOLIC SYNDROME INCIDENCE RELATED TO AIRWAY OBSTRUCTION IN KOREAN: A COMMUNITY-BASED COHORT STUDY

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Background and Aims: There are many studies about the relationship between metabolic syndrome and chronic obstructive pulmonary disease (COPD). But the incidence of metabolic syndrome in COPD patient is not investigated. The aim of this study is evaluation of the incidence of metabolic syndrome in subject with airway obstruction using community-based cohort.

Methods: We analyzed the 4 years data from Ansung-Ansan cohort. A total of 6184 adults aged over 40 who performed spirometry were enrolled in this study. Airway obstruction is defined by forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC)<70% and metabolic syndrome is defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. Results: 419 patients were diagnosed newly as metabolic syndrome based on the NCEP ATP III guidelines during follow-up period. Metabolic syndrome was higher in COPD subjects compared with non-COPD subjects in both gender (10.0% vs. 14.7% in male and 11.8% vs. 14.7% in female). In male, the risk of metabolic syndrome was higher in subjects with airflow obstruction than in those without, after adjusting by age, body mass index and smoking.

Conclusions: Our study suggested that metabolic syndrome was higher in male airflow obstruction group compared to the healthy subjects.

CURRENT HOSPITAL MONITORING PRACTICES AND THE IMPACT OF GLYCAEMIC LEVELS ON PATIENTS ADMITTED WITH ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Chronic obstructive pulmonary disease (COPD) is a significant cause of hospital admissions and health care costs. Identifying the causes of poor patient outcomes is therefore important in reducing complications and length of hospital stay. The relationship between patient outcomes and abnormal glycaemic levels in patients with acute exacerbations of COPD is unclear as both hypoglycaemia and hyperglycaemia have been associated with adverse clinical outcomes including length of hospital stay, new cardiac, renal, neurological or nosocomial infective events, and mortality.

Aim: To review current glycaemic monitoring practices in patients admitted with acute exacerbations of COPD. To examine the association between abnormal glycaemic levels and clinical outcomes in these patients.

Methods: Retrospective review of patients admitted with acute exacerbations of COPD to Campbelltown Hospital over a 12 month period (June 2015 to May 2016). Data extracted from medical records included patient demographics (age, sex, smoking history, diabetes history, corticosteroid use), blood sugar levels (frequency of monitoring, admission blood sugar level, average blood sugar levels, number of hyper and hypo-glycaemic events, intervention), and patient outcomes (length of hospital stay, mortality; cardiac, renal, infectious and neurological complications).

Results: 346 patients (150 males) were admitted and all received systemic corticosteroids. 74 patients (21%) had known previous diabetes mellitus. Only 183 patients (53%) had glycaemic monitoring. 6 diabetic patients (8%) did not receive monitoring. 34 non diabetic patients (13%) had hyperglycaemia on admission but were not regularly monitored. 126 non diabetic patients (46%) had hyperglycaemia during admission. The rate of cardiac complications (atrial fibrillation, fluid overload and myocardial infarction) were higher in patients with abnormal glycaemic control. There was no difference in length of stay, nosocomial infections, renal and neurological complications and mortality.

Conclusion: Glycaemic monitoring was not universally conducted and a protocol for this is indicated. Poor glycaemic control was associated with increased cardiac complications.

PREVALENCE OF RIGHT VENTRICULAR DYSFUNCTION AMONG STABLE COPD PATIENT IN PERSAHABATAN NATIONAL RESPIRATORY CENTER HOSPITAL: A PRELIMINARY STUDY

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Background and Aim: Cardiovascular disease is a frequent comorbidity and cause of death in chronic obstructive pulmonary disease (COPD). Right ventricular dysfunction is one of predictive of survival in COPD. Echocardiography provides accurate and rapid information to evaluate cardiac function. The aim of this study is to elucidate the right ventricle contraction in stable COPD patients in the Persahabatan Hospital Jakarta.

Methods: This is a preliminary, cross-sectional study among stable COPD patients in Persahabatan Hospital Jakarta who visit the COPD outpatient clinic and signed an informed consent form and meet the criteria. Spirometry confirmed the pulmonary function. COPD severity was defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Echocardiography performed to assess right ventricle contraction among stable COPD patients. Right ventricle contraction was measured with tricuspid annular plane systolic excursion (TAPSE) values in echocardiography.

Results: A total 22 COPD patients were selected to performed spirometry and echocardiography. Echocardiographic evaluation of COPD revealed 19/22 (86.4%) cases had normal right ventricle contraction. There were 3/22 (13.6%) subjects had decreased right ventricular contraction. Right ventricular contraction was decreased in 2/13 (15.4%) and 1/9 (11.1%) cases among severe COPD (C+D group) and mild COPD (A+B group). All subject with reduced right ventricular contraction did not have a history of heart diseases.
Abstracts

Conclusion: The prevalence of right ventricular contraction dysfunction among stable COPD patient in Persahabatan Hospital Jakarta was 13.6%.

AP040

PULMONARY ARTERIAL ENLARGEMENT DURING EXACERBATION OR PNEUMONIA AND ITS ASSOCIATION WITH CLINICAL INDICES OF ACUTE AND STABLE STAGE IN COPD

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Background and Aims: Pulmonary artery to aorta ratio (PA/A=1) on CT scanning in stable COPD is associated with future exacerbation and is useful in detecting patients at risk. However routine CT images are not recommended for COPD at stable stage in clinical practice. PA/A during exacerbation of COPD and its association with severity of exacerbation have been reported, however its relation with clinical indices of stable stage are unknown. Our aims were to evaluate PA/A of acute stage of COPD and its association with clinical indices of both acute and stable stage.

Methods: We retrospectively evaluated 102 COPD patients admitted to our hospital for exacerbation or pneumonia from January 2014 to December 2015. The diameter of pulmonary artery, ascending aorta, and the PA/A ratio were measured on CT scans. We divided patients into PA/A>1 and PA/A<=1 group and compared clinical indices of acute stage such as ICU admission and use of mechanical ventilation and those of stable stage such as pulmonary function, use of home oxygen therapy, history of severe exacerbation in the previous year and cardiac comorbidities. The difference and correlation between PA/A of acute and stable stage were evaluated in 51 patients who had CT scan on stable stage.

Results: Eighty two patients (80%) had CT scan at the time of hospitalization and PA/A=1 (n=21) and PA/A=1 group (n=61) were compared. More patients in the PA/A=1 group had severe exacerbation in the previous year (p=0.04), although no other indices of stable stage nor severity of acute stage were different. PA/A of acute stage were larger than that of stable stage (p=0.02), however both were well correlated (r=0.78, p<0.01).

Conclusions: PA/A in the acute stage correlates well with that in the stable stage and is associated with severe exacerbation.

AP041

THE INCIDENCE AND RISK FACTORS OF ATRIAL FIBRILLATION IN ASIAN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background and Aims: Atrial fibrillation (AF) is commonly observed in chronic obstructive pulmonary disease (COPD) patients in clinical practice. A wide variety of factors can cause and trigger AF in patients with COPD. There is a paucity of information on AF incidence and risk factors in patients with COPD and lack information regarding Asian populations.

The aim of our study is to investigate the incidence and risk factors of AF in Asian COPD patients.

Methods: We selected a study population over the age of 40 years with a COPD diagnosis and used at least one inhaled bronchodilator medication between 1998 and 2012. The date of the index COPD diagnosis was defined as the index date. We excluded patients with a history of AF, significant mitral valve disease, disorders of the thyroid gland, or ischemic heart disease before the index date. We followed all patients from the index date to the day of AF occurrence, the day of death, the date of December 31, 2013. The baseline of comorbidities was identified before the index date. Comorbidities included hypertension, diabetes mellitus, end-stage renal disease, congenital heart failure, stroke, peripheral arterial occlusive disease or malignancy.

Results: We included 6,208 COPD patients and 12,409 patients without COPD. The incidence of AF was higher in COPD patients than in those without COPD. The adjusted hazard ratio (HR) for AF among those with COPD was 2.23 with a 95% confidence interval (CI) of 1.98 to 2.51 compared to those without COPD. After multiple analyses, patients with hypertension [HR 1.43 (95% CI=1.26-1.62)] or heart failure [HR 2.36 (95% CI=1.81-3.08)] were found to have a significantly higher incidence of AF than those without these conditions.

Conclusions: It is important for physicians to monitor, prevent, and provide early intervention for AF in COPD patients with hypertension or heart failure.

AP042

IMPACT OF AIRFLOW LIMITATION ON RECURRENCE OF VENOUS THROMBOEMBOLISM AMONG PATIENTS WITH PULMONARY EMBOLISM

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a well-known risk factor for venous thromboembolism (VTE). However, there is limited evidence regarding the impact of COPD on the recurrence of VTE. This study aims to evaluate the impact of airflow limitation on the recurrence of VTE among patients with pulmonary embolism (PE).

Methods: This is a retrospective cohort study of PE patients at a university-based hospital in Seoul, Korea, from April 2010 to December 2013. PE was confirmed using a contrast-enhanced computed tomography (CT) scan. Airflow limitation (AL) was defined as pre-bronchodilator FEV1/FVC less than 0.7 within two years of PE diagnosis. VTE recurrence was defined as composite of recurrence as PE, DVT, or both. Considering that malignancy is a strong risk factor for VTE, we performed all analyses stratifying patients based on cancer diagnosis. Cox proportional hazards models were used to determine the impact of AL on VTE recurrence.

Results: Among patients with (n=401) and without cancer (n=98), 31.4% and 31.6% patients had AL, respectively. Non-cancer patients with AL had a 9.6-fold higher risk of VTE recurrence (95% CI=1.98-25.1) than those without AL after adjusting for age, sex, body mass index, smoking status, treatment for PE, and surgery or immobilization. Cancer patients with AL had a 1.2-fold higher risk of VTE recurrence (95% CI 0.66-2.31) than those without AL, which did not achieve statistical significance after adjusting for confounders and provoking factors.

Conclusions: The presence of airflow limitation independently increased the risk of VTE recurrence in PE patients, and the increased risk was more evident in non-cancer patients.

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AIRFLOW LIMITATION IN PREOPERATIVE PATIENTS WITH THORACIC SURGERY

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**Background and Aim:** Spirometry is crucial for diagnosing chronic obstructive pulmonary disease (COPD) that is generally slowly progressive and tends to be underdiagnosed. In the present study, we investigated the incidence of undiagnosed COPD based on airflow limitation evaluated by preoperative respiratory function test for thoracic surgery.

**Methods:** A total of 257 patients in whom preoperative respiratory function test for thoracic surgery were performed between June 2012 and May 2013 were retrospectively evaluated based on information from medical records.

**Results:** The mean age of 257 participants was 67.3 ± 13.1 years old. Among these 257 patients, 91 (35%) patients had obstructive pulmonary impairment included 4 cases with bronchial asthma, and the mean age of the rest 87 patients (65 males/22 females) without bronchial asthma was 72.3 ± 10.3 years old. Based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, the percentages of patients with mild (GOLD 1), moderate (GOLD 2), severe (GOLD 3) and very severe (GOLD 4) were 63% (55/87), 36% (31/87), 1% (1/87), and none, respectively. Among these 87 patients, 66 (76%) had smoking history (20 current smokers/ 46 ex-smokers/6 never-smokers/ 15 history unknown) with average Brinkman index of 1074 ± 717, and 56 patients (64%) with airflow limitation had no respiratory symptoms. The rates of smoking in patients with or without respiratory symptoms were 92% (24/26) and 91% (42/46), respectively, and the rates of treatment intervention with bronchodilators for COPD in both two groups were 24% (7/29) and 20% (11/56), respectively.

**Conclusion:** This study reveals that 34% of patients in whom thoracic surgery was performed were suspected COPD About 80% of these patients were undiagnosed before, and about 90% of these patients had smoking history. Preoperative and postoperative treatment interventions according to the results of preoperative pulmonary function test may improve respiratory functions and reduce operative complications, and physicians and surgeons should be aware of it.

**Table 1. VTE recurrence by risk group category**

<table>
<thead>
<tr>
<th></th>
<th>No Cancer</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Airflow Limitation</td>
<td>With Airflow Limitation</td>
</tr>
<tr>
<td><strong>No. of Cases (%)</strong></td>
<td>2 (3.0)</td>
<td>5 (16.1)</td>
</tr>
<tr>
<td><strong>Incidence Rate (/1,000 Person-Years)</strong></td>
<td>1.1</td>
<td>10.6</td>
</tr>
<tr>
<td><strong>Crude HR (95% CI)</strong></td>
<td>Reference</td>
<td>8.20 (1.58, 42.50)</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td>Reference</td>
<td>10.87 (1.27, 83.10)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td>Reference</td>
<td>9.63 (1.11, 83.49)</td>
</tr>
</tbody>
</table>

*One patient who died on the day of PE diagnosis was excluded in analysis.
Model 1 adjusted for age, sex, BMI, smoking (never/ever) and treatment for PE
Model 2 further adjusted for surgery or immobilization

VTE, venous thromboembolism; HR, hazard ratio; CI, confidence interval; PE, pulmonary embolism

**Abstracts**
Abstracts

EVALUATION OF IRON DEFICIENCY WITHOUT ANEMIA IN PATIENTS WITH COPD
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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease and a major cause of morbidity and mortality worldwide. Iron deficiency may have a significant role to play in COPD also. This study has been conducted to investigate association of iron deficiency in non-anemic patients of COPD with functional status, disease severity and quality of life.

Methods: Stable COPD patients without anemia were divided into two groups: Iron replete (IR) and iron deficient (ID), based on their serum ferritin and transferrin saturation. Spirometry, six minute walk distance (6MWD) and St. George Respiratory Questionnaire (SGRQ) were performed in patients of both the groups and their exacerbation history in previous year was noted.

Results: Out of 79 patients, iron deficiency was seen in 36 (45.5%) patients with COPD. ID patients had lower mean 6MWD (354.28 ± 82.4m vs 432.5 ± 47.21m; P = 0.001), greater number of exacerbations in a year (P=0.003), higher SGRQ symptom score (61.41 ± 18.95 vs. 47.69 ± 21.30; P=0.003), but no significant difference in airflow limitation.

Conclusions: Iron deficiency is associated with worse exercise tolerance, worse dyspnea grading and more number of acute exacerbations in patients with COPD. Poor exercise tolerance and dyspnea grading suggest a poor functional status of patient and more number of exacerbations is poor prognostic marker of COPD. Thus, all patients of COPD, whether or not anemic, should be evaluated for iron deficiency.

PREVALENCE OF BRONCHIECTASIS AMONG COPD PATIENTS IN CENTRAL SRI LANKA
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Introduction: Clinical behaviour of COPD may be disproportionate to lung function stages. It correlate with BMI, Dyspnoea level and exercise capacity. There may be additional factors other than these known factors. Therefore it is vital to recognize additional pathologies that could coexist. Bronchiectasis has been recognized as a potential new phenotype of COPD.

Objective: To identify the prevalence of Bronchiectasis among COPD patients.

Methodology: A descriptive cross sectional study, selected randomly. An interviewer administered structured questionnaire was used to collect data. All the patients were examined by a clinician and lung function tests and other relevant investigations were carried out in a single laboratory. Data were analysed using Microsoft Excel.

Results: 82 male patients ,mean age was 66 yrs,mean FEV1 43.78%. There were 14 (17.07%), 35(42.68%), 32(39.02%), 01(1.21%) between 50-59, 60-69, 70-79, 80-89 yrs respectively and 19 (23.17%),40 (48.78%), 17 (20.73%), 6 (7.31%) with very severe, severe, moderate and mild COPD respectively. Overall prevalence is 71.95% (59).most commonly involved mid zones (53patients,89.83%). The most prevalent morphological type the tubular type (51 , 86.44%). The prevalence did not show any association with disease severity of COPD (6.77%, 20.33 %, 47.45% and 25.42% in mild, moderate, severe, very severe COPD respectively) and increasing age (20.33% in 50-59 yrs, 38.98% in 60-69 yrs, 38.985 in 70-79 yrs and 1.69% in 80-89 yrs).Exacerbation frequency of COPD did not have a positive correlation with prevalence of bronchiectasis ( 22.03%, 25.42%, 20.33%, 8.47%, 10.16%, 13.55% in those with 0, 1, 2, 3, 4 and >=5 exacerbations per year, respectively).

Conclusion: The prevalence is high as 71.95%,the distribution (89.83%) involved the mid zones and predominantly (86.44%) of the tubular type.

LONGITUDINAL TRAJECTORY OF SEXUAL FUNCTION IN MEN WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE
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Background and Aims: Patients with chronic obstructive pulmonary disease (COPD) commonly experience an aggregate of symptoms. As time goes on, functional deterioration and disease progression stimulates a cycle of decline that includes dyspnea, diminished exercise capacity, physical inactivity, deconditioning, disability, and poor health-related quality of life. Although sexual function is one of the most important issues for better QoL, but there are limited information on longitudinal changes of sexual function over time with the illness trajectory model. This study is to identify different patterns of sexual function changes in longitudinal data, and to examine predictors of these trajectories.

Methods: Data were extracted from the KOLD cohort for which patients with obstructive lung diseases had been recruited from 11 secondary or tertiary hospitals in South Korea from 2005 to 2012. A total of 185 participants met inclusion criteria. Baseline data of sexual function measured with the International Index of Erectile Function-5 (IIEF-5) were collected at the point of cohort entry and follow up at every 12 months over four years. Growth mixture modeling was used to estimate distinct patterns and ordinal, multinomial logistic regression were used to determine factors affecting different trajectory patterns of sexual function.

Results: The four classes were then defined according to their baseline IIEF-5 level and deterioration or improvement trends over the 5 years. Four distinct patterns of sexual function were identified: class I=persistently good, class II=rapidly worsen and then rapidly improved, class III=gradually improved and then gradually worsen, and class IV=persistently bad. Distinct patterns in sexual function are significantly associated with age, income, and perceived health status level.

Conclusions: Understanding sexual function trajectories and the factors that affect them provides professional insights and relevant knowledge for evidence-based nursing care and positive patient outcomes.
Background: Patients with chronic obstructive pulmonary disease (COPD) often have poor health-related quality of life (HRQoL) that is disproportionate to their degree of airflow limitation. This study evaluated the association between St. George’s Respiratory Questionnaire for COPD (SGRQ-C) score and forced expiratory volume in one second (FEV1) and investigated factors responsible for high SGRQ-C score according to severity of airflow limitation.

Methods: Data from 1,264 COPD patients were obtained from the Korean COPD Subgroup Study cohort. Patients were categorized into two groups according to severity of airflow limitation: mild-to-moderate and severe-to-very severe COPD groups. We evaluated the clinical factors associated with high SGRQ-C score (≥25) in each COPD patient group.

Results: Of the 1,264 COPD patients, 902 (71.4%) had mild-to-moderate airflow limitation and 362 (28.6%) had severe-to-very severe airflow limitation. Of the mild-to-moderate COPD patients, 59.2% (534/902) had high SGRQ-C score, while 80.4% (291/362) of the severe-to-very severe COPD patients had high SGRQ-C score. The association between the SGRQ-C score and post-bronchodilator FEV1 (% predicted) was very weak in the mild-to-moderate COPD patients (r = -0.103, p = 0.002) and weak in the severe-to-very severe COPD patients (r = -0.219, p < 0.001). Multiple logistic regression analysis revealed that age, being an ex-smoker, a lower level of education, cough, dyspnea with congestive heart failure, hypertelidemia, and depression were significantly associated with high SGRQ-C score in mild-to-moderate COPD patients. In comparison, an ex-smoker and having respiratory symptoms including sputum and dyspnea were independent factors associated with high SGRQ-C score in severe-to-very severe COPD patients.

Conclusions: Besides respiratory symptoms with dyspnea and cough, high SGRQ-C score was affected by extra-pulmonary comorbidities in mild-to-moderate COPD patients. However, only respiratory symptoms such as sputum and dyspnea were significantly associated with high SGRQ-C score in severe-to-very severe COPD patients. This indicates a need for an improved management strategy for relieving respiratory symptoms in COPD patients with poor HRQoL. In addition, attention should be paid to extra-pulmonary comorbidities, especially in mild-to-moderate COPD patients with poor HRQoL.

A SELF-MANAGEMENT PROGRAMME OF RESCUE PACK FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS

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Background and Aims: COPD is one of the common causes of morbidity and mortality affecting adults worldwide. This study was to determine if a rescue pack would decrease readmission to the hospital within 30 days of discharge and the length of hospitalization.

Methods: Patients admitted to acute male medical ward of Caritas Medical Centre (Hong Kong) between December 2015 and December 2016 with a diagnosis of COAD were recruited for the study. Patients with mental incapacities to understand the program such as dementia, impaired level of consciousness and confusion were excluded. A respiratory nurse specialist assessed and provided education including inhaler technique, lifestyle modification, breathing technique and smoking cessation to all recruited patients. To compare the effectiveness of rescue pack, patients were assigned to either the control group or the “Rescue Pack” group.

Results: In total 63 patients were recruited, 30 (47.6 %) to control and 33 (52.4 %) to rescue pack group. 14 of 30 in the control group (46.7 %) and 15 of 33 in the rescue pack group (45.5%) were readmitted within 30 days. The frequency of 30 days readmission was similar between groups. Patients in the rescue pack group recorded a shorter length of hospitalization. In the control group, patients with inadequate inhaler technique (n=11) have a longer length of hospitalization (M=6.6). Among these patients (n=7) were readmitted within 30 days.

Conclusions: Only prescription of rescue pack for patients with COPD was not enough to reduce the 30-day readmission rate. Inhaler technique is also an important factor to affect the readmission rate and hospital stay. In order to improve the programme, patients should be reassessed to see whether they have any misunderstandings of self-management of rescue pack or they have any other problems leading to readmission when they were readmitted.

HANd GRIP STRENGTH IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim: Hand grip strength is a simple way of predicting the risk of cardiovascular disease and all-cause mortality in the general population. However, the practical significance of grip strength in patients with chronic obstructive pulmonary disease (COPD) is uncertain. The aim of this study was to compare hand grip strength between subjects with and without COPD and to evaluate its clinical relevance in patients with COPD using a national survey.

Methods: Data were collected from the Korean National Health and Nutrition Examination Survey. The study included 421 adults with COPD and 2542 controls who completed questionnaires, spirometry, and a hand grip strength test. Hand grip strength was compared between subjects with and without COPD, and the association between grip strength, lung function, and quality of life was evaluated.

Results: The mean hand grip strength was 33.3±9.1 kg in the COPD group and 29.9±9.5 kg in the non-COPD group; adjusted hand grip strength was 30.9±0.33 kg and 30.9±0.11 kg, respectively (P=0.99).

Conclusions: Hand grip strength was not different between subjects with and without COPD, and the association between grip strength, lung function, and quality of life was evaluated.

IMPACT OF LOWER-LIMB ENDURANCE TRAINING ON DYSPNEA SCALE AND PULMONARY FUNCTION TEST RESULTS IN COPD PATIENTS

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Background and Aims: Patients with COPD exhibit persistent dyspnea in daily activities and irreversible airflow obstruction. These will finally lead to inability to carry on daily activities and markedly decrease their quality of life. Endurance training was now considered as therapy modality to alleviate several symptoms experienced by COPD patients. The aim of this study is to identify the impact of lower-limb endurance training on dyspnea symptom and pulmonary function test results in COPD patients.

Methods: We performed experimental study in July 2017 on 20 stable COPD patients divided both in group C and D according to GOLD 2017 criteria. Patients were given individualized dose of stationary cycling twice a week for one month in which every session lasted 5-20 minutes gradually. Before and after rehabilitation program, pulmonary function tests were measured by spirometry to obtain percent predicted of FEV1, FVC, PEFR and FEF 25-75, while dyspnea scale was measured by mMRC index. Statistical analysis was performed by Wilcoxon and T-dependent test.

Results: Baseline value of FVC (49.6±21.6%) increased significantly to 59.65±16.53% after one month of endurance training program (p<0.01). Surprisingly, there was also significant increase of FEV1 value from 46.9±21.7 to 52.9±20.7% (p<0.005). The increase of FVC and FEV1 in group C was slightly higher than in group D although not statistically significant (p=0.29; p=0.25 respectively). However, no difference was observed in PEFR and FEF25-75 value (p=0.05). Patients’ dyspnea index also showed significant improvement (p<0.001) from mMRC median scale 2 (range 1-3) to 1 (range 0-2) in both group C and D. There was no exacerbation found during rehabilitation program.

Conclusions: Twice a week lower-limb endurance training for one-month improved dyspnea scale and pulmonary function test results of COPD patients safely and effectively

Keywords: COPD, pulmonary function, lower-limb endurance training, mMRC scale

CLINICAL IMPORTANCE OF CROSS-SECTIONAL AREA OF INTERCOASTAL MUSCLES IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Limb muscle wasting is one of main systemic manifestation of chronic obstructive pulmonary disease (COPD). However, the change of respiratory muscle is unclear. This study assessed the cross-sectional area (CSA) of the intercostal muscles (ICMs) in patients with COPD, using chest computed tomography (CT) and determined its association with the clinical characteristics of COPD.

Methods: They retrospectively reviewed 60 patients with stable COPD and compared them with 30 controls. CSA (mm2) of the ICM on chest CT was measured at the midline level of the lateral arch of the bilateral first rib with a 3-mm slice thickness by using CT histogram software. The association with the clinical characteristics of COPD and with the control groups was assessed.

Results: CSA of the ICM and the CSA/body mass index (BMI) were lower in the COPD group than in the control group. Patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 4 had a significantly lower CSA of the ICM than patients with stage 1, 2, and 3. CSA of the ICM was positively associated with FEV1, %FEV1 predicted, FEV1 /FVC ratio, and BMI and negatively associated with age. However, there were no associations with PaO2, PaCO2, smoking status, 6-minute walk test, frequency of acute exacerbation of COPD, and serum C-reactive protein level.

Conclusions: Intercostal muscle atrophy occurs in COPD patients and is associated with severity of airway obstruction, BMI, and increasing age.

PATTERN OF DAILY PHYSICAL ACTIVITY IN STABLE THAI CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background and Aims: Daily physical activity (PA) predicts prognosis and mortality in chronic obstructive pulmonary disease (COPD) patients. Pattern of daily PA may be different among populations due to various cultures. Information about PA in Thai COPD patients is deficient. This study was aimed to evaluate the physical activity pattern of Thai COPD patients.

Methods: We have enrolled stable GOLD stage 2 and 3 COPD patients to participate in physical activity monitoring study as a part of pulmonary rehabilitation program. Subjects were asked to wear pedometers on their waist during the day for 2 consecutive weeks before and after joining the pulmonary rehabilitation program. Baseline demographic and physiologic data, including spirometry, 6-minute walking distance (6MWD) and cardiopulmonary exercise testing (CPET) data were recorded. We used paired t-test to compare between weekday and weekend daily step counts. Independent sample t-test was used to compare daily step counts between groups.

Results: We included 26 stable COPD patients in the study, which 23 (88.5%) were males. Subjects’ age (mean ±SD) was 67.7±7.6 years and average FEV1 %predicted was 58.7 ± 13.6%.

The weekday and weekend daily step count were comparable, 4837±3115 vs 4725±2464 steps respectively (P= 0.740). Remarkably, the average step count between GOLD stage 2 and GOLD stage 3 were not significantly different. However, the overweight COPD patients demonstrated less daily step count than normal weight COPD patients, 3573±2207 steps vs 6110±3093 steps respectively (P=0.023). There were moderate correlations between daily PA (step counts) and 6MWD (m) (r = 0.448, p<0.05)

Conclusions: We have demonstrated pattern of weekday and weekend physical activity in Thai COPD patients. Daily step count in COPD patients moderately correlated with 6MWD.

THE DEVELOPMENT OF NEW-GENERATION APPLICATION SOFTWARE OF TABLET PC THAT INTERACTIVELY CARRY OUT PERSONALIZED SELF-MANAGEMENT EDUCATION TO PATIENTS WITH COPD RECEIVING LTOT

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Background and Aims: The skills for self-management are essential in improving health status in patients with COPD receiving long term oxygen therapy (LTOT). However, the opportunities for receiving education program in clinical settings were hard to come by and this underuse, including pulmonary rehabilitation, has been pointed out as global issues that needed to be solved. It is necessary to switch to new intervention techniques based on innovative ideas. To improve the implementation and delivery of self-management education, we organized the multidisciplinary team to develop new-generation application software (app) that itself carry out personalized self-management education interactively.

Methods: The team consists of clinicians, nurses, physical therapist, and health IT developers and algorithm for app was designed and tested.

Results: The main characteristic of app developed are as follows: 1) the app speaks to patient by using voice actor's voice, 2) health condition is assessed by default setting, and the personalized action plan will be given when they have signs of exacerbations, 3) use of personalized video clips for technical guidance on oxygen equipments, stretching exercise and inhaler technique, 4) behavioural modification intervention by praising or encouraging patients.

Conclusions: The tools for the self-management education can be classified into four generations. The first-generation would be enlightenment tools such as posters, second would be commonly used tools such as textbooks, DVDs and e-books, and third generation would be the apps which need human resources to make bidirectional communication, such as tele-monitoring and tele-nursing of symptoms, steps and SpO2. The benefits of the new fourth-generation we developed is the availability of personalized interactive approach which will enhance the patient adherence (make learning fun) and save the time of medical staffs.

Conclusions: The 6 weeks pilot study is scheduled. The new-generation app may be useful in disseminating standardized self-management education for COPD patients receiving LTOT.

Background and Aims: In patients with COPD, physical activity is considered increasingly important due to the beneficial influence of regular physical activity on the prognosis. The aim of this study was to evaluate the effects of a self-managed physical activity program using a pedometer and diary on physical function, ADL, and QOL in COPD.

Methods: Outpatients with COPD were assessed for dyspnea, muscle strength, exercise tolerance, ADL, and QOL at baseline and after 3 months of intervention. Patients were randomly assigned to “Control” group or “Diary” group. In the Diary group, the number of steps was counted with a pedometer and recorded in a diary together with self-evaluation of physical activity, while patients assigned to the control group did not use a pedometer or keep a diary. In both groups, patients were not given a target number of steps or target level of physical activity.

Results: 16 patients completed follow-up. The Diary group showed significant increase in the step count was 7259.8±3110.7 per day during the initial 2 weeks of the study versus 7960.5±3083.2 per day during the final 2 weeks (p<0.05). Significant differences found between the Diary and Control groups with regard to the extent of change in the 6-minute walking test (44.5±43.2m vs. -10.8±20.2m, p<0.01) and 30-second chair stand test (3.9±2.9times vs. -2.1±1.4times, p<0.01) after 3 months.

Conclusions: This study suggests that a self-managed physical activity program using a pedometer and diary can increase the level of physical activity, and that a pedometer is an effective device for self-monitoring.
RELATIONSHIP BETWEEN FEV1, AND 6MWD (SIX-MINUTE WALK DISTANCE) ON DYSPNEA SCORE AND FUNCTIONAL STATUS IN COPD AT UTTARADIT HOSPITAL
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Background and Aims: Spirometry is noninvasive test for diagnosis, assessment airflow limitation and to plan management in COPD. GOLD guideline recommended to evaluate staging in airflow obstruction by post-bronchodilator FEV1 level before treatment. FEV1 may be correlated with dyspnea symptoms and health status but takes time to evaluate for outpatient visit. The 6-minute walk test (6MWT) is a practical simple test that requires no expensive equipment or advanced training technicians and correlates better to measure functional capacity. This study was aimed to determine correlation and efficacy between FEV1 and 6MWD on dyspnea symptoms and functional status in COPD patients.

Methods: Retrospective study conducted of 493 diagnostic COPD patients who attending outpatient department between 2014 to 2016. All patients underwent spirometric measurement post-bronchodilator FEV1. 6MWT was performed following American Thoracic Society (ATS) which distance was recorded in meters. Baseline characteristics. Modified British Medical Research Council (mMRC) Questionnaire and COPD Assessment Test (CAT) were recorded and calculated. Correlation coefficient (r) analysis by Spearman rank correlation.

Results: This study showed significantly linear correlation of FEV1 (L/min) with 6MWD (r = 0.33, P < 0.001), mMRC (r = 0.33, P < 0.001), and CAT (r = 0.22, P = 0.001), otherwise there was inverse linear correlation significantly between 6MWD with mMRC (r = -0.29, P < 0.001) and CAT (r = -0.24, P < 0.001).

Conclusions: 6MWD can be useful for evaluation and follow-up stable COPD patients effectively when the facility of spirometry is limited.

EVALUATION OF GAIT SYMMETRY AND THE CENTER OF MASS DISPLACEMENT BY A TRUNK ACCELERATION DURING WALKING IN COPD PATIENTS
YOSHINO TERUI1, MASAIHRO IKAWURA1,2, ERIKO SUTOJ1, KEIYU SUGAWARA1, HITOMI TAKAHASHI1, IKUO KAWAKABAYASHI1, TAKANOBU SHIOYA2
1Department of Physical Therapy, Akita University Graduate School of Health Sciences, Akita, Japan, 2Department of Pulmonary and Tuberculosis, Department of Internal Medicine, Uttaradit Tertiary Hospital, Naresuan University – Affiliated Hospital, Uttaradit, Thailand

Background and Aim: COPD patients have a high probability of falling. The gait of COPD patients should be evaluated accurately to prevent falling. The new software calculate the center of mass (CoM) displacement by trunk acceleration during walking has been developed recently.

The aim of this study was to assess the CoM displacement and gait symmetry using a tri-axial accelerometer in elderly COPD.

Methods: Sixteen elderly COPD (age: 71±3.9 years, FEV1: 58±4.01±3.9±2 years, 20 healthy age-matched subjects (age: 63.3±3.0 years) walked 10 m wearing a tri-axial accelerometer at the level of the L3 spinous process. CoM displacements and motion trajectory figures from the acceleration were exported by designated software.

Medio-lateral (ML) and vertical acceleration were expressed as continuous waveforms and the bilateral surrounded area by waveforms was analyzed as Lissajous Index (acceleration LI). The bilateral surrounded area by motion trajectory figures was analyzed as Lissajous Index (trajectory LI). LI of 0 indicates perfect symmetry. Pulmonary function, leg muscle strength and one-leg standing test (OLST) were evaluated in COPD patients. The CoM displacement, acceleration LI and trajectory LI were compared between COPD patients and healthy subjects. Correlation between the CoM displacement, acceleration LI and trajectory LI were assessed with their physical functions.

Results: ML CoM displacement, anterior-posterior CoM displacement and acceleration LI of COPD patients were significantly larger than that of healthy subjects (p=0.003, p=0.049, and p=0.017, respectively). The multiple regression analysis showed that mMRC was significantly associated with ML CoM displacement (p=0.009). The acceleration LI and the trajectory LI were significantly correlated with OLST and BMI (r = -0.530, and r = -0.524, respectively).

Conclusion: Gait symmetry from acceleration LI and trajectory LI were significantly correlated with standing balance and BMI, respectively in COPD. LI using a tri-axial accelerometer is useful in evaluating gait disturbance in COPD.

LONGITUDINAL RELATIONSHIP BETWEEN GAIT SPEED AND PHYSICAL ACTIVITY IN COPD
MASAHIRO IWAKURA1,2, KAZUKI OKURA1, KAZUYUKI SHIBATA1,2, ATSUYOSHI KAWAGOSHI1, KEIYU SUGAWARA1, HIRONOSHU TAKASHI1, IKUO KAWABAYASHI1, TAKANOBU SHIOYA2
1Department of Pulmonary and Tuberculosis, Department of Internal Medicine, Uttaradit Tertiary Hospital, Naresuan University – Affiliated Hospital, Uttaradit, Thailand, and 2Department of Physical Therapy, Akita University Graduate School of Health Sciences, Akita, Japan

Background: Reduced gait speed is often observed in elderly patients with COPD, and previous cross-sectional studies have found an association between reduced gait speed and physical inactivity. However, the longitudinal relationship between gait speed and physical activity remains unclear. We investigated the relationship between changes in gait speed and physical activity in elderly patients with COPD.

Methods: Overall, 12 outpatients with COPD (age, 71 ± 6 years; FEV1, 57 ± 31 %pred) participated in this study. Usual gait speed, steps per day, time per day spent in moderate to vigorous physical activity (MV-PA), body weight, fat free mass index, 6-min walk distance, maximum voluntary isometric quadriceps contraction, modified Medical Research Council dyspnea score, and COPD assessment test scores were obtained, for all patients, at baseline and 3 months post assessment to calculate change. All participants received pulmonary rehabilitation during that period. We used Pearson’s correlation coefficient (r) to assess the strength of correlation of changes in gait speed and other outcomes with changes in steps per day and MV-PA pre- and post-pulmonary rehabilitation.

Results: The means of gait speed, daily steps, and MV-PA from baseline to 3 months were 1.13 ± 0.13 m/s, 1.13 ± 0.23 m/s, 4628 ± 2484 steps/day, 6415 ± 3362 steps/day, 15.9 ± 15.8 min/day, 26.0 ± 21.9 min/day, respectively. Gait speed had a significant and positive correlation to changes in steps per day (r = 0.853, p < 0.001) and MV-PA (r = 0.726, p = 0.007).

Conclusions: Our findings revealed a strong longitudinal relationship between gait speed and physical activity, suggesting the importance of evaluation and intervention on gait speed in elderly patients with COPD. Further research is required to clarify the causal direction between reduced gait speed and physical inactivity in elderly patients with COPD.
AP058
THE EFFICACY OF 30-BREATH SESSIONS MODERATE-INTENSITY INSPIRATIONAL MUSCLE TRAINING (IMT) FOR THE ELDERLY PATIENTS WITH COPD
TAKANOBU SHIOYA1, MASASHIRO SATAKE1, SACHIKO UEMURA1, YOSHIHO TERUI1, YUKI KAGAYA2, KAZUKI OKURA2, ATSUYOSHI KAWAGOSHI2, YUTAKA FURUKAWA2, MASASHIRO IWAKURA1, KENYU SUGAWARA2, HITOMI TAKAHASHI3, MITSUNOBU HOMMA4
1Akita University School of Health Sciences, Akita, Japan, 2Research Institute for Brain & Blood Vessels-Akita, Akita, Japan, 3Akita City Hospital Department of Rehabilitation, Akita, Japan, 4Akita City Hospital Department of Pulmonary Medicine, Akita, Japan

Background: The standard IMT training for COPD patients was low intensity (>30%PImax) for 30 minutes until Langer (2015) showed that high intensity (>50% of PImax) training of 30 breaths (3-5 minutes) was effective.

Aim: To investigate the efficacy of moderate intensity, 30 breath IMT sessions in the elderly COPD patients with COPD.

Methods: Twenty outpatients with stable COPD (Age: 71 ± 8 years, FEV1: 56.6 ± 21.1%, predicted) followed for three months a combined protocol of low-intensity exercise training and two, 30 breath IMT sessions using the POWERBreathe™ set at 40% of their PImax. Respiratory muscle strength, the 6 minute walking test (6MWT), and the quadriceps femoris muscle force (QF) were measured before and after IMT.

Results: PImax (P < 0.001), PEmax (P < 0.001), and 6MWT (P = 0.005) improved significantly after the combined IMT/ET interventions. QF didn’t strengthen significantly (P = 0.168). The correlation between the increase in PImax (mean of difference: 32.7cmH2O) and the improvement of 6MWT (mean of difference: 32.7m, r = 0.664, P = 0.001) was high and significant.

Conclusion: Our data suggest that two daily, 30 breath sessions of moderate IMT increases the exercise capacity of elderly COPD patients. Quicker training sessions might lead to improved adherence to IMT protocols.

AP058A
COMPARATIVE STUDY ON MEDICAL UTILIZATION AND COSTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH GOOD LUNG FUNCTION
SHIN BUM KIM1, JEONG UK LIM1, KWANG HA YOO2, KI-SUCK JUNG3, CHIN KOOK RHEE1, YONG IL HWANG1, YONG IL HWANG2
1Division of Pulmonary, Critical Care and Sleep Medicine, Department of Internal Medicine, St. Paul’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea, 2Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Republic of Korea, 3Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Hallym University Medical Center, Hallym University College of Medicine, Anyang, Republic of Korea, and 4Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Introduction: Mild to moderate chronic obstructive pulmonary disease (COPD) patients are underdiagnosed and undertreated due to the asymptomatic nature, compared to severe COPD patients. Previous studies on mild COPD patients have focused on symptomatic patients, and few studies are available on asymptomatic patients.

Methods: We evaluated hospital visits, medical costs per person, COPD medication use, and compared medical resource utilization screened from the general population and COPD cohort patients. COPD patients aged 40 or older with forced expiratory volume in 1 s (FEV1) ≥ 60% were selected from the 2007–2012 Korean National Health and Nutrition Examination Survey (KNHANES) data. Data including the number of outpatient clinic visits, hospital admission, COPD-related medications, medical costs were obtained from the Health Insurance Review and Assessment Service and were compared to COPD patients with FEV1 ≥ 60% from the Korean COPD Subtype Study (KOCOSS) cohort during the study period.

Result: 3.6% of COPD patients with FEV1 ≥ 60% from the KNHANES group visited medical facilities in 2007 and 5.9% visited in 2012. 30% of COPD patients with FEV1 ≥ 60% from the KOCOSS cohort visited medical facilities in 2007, and 87.1% in 2012. Total medical costs per person per year increased from 264.37 ± 663.41 United States Dollars (USD) in 2007 to 797.00 ± 2724.21 USD in 2012 for the KNHANES group. For the KOCOSS group, total medical costs increased from 447.08 ± 947.91 USD in 2007 to 856.94 ± 2284.24 USD. In 2012, 20.7% of patients from the KNHANES database received long-acting muscarinic agonists (LAMA); however, 78.7% of KOCOSS cohort received LAMA.

Conclusion: Medical resource utilization and medical costs per person for early COPD patients in Korea increased during the study period. However, asymptomatic COPD patients from the KNHANES group do not receive adequate long-term treatment and require more clinical attention.

Lung Cancer 1
AP059
A DESCRIPTIVE STUDY REGARDING THE HISTOLOGICAL SUBTYPES OF LUNG CANCER IDENTIFIED IN A COHORT OF PATIENTS IN CENTRAL SRI LANKA
SACHINI SENEVIRATNE1, SUMEDHA HEENAGAMAGE1, SAMADARA NAKANDALA1, PREMALI MANORANGI1, ISURU CHANDRADASA1, DUSHANTHA MADEGEDARA1
1Respiratory Disease Treatment Unit 2, Teaching Hospital Kandy, Sri Lanka, Kandy, Sri Lanka

Background and Aims: Lung cancer remains to be one of the most common cancers globally. This study is a descriptive analysis of the histological subtypes of lung cancer among a group of patients who were histologically proven to have lung cancer at respiratory disease treatment unit 2 of Teaching Hospital, Kandy, Sri Lanka.

Methods: A retrospective analysis of data of patients diagnosed with lung cancer from 2013 to 2017

Results: The total number of patients is 127 of which (85%) were male (n=108) and 15% were female (n=19). Out of the 19 female patients 14 had adenocarcinoma (73.68%), of which 1, 9, 2 and 1 patients had well differentiated, moderately differentiated, poorly differentiated or invasive adenocarcinoma respectively. Four (21.05%) had squamous cell carcinoma, out of which 3 were poorly differentiated. One female patient had Non small cell carcinoma (NSCLC-NOS). Squamous cell carcinoma was the most common histological subtype identified in males (n=51, 47.22%), out of which 9, 32 and 10 patients had well differentiated, moderately differentiated or poorly differentiated carcinoma respectively. 34 male patients (31.48%) had adenocarcinoma, out of which 6, 16, 10 and 2 patients had well differentiated, moderately differentiated, poorly differentiated and invasive types respectively. Small cell carcinoma was identified in 11 (10.18%) patients. Of the male patients 3, 7 and 2 patients had NSCLC-NOS, poorly differentiated carcinoma and a mixed histological type respectively.

Conclusion: The vast majority of patients diagnosed with lung cancer in Sri Lanka are male and the commonest histological type among them is squamous cell carcinoma. This difference is most likely to be due to the high prevalence of smoking among males and the near
nonexistence of this risk factor among females in Sri Lanka. However
related etiological factors such as influence of biomass fuel exposure and
influence of environmental pollution needs to be analyzed.

BIOLGICAL AND CLINICOPATHOLOGICAL SIGNIFICANCE
OF GALECTIN-3 EXPRESSION IN HUMAN LUNG
ADENOCARCINOMA
YOKO KATAOKA1, YASUHIKO OHSHIO1, TOMOYUKI Igarashi1,
KOJI TERAMOTO1, JUN HANAOKA1
1Department of Surgery, Shiga University of Medical Science, Shiga,
Japan

Background and Aim: Galectin-3, a β-galactoside-binding lectin,
have been shown to be involved in tumor development. However the signif-
ificance of galectin-3 expression in lung cancer remains unclear. Recently,
several studies demonstrated that galectin-3 is upregulated by hypoxia-
inducible factor 1α (HIF-1α) in several types of cancers other than lung
cancer. We hypothesized that hypoxia would promote tumor progression
via upregulation of galectin-3 in lung cancer. The aim of this study is to
evaluate the biological role of galectin-3 in human lung adenocarcinoma
and clarify its prognostic significance in patients.

Methods: (1) Galectin-3 or scrambled shRNA were transfected into
human lung adenocarcinoma cell line. A549 to evaluate the effect of hy-
oxia in vitro. Cell migration and invasion assays were performed under
hypoxia. To study RhoA activation, pull-down assay was done to assess
GTP-bound RhoA. (2) Galectin-3 expression was analyzed by immu-
nohistochemistry in 57 patients with stage I lung adenocarcinoma who
underwent surgical resection.

Results: (1) Hypoxia induced the upregulation of HIF-1α and
galactin-3, and increased cell migration and invasion. Silence of galectin-
3 expression in A549 significantly decreased cell migration and invasion
in hypoxic condition. Activation of RhoA was signifi-
cantly decreased in galectin-3 knockdown cells compared with control cells.
(2) Galectin-3 expression was observed in 20 patients (35.1%), and significantly associ-
ated with the incidence of recurrences (p<0.001) and the relapse-free sur-
vival time (p=0.001).

Conclusion: These data suggest that glycogene-3 would contribute to
tumor invasion in hypoxia through RhoA activation and indicate that
galactin-3 expression on tumor cells would serve as a prognostic marker
in lung adenocarcinoma. Therefore, galactin-3 could be a potential ther-
aputic target in human lung adenocarcinoma.

AP060

A COMPARISON OF ARMS-PLUS AND DROPLET DIGITAL
PCR FOR DETECTING EGFR ACTIVATING MUTATIONS IN
PLASMA
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1Department of Pulmonary Medicine, Xijing Hospital, Fourth Military
Medical University, Xi’an, China

Background and Aims: The majority of currently available circulat-
ing tumor DNA (ctDNA)-based genotyping assays possess low sensitivity
and are nonquantitative. Herein, we evaluated the performance of a novel
amplification refractory mutation system (ARMS)-based assay, namely
ARMS-Plus, in detecting plasma EGFR mutations in NSCLC patients,
compared to droplet digital PCR (ddPCR), and assessed the power of
plasma EGFR mutations in predicting efficacy of EGFR-TKI regimen.

Methods: Analytical sensitivity were determined by pre-clinical tests.
A total of 122 advanced NSCLC patients were enrolled (Table 1). Tissue
EGFR mutation status was confirmed by conventional ARMS PCR.
A total of 122 advanced NSCLC patients were enrolled (Table 1). Tissue
EGFR mutation status was confirmed by conventional ARMS PCR.

Results: The detection limit of ARMS-Plus is at least 0.015%.
For the 116 plasma samples analysed by ARMS-Plus, the sensitivity,
specificity, and concordance rate were 77.27% (34/44), 97.22% (70/72),
and 89.66% (104/116; k=0.77, P<0.0001), respectively (Table 2). Among
the 71 plasma samples analysed by both ARMS-Plus and ddPCR,
ARMS-Plus showed a higher sensitivity than ddPCR (83.33% versus
70.83%). (Table 3)

Conclusions: ARMS-Plus is sensitive and specific for the detection
of EGFR activating mutations in advanced NSCLC patients, with a diag-
nostic performance comparable to that of ddPCR. Considering that
ARMS-Plus can be performed simply with real-time PCR devices, it could
be an effective and economic method for plasma genotyping of EGFR
mutations when tissue is not available.

AP061

DIAGNOSTIC VALUE OF MICRORNAs DERIVED EXOSOMES
FROM BRONCHOALVEOLAR LAVAGE FLUID IN EARLY
STATE LUNG ADENOCARCINOMA: A PILOT STUDY
MI-HYUN KIM1, JUNG SEOP EOM2, JUNG HA MOOK1, HYE-KYUNG
PAIK1, MIN KI LEE1
1Department of Internal Medicine, School of Medicine, Pusan National
University, 179, Gudeok-ro, Seo-gu, Busan, South Korea

Background and Aims: Low-dose computed tomography for lung
screening is able to identify smaller nodules more often than can chest
radiographs. However, complications of invasive diagnostic procedures of
detected nodules are common in practice. Exosomes, membrane vesicles
released from cells, contain a diverse array of biomolecules that closely
reflect the biologic state of cell and tissue from which they are released.
The aim of this study is to investigate diagnostic values in bronchoalveo-
lar lavage (BAL) fluid exosomal micro (m)RNA in early stage lung
adenocarcinoma.

Methods: We chose candidate miRNAs (miR-7, miR-21, miR-126,
Let-7a, miR-17, and miR-19) known as having a diagnostic value of lung
adenocarcinoma. Exosomes were isolated from BAL fluid from control
subjects (n = 15) and patients with lung adenocarcinoma (n = 13). Exoso-
mal RNA was analyzed by using commercial kit containing probes for
selected 6 miRNAs. Results were validated with quantitative RT-PCR.

Results: The presence of miRNAs was confirmed in exosomes from
BAL fluid of both lung adenocarcinoma patients and control subjects.
miR-126 (p<0.001) and Let-7a (p=0.015) were present in significantly
higher levels in the BAL fluid of lung adenocarcinoma patients than in
control subjects. The BAL fluid miRNA signature was confirmed using an
independent set of paired adenocarcinoma and normal tissue samples
(n = 4). Lung adenocarcinoma tissues showed increased expression of
miR-126 (p=0.039) as compared to normal tissue samples.

Conclusion: We identified that a close correlation between the BAL
fluid exosomal miRNAs and tumor miRNAs. BAL fluid exosomal miRNAs
obtained by noninvasive methods could serve as diagnostic biomarkers in
early stage lung adenocarcinoma.
Figure 1. Flow chart of patient enrollment. NSCLC, non-small cell lung cancer; EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor

Figure 2. Correlation between radiological responses and the concentration of EGFR mutant alleles in plasma: a case report of a T+P+ patient. (a) Serial CT images of the patient. The diagnosis was made at 2015-10 and responses to gefitinib were evaluated every two months thereafter. (b) Longitudinal monitoring of plasma EGFR 19del concentration using ARMS-Plus.

Table 1. Patient demographics

<table>
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<th>n(%)</th>
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<td>Patients no.</td>
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</tr>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>Median (Range)</td>
<td>59 (30-85)</td>
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<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Male</td>
<td>65 (53.3)</td>
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<td>Female</td>
<td>57 (46.7)</td>
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<td>Histologic type</td>
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<tr>
<td>Adenocarcinoma</td>
<td>99 (81.1)</td>
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<tr>
<td>Squamous cell carcinoma</td>
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</tr>
<tr>
<td>Stage</td>
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<tr>
<td>IIA</td>
<td>7 (5.7)</td>
</tr>
<tr>
<td>IIB</td>
<td>36 (29.5)</td>
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<tr>
<td>IV</td>
<td>79 (64.8)</td>
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<tr>
<td>Performance status</td>
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<tr>
<td>0–2</td>
<td>115 (94.3)</td>
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<td>3–4</td>
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<tr>
<td>EGFR mutation status (by tissue genotyping)</td>
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<tr>
<td>EGFR activating mutation positive</td>
<td>45 (36.9)</td>
</tr>
<tr>
<td>EGFR activating mutation negative</td>
<td>77 (63.1)</td>
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<tr>
<td>Received EGFR-TKIs treatment</td>
<td>44 (36.1)</td>
</tr>
<tr>
<td>Objective response rate</td>
<td>18/44 (40.9)</td>
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<tr>
<td>Disease control rate</td>
<td>41/44 (93.2)</td>
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Table 2. Performance of ARMS-Plus and ddPCR for the detection of EGFR mutations in plasma

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<tr>
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<th>ARMS-Plus</th>
<th>ddPCR</th>
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<tr>
<td></td>
<td>%</td>
<td>n</td>
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<tr>
<td>Overall</td>
<td>77.27</td>
<td>34/44</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
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<tr>
<td>19del</td>
<td>79.31</td>
<td>23/29</td>
</tr>
<tr>
<td>L858R</td>
<td>68.75</td>
<td>11/16</td>
</tr>
<tr>
<td>Overall</td>
<td>97.22</td>
<td>70/72</td>
</tr>
<tr>
<td>Specificity</td>
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<td></td>
</tr>
<tr>
<td>19del</td>
<td>90.85</td>
<td>86/87</td>
</tr>
<tr>
<td>L858R</td>
<td>99.00</td>
<td>99/100</td>
</tr>
<tr>
<td></td>
<td>% (k)</td>
<td>n</td>
</tr>
<tr>
<td>Overall</td>
<td>89.66</td>
<td>104/116</td>
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<tr>
<td>Concordance*</td>
<td>93.97</td>
<td>109/116</td>
</tr>
<tr>
<td></td>
<td>(0.77)</td>
<td>(0.78)</td>
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<tr>
<td>L858R</td>
<td>94.83</td>
<td>110/116</td>
</tr>
<tr>
<td></td>
<td>(0.76)</td>
<td>(0.93)</td>
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</table>

*All results in concordance had a P value of less than 0.0001

Table 3. A head-to-head comparison of the performance of ARMS-Plus and ddPCR in a subset of 71 patients tested by both assays

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<td></td>
<td>%</td>
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</tr>
<tr>
<td>Overall</td>
<td>83.33%</td>
<td>20/24</td>
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<tr>
<td></td>
<td>100%</td>
<td>(47/47)</td>
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<tr>
<td></td>
<td>94.37%</td>
<td>(67/71)</td>
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<tr>
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<td>94.37%</td>
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<td>Concordance</td>
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<td>L858R</td>
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CT revealed a heterogeneous mass in the lower lobe of the right lung associated with ‘crazy paving’ appearance. CT-guided biopsy revealed invasive moderately differentiated adenocarcinoma of the lung.

She was commenced on tyrosine-kinase inhibitor (TKI), Geﬁtinib (epidermal growth factor receptor [EGFR] status was positive). Her disease showed partial response initially but later progressed. A repeat CT showed an increment in tumour size. The previously seen area of ‘crazy paving’ was completely replaced by solid tumour, suggestive of inﬁltration. A second-line TKI, Afatinib was introduced but the disease continued to progress. She also developed right humeral fracture secondary to bone metastasis. A few months later, treatment was discontinued due to intolerable mucocutaneous skin rashes and patient’s wishes. She was referred to palliative and rehabilitation teams.

Primary lung carcinoma usually appears as solid or subsolid nodules or mass on CT. Invasive adenocarcinoma may show various CT appearances including consolidation, ground glass or tree-in-bud opacities, or ‘crazy paving’. ‘Crazy paving’ refers to the superimposition of ground-glass opacity and linear pattern resembling irregularly shaped paving stones on CT images. It was historically described as a pathognomonic sign for alveolar proteinosis. This pattern was later reported in a variety of other lung disorders-idopathic, neoplastic, infectious, inhalational, lymphangitic carcinomatosis and superimposed pulmonary infection. In the context of lung carcinoma, this pattern is more commonly seen in mucinous than non-mucinous type of invasive adenocarcinoma.

Background and Aim: Lung cancer is the leading cause of cancer related death. Despite recent advances in the treatment, lung cancer remains an incurable disease. Matrine is a natural component from the traditional Chinese medical herb Sophora ﬂavescentes that exhibits strong antioxidant effects. However, the protective effects and molecular mechanisms of matrine in lung cancer remain not entirely clear. This study sought to explore the protective effects and molecular mechanisms of matrine in lung cancer cells.

Methods: A549 or H1299 cells were cultured in complete DMEM medium, contained with 0.5mg/ml matrine. Cell proliferation was evaluated by using CCK-8 assay, Edu assays and colony formation assays. Wound healing assay and transwell approach were used to detect the effects of matrine on A549 or H1299 cell migration and invasion. Hoechst 33342 and DAPI staining and Flow cytometry are used for assessing cell apoptosis. Western Blot was performed to detect the expressions of AKT, p-AKT, GSK3β, p-GSK3β.

Results: Matrine signiﬁcantly suppressed the proliferation and colony formation of lung cancer cells. By cell apoptosis analysis, wound healing and transwell assays, the results showed that matrine induced cell apoptosis and inhibited migration of lung cancer cells. Further results indicated that matrine inhibited cell proliferation and migration through down-regulating AKT and GSK pathways. Moreover, matrine induced lung cancer cell apoptosis in a dose dependent manner.

Conclusion: Matrine play a vital role in inhibiting lung cancer proliferation and migration through inhibiting AKT/GSK signaling pathways.

Acknowledgments: This work was supported by the National Natural Science Foundation of China (81370174)
expression of CAP1 have low survival and poor prognosis with lung cancer, ovarian cancer, breast cancer, colon cancer, and blood-related cancers. ICGC database show that CAP1 had the highest rate of change in melanoma and lung cancer. eBioPortal database show that CAP1 was mainly mutated and amplified in lung cancer. STRING database shows that CAP1 was Co-expression with CFL1 (0.996), and ACTIN-related protein (0.978). Cell immunofluorescence confirmed that CAP1 and ACTIN, ColIa were coexpressed in lung cancer cells.

**Conclusion:** CAP1 has abnormal amplification in most cancers, and high expression of CAP1 suggested that poor prognosis in patients with lung cancer. It is revealed that CAP1 play a critical role in the tumorigenesis and progression of cancer.

**Key words:** lung cancer, Gene, Database, Amplification

**AP066**

**EXPRESSION OF CAP1 IS ASSOCIATED WITH METASTASIS AND PROGNOSIS OF LUNG CANCER**

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**Objective:** To investigate the expression level of CAP1 and its association with the clinic features and tissue pathology grade in the metastasis of lung cancer.

**Methods:** 120 non small cell lung cancer patients were enrolled and the clinical data were collected after 4 years of follow-up. Immunohistochemical and western blot analyses were performed in metastatic tissues of NSCLC. The relationship between the expression of CAP1 and the clinical features, pathological grade and prognosis was analyzed by single factor variance and multivariate COX regression analysis, ROC curve was used to analyze the sensitivity and specificity of CAP1 in the brain metastasis of lung cancer. Survival analyses were performed by using the Kaplan-Meier method.

**Results:** The model comprises 120 cases of NSCLC that were treated and followed up for 4 years. The patients were divided into the BM (n=50) and non-BM (other visceral metastasis and those without recurrence) (n=70) groups. CAP1 protein content and immunoreactivity were significantly increased in BM specimens compared to other-metastatic specimens. There was no significant difference in age, sex, pathological stage, histological type and tumor size between the brain metastases group and the control group (p>0.05). No correlation was found between the overexpression of CAP1 and sexuality, tumourigenesis and progression and patient age, respectively (p>0.05), except tumor diameter by Univariate variance and multivariate COX regression analysis. The Kaplan-Meier survival analysis revealed the poor outcome of patients in the high-level CAP1-expression group, and 5-year survival rates were 19 and 59% in the high- and low-level groups (p=0.030, log-rank test).

**Conclusion:** The CAP1 molecular model may be useful in the prediction of the risk of BM in NSCLC.

**Key words:** Metastasis, Prognosis, Survival rate, Biological markers

**AP067**

**THE RELATIONSHIP BETWEEN CAP1 AND ITS BIOLOGICAL CHARACTERISTICS IN LUNG CANCER**

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**Objective:** To investigate the relationship between CAP1 and biological characteristics in lung cancer.

**Methods:** The expression level of CAP1 were detected by WB analysis in lung cancer cell lines. GFP-CAP1 Knockdown and RFP-CAP1 overexpression of lentivirus were transplanted into lung cancer cell lines (A549, H1299 and 95D). The cell transfection efficiency was determined by PCR and Western Blot. To assess the function of CAP1, stable transfected cells were established, and functional analyses were performed. Cell migration ability was determined by clonal formation assay and CCK8. The ability of cell migration was detected by scratch test. Transwell invasion assay was used to detect invasive ability. Skeleton staining was used to detect cytoskeleton changes.

**Results:** Tumor was implanted by subcutaneous injection of 1.0×10⁶ cells/mouse in 200ul of a 50/50 dilution of DMEM in PBS into the left flanks of the nude mice. All mice were executed in 6 weeks after the inoculation, stripped and put out the tumor which to be calculated the tumor volume according to the formula. overexpression, interference on lung cancer cell tumorigenicity. All the specimens were fixed with 10% formaldehyde solution, and the expression of CAP1 protein and nucleic acid in tumor tissue was detected by Western Blot and IHC.

**Conclusion:** CAP1 expression was successfully up regulated in lung cancer cells. CAP1 could enhanced lung cancer cell invasion and migration. However, CAP1 had no effect on the proliferation of lung cancer cells.

**Key words:** Invasion, Proliferation, Migration, Cytoskeleton
methylations of 12 genes (RARB, MDFI, HOXD11, SIM-1, PCDH10, GDNF, Retclp, HS3ST2, DCC, miRNA137, KLK10, and TIMP3) were analyzed using methylation-specific PCR analysis. The clinical relevance of methylation profiling and serum ROM levels on the outcome of disease was evaluated.

Results: Kaplan–Meier survival analysis revealed that serum ROM levels were significantly associated with overall survival after curative resection of pathologically node-negative NSCLC (log rank test; \( p = 0.0165 \)). Serum ROM levels were significantly associated with the degree of tumor differentiation \( (p = 0.0061) \). DNA methylation profiling revealed that aberrant PCDH10 methylation was associated with serum ROM levels \( (p = 0.0478) \). The average levels of serum ROM were 361.9±11.8 in patients with methylated PCDH10 \((n = 36)\) and 312.8±13.1 in patients without PCDH10 methylation \((n = 29)\) \( (p = 0.0071) \).

Conclusions: The results of this study indicate that serum ROM levels cause poor prognosis in patients with curatively resected node-negative NSCLC and may play a substantial role in inducing epigenetic alterations in specific genes such as PCDH10.

Figure. Overall survival curves of patients classified according to serum oxygen metabolite levels.

**AP069**

**PROGRAMMED CELL DEATH-LIGAND 1 EXPRESSION AND IMMUNOSCORE IN STAGE II AND III NON-SMALL CELL LUNG CANCER PATIENTS RECEIVING ADJUVANT CHEMOTHERAPY**

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Background and Aim: Programmed cell death 1 (PD-1) receptor–ligand interaction is a major pathway that is often hijacked by tumors to suppress immune control. Immunoscore (IS), a combinational index of ligand interaction is a major pathway that is often hijacked by tumors to

Conclusions: The results of this study indicate that serum ROM levels cause poor prognosis in patients with curatively resected node-negative NSCLC and may play a substantial role in inducing epigenetic alterations in specific genes such as PCDH10.

**AP070**

**EXPERIENCE ON OSIMERTINIB THERAPY IN THE ACTUAL CLINICAL SETTING**

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Background and Aims: Osimertinib was approved in Japan in March 2016 and is now available at community hospitals for the treatment of patients(pts) with T790M+ lung cancer that is resistant to EGFR-TKI. Drug approval was granted based on the combined results of the AURA and AURAZ2 clinical trials, which included 80 Japanese pts of the 411 pts enrolled.

We aimed to investigate the efficacy and safety of osimertinib in Japanese pts with T790M+ lung cancer at a community hospital in Japan.

Methods: 30 pts at Sapporo Minami-sanjo Hospital (Sapporo, Hokkaido, Japan) were treated with osimertinib between May 2016 and April 2017.

Results: The median age was 65 years (range, 43–85 years). 29 pts had a history of EGFR-TKI therapy with gefitinib in 21 pts, erlotinib in 19 pts, and afatinib in 15 pts. Upon the initial EGFR mutation testing, 18 pts had exon 19 deletion, 8 patients had L858R, 2 pts had combined L858R and T790M, and 2 pts had unknown results.

Central nervous system (CNS) lesions were observed in 19 patients (63%). T790M was confirmed by histologic evaluation in 27 patients and by plasma screening alone in 3 patients.

The response rate was 67% and the disease control rate was 100%.

The data on median progression-free survival (PFS) was immature; nevertheless, the PFS rate at 9 months was 63%. There were no Grade ≥3 adverse events (CTCAE v4.0).

Conclusions: This study demonstrated similar results on osimertinib compared with those of the AURA clinical trials, despite the relatively high prevalence of CNS lesions in this population of community hospital patients. In the actual clinical setting, osimertinib was effective in Japanese patients with T790M+ lung cancer that is resistant to EGFR-TKI therapy.

**AP071**

**A CASE OF CHEMICAL PULMONARY DISORDER DUE TO ALECTINIB**

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Background and Aims: Second-generation anaplastic lymphoma kinase (ALK) inhibitor, alectinib is known as a first-line drug for inoperable non-small cell lung cancer (NSCLC) in ALK gene translocation positive patients. Serious side effects of alectinib include interstitial pneumonia; however, the frequency is low. We report a case of chemical pulmonary disorder due to alectinib in a patient with NSCLC.

Methods: Case Report: A 72-year-old Japanese woman who was positive for gene translocation with ALK-rearranged stage IV lung
Clinical analysis of Afatinib in EGFR-Tyrosine Kinase Inhibitor naïve patients with non-small cell lung cancer harboring EGFR mutations

Shingo Nasu, So Takeata, Kentaro Matsuhiro, Satomo Morita, Kaori Iwata, Noriko Ryota, Yukioka Okada, Yosie Tokucu, Yuki Ueda, Akinori Kudoku, Naoko Usui, Ayako Tanaka, Takayuki Shiroyama, Naoko Morishita, Hidekazu Suzuki, Norio Okamoto, Tetsunori Hirashima

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Background and Aims: Afatinib, a second-generation epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitor, has been reported to significantly improve overall survival rates in patients with exon 19 deletions compared to chemotherapy in the combined analyses of the LUX-Lung 3 and LUX-Lung 6 trials. However, in many patients, treatment is difficult to continue because of adverse reactions. There are no supporting data from clinical practice. We aimed to retrospectively assess the clinical course of EGFR mutation-positive cases of non-small cell lung cancer in which afatinib was first introduced as an EGFR-tyrosine kinase inhibitor.

Methods: We investigated the clinical backgrounds, therapeutic effects, side effects, and prognoses of patients treated with afatinib for the first time from May 2014 to April 2016. The side effects were managed by doctors, pharmacists, and nurses.

Results: Thirty-two patients were treated with afatinib within the study period. There were 13 men and 19 women. The median age was 66 years (range 39–83 years). EGFR exon 19 deletion, L858R, and exon 19 deletion plus L858R were present in 22, 9, and 1 patient(s), respectively. The starting dose was 40 mg in 24 patients and 30 mg in 8 patients. Some of the patients developed adverse effects of grade 3 and above, including diarrhea (15.6%), paronychia (6.2%), and stomatitis (6.2%). As of March 31, 2017, 18 patients had discontinued treatment (owing to progressive disease in 16 patients, drug-induced fever in 1, and diarrhea in 1). The overall response rate was 78.1% and the median afatinib oral dose period was 480 days (95% confidence interval: 338–NA).

Conclusions: Afatinib first introduced as an EGFR tyrosine kinase inhibitor was suggested to be relatively safe and effective in treating EGFR mutation-positive cases of non-small cell lung cancer with reduced side effects.

Efficacy and Safety of Salvage Chemotherapy Following Exposure to Immune Checkpoint Inhibitors in Patients with Non-small Cell Lung Cancer

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Background: Immune checkpoint inhibitors (ICIs) are active for patients with metastatic and recurrent non-small cell lung cancer (NSCLC), nevertheless, response to these agents are limited. We evaluated efficacy and safety to chemotherapy in patients who had progressed on ICIs.

Methods: Clinical data for eligible 38 patients with metastatic and recurrent NSCLC, and treated with nivolumab between January 2016 and March 2017 were retrospectively analyzed.

Results: Among the 38 patients who had progressed on ICIs, 21 patients received salvage chemotherapy, and 17 patients did not
Abstracts

received. Response rate and disease control rate were 21 % and 37 % respectively, and median progression-free survival (PFS) was 2.8 months. Drug induced interstitial pneumonia were identified in 3 patients (14.3 %) of all patients received salvage chemotherapy.

Conclusion: In NSCLC, efficacy of salvage chemotherapy after immunotherapy exposure may be superior to historical data of the pre-ICIs era. Careful monitoring is important to prevent the worsening of interstitial pneumonia in patients of salvage chemotherapy after ICIs.

CONFORMITY OF EGFR MUTATION STATUS BETWEEN BLOOD PLASMA AND TUMOR TISSUE SAMPLES IN NSCLC ADENOCARCINOMA, AT DR. H. A. ROTINSULU LUNG HOSPITAL, A PRELIMINARY STUDY

REZA KURNIAWAN TANUWHARDJA1, HANNY ROESMARGONO2
1Pulmonary Department, Dr HA Rotinsulu Lung Hospital, Bandung, Indonesia, and 2PT Prodia Widyahasada, Jakarta, Indonesia

Background and Aim: Lung cancer: the leading cause of cancer-related deaths worldwide about 85% of lung cancers are NSCLC with Adenocarcinoma in predominance EGFR-TKI became a current standard treatment in elderly patients with advanced squamous non-small-cell lung cancer. Eligibility criteria included an overall performance status (Karnofsky Index) of ≤80%, Eastern Cooperative Oncology Group (ECOG) performance status of ≤2, age of ≥70 years, and receive carboplatin plus paclitaxel in elderly patients with previously untreated advanced squamous non-small-cell lung cancer, selected based on the Mini Nutritional Assessment-short-form scores (MNA-SF)

Methods: This multicenter, single-arm, open-label, phase 2 study assessed the efficacy and safety of carboplatin plus weekly nanoparticle albumin-bound paclitaxel in elderly patients with previously untreated advanced squamous non-small-cell lung cancer, selected based on the Mini Nutritional Assessment short-form scores (MNA-SF).

Results: Thirty patients with a median age of 76 (range, 70–83) years were enrolled. The objective response rate was 50.0% (95% confidence interval: 31.3–68.7%), which met the primary objective of this study. The disease control rate was 73.3% (95% confidence interval: 54.1–87.7%). At a median follow-up of 15.0 months, the median progression-free and overall survival was 7.1 and 19.1 months, respectively. The most common treatment-related adverse event of Grade ≥3 was neutropenia (66.7%). Well-nourished patients, based on the MNA-SF, experienced fewer adverse events of Grade ≥3 compared to patients at risk of malnutrition. All treatment-related adverse events were tolerable and reversible. There were no treatment-related deaths.

Conclusion: Carboplatin plus weekly nanoparticle albumin-bound paclitaxel is effective and well tolerated as a first-line treatment for elderly patients with advanced squamous non-small-cell lung cancer. Eligibility based on MNA-SF screening may be useful in determining acceptable toxicity.
AP077

THE EFFECT OF CARBOPLATIN PACLITAXEL AND BEVACIZUMAB FOR ADVANCED NON-Small Cell Lung Cancer with Malignant Pleural Effusion

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Background: It is difficult to treat the patients with lung cancer with malignant pleural effusion (MPE). Recently, the effect of the chemotherapy including Bevacizumab regimen is suggested.

Aims: We assessed the effect of the chemotherapy of Carboplatin, Paclitaxel and Bevacizumab (CPB) regimen for lung cancer patients with MPE.

Methods: Since 2011 to 2016, 21 patients with MPE received first line chemotherapy with CPB regimen. We assessed treatment effect of the patients for rate of decreased pleural effusion, progression free survival (PFS) and overall survival (OS). And compared with 20 patients without MPE received first line chemotherapy with CPB regimen.

Result: 21 patients with MPE, histology (all adenocarcinoma), male (15 patients), median age (69, 52-77 years), ECOG performance status 0-1 (19 patients). Pleural effusion decreased in 18 patients (85.7%). PFS median was 6.1 months and OS median was 9.5 months. 17 patients had positive histologic or cytologic evidence. Compared with positive and negative histologic or cytologic evidence, no statistical difference was shown in PFS (positive 6.1 months vs negative 5.5 months, p=0.939) and OS (positive 8.8 months vs negative 9.4 months, p=0.931). Compared with no MPE patients, no statistical difference were shown in PFS and OS (no MPE 7.2 months vs MPE 6.1 months, p=0.261) and no MPE 13.8 months vs MPE 9.5 months, p=0.256)

Conclusion: Compared with no MPE and MPE, MPE tended to poor prognosis, but there was no statistical difference in PFS and OS. These results suggest the chemotherapy including Bevacizumab regimen has good control for MPE.

AP078

EFFICACY OF ANTIEMETIC THERAPY FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN ELDERLY PATIENTS WITH ADVANCED LUNG CANCER RECEIVING CARBOPLATIN COMBINATION CHEMOTHERAPY

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Background: Chemotherapy-induced nausea and vomiting (CINV) are major adverse effects, and various guidelines recommend using neurokinin-1 receptor antagonists (NK1RAs), 5-hydroxytryptamine-3 receptor antagonists (5-HT3RAs), and dexamethasone to control these symptoms. The risks of higher toxicity, such as CINV, need to be minimized to determine efficacy of chemotherapy in elderly patients with cancer. It is suggested that carboplatin (CBDCA)-based chemotherapy can be safely used in elderly patients with lung cancer, but moderate emetogenic chemotherapy (MEC) is required for controlling CINV.

Aim: This retrospective study evaluated the prevalence of CINV in elderly lung cancer patients who received CBDCA combination chemotherapy.

Methods: Patients aged ≥75 years (n=54) with advanced lung cancer who received CBDCA combination chemotherapy between April 2012 and March 2017 were analyzed retrospectively. The antiemetic regimen for chemotherapy consisted of 5-HT3RA, dexamethasone, and/or NK1RA based on the Japan Society of Clinical Oncology guidelines. Primary outcomes were to determine the rates of complete response (CR; no emesis and no rescue medication during 0–120 h) and complete control (CC; CR and only mild nausea during 0–120h). Further, the clinical episodes of CINV, anorexia, rescue medication, and change in antiemetic therapy or chemotherapy were assessed.

Results: The median age was 77 (range, 75–85) years, and 10 patients (18.5%) were female. Small cell lung cancer was diagnosed in 31.5% of patients and 68.5% had non-small cell lung cancer. Ten chemotherapy schedules were used, and all patients received a doublet or triplet with CBDCA plus other drugs. The CR rate was 94.4%, whereas the CC rate was 92.6%. From cycle 2, 11 patients (20.4%) adjusted to the change in antiemetic therapy.

Conclusion: Although our cohort was small, elderly lung cancer patients can help determine the success of CBDCA combination chemotherapy if CINV is better managed using antiemetic therapy.

AP079

COMPARISON OF CHEMOTHERAPY RESPONSE AND ADVERSE EFFECTS OF DOUBLE-PLATINUM PLUS EGFR-TKI VERSUS DOUBLE-PLATINUM ALONE ON PATIENTS WITH NSCLC WHO HAD DISEASE PROGRESSION FOLLOWING EGFR-TKI TREATMENT

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Background and Aim: EGFR-TKI is the first-line therapy for EGFR-mutant patients. Nevertheless, patients will have disease progression (median PFS 10 – 12 months) due to resistance. The treatment options are still limited in developing countries for such cases, thus double-platinum chemotherapy is the next option. Although IMPRESS study reported no difference in terms of PFS and OS between double-platinum and double-platinum plus EGFR-TKI, several local studies reported benefit of continuing EGFR-TKI in combination with double-platinum chemotherapy (treatment beyond progression). The Aim is to Compare chemotherapy effects of Double-Platinum Plus EGFR-TKI Versus Double-Platinum alone on patients with NSCLC progression following EGFR-TKI treatment.

Methods: This is an analytical descriptive study using prospective cohort design, involving 30 patients with disease progression following EGFR-TKI treatment that meet inclusion criteria in Dr. Soetomo General Hospital. Subjects then observed in 3 cycles of double-platinum chemotherapy. Subjective response (body weight and EQ5D questionnaire) were analyzed, chest CT scans were evaluated using Recist criteria, and adverse effects were monitored. This study was conducted in accordance with GCP principles and has received ethics certificate from Dr. Soetomo General Hospital ethics committee (No.08/Panke.KKE/I/ 2017).

Results: Subject characteristics between two arms are insignificantly different (p ≥ 0.05). The most common EGFR mutation is exon 21 (50% on arm A and 60% on arm B), Chi square test on subjective response parameter (EQ5D (p=0.483)), T2 free sample test on semi-subjective parameter (body weight (p=1.00)). Comparison test on both groups after cycle 2 and 4 showed p value ≥ 0.05. Statistical test on adverse effect between both groups showed p value = 0.526.
Conclusion: This study showed no significant difference between double-platinum and double-platinum plus EGFR-TKI on patients who had disease progression following EGFR-TKI treatment.

Keywords: NSCLC, EGFR-TKI, disease progression, double-platinum

Efficacy of 1st/2nd-Generation EGFR-TKIs in Patients with Non-Small-Cell Lung Cancer (NSCLC) and Pleural Effusion

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Background and Aims: Although epidermal growth factor receptor (EGFR) - tyrosine kinase inhibitors (TKIs) are effective in patients with mutated non-small-cell lung cancer (NSCLC), pleural or pericardial effusion is a known negative factor in EGFR-TKI monotherapy and suggested taking time to response for effusion. But the difference between some EGFR-TKIs for controlling effusion is still unknown. We analyzed the efficacy of 1st/2nd-generation EGFR-TKIs in EGFR-positive patients with pleural effusion.

Methods: The NSCLC patients treated with Gefitinib, Erlotinib and Afatinib were evaluated at Yokohama City University Medical Center. Treatment responses of tumor and effusion were measured in first evaluation CT and analyzed retrospectively in patients with and without pleural effusion.

Results: 76 cases in 63 patients (10 patients had a history of several EGFR-TKI re-challenge) were treated with 1st/2nd-generation EGFR-TKIs, and 32 of Gefitinib, 25 of Erlotinib and 12 of Afatinib cases were evaluated between January 2012 and December 2016. 34 of the patients had no pleural effusion, of which 32 were evaluable for tumor response (responded or stable). 34 cases with pleural effusion were evaluated; of these, 31 cases had no progression and 3 patient had tumor progression during a 1st evaluation time treatment with 1st/2nd-generation EGFR-TKIs. Regarding the pleural effusion, the effusion decreased in 17 cases and, was stable in 12 patients; in 6 cases, there was a slight or moderate increase despite the administration of 1st/2nd-generation EGFR-TKIs.

Conclusions: Although an active agent in clinical practice, 1st/2nd-generation EGFR-TKIs might not provide an early response for pleural effusion.

ORAL GLUTAMINE SUPPLEMENTS REDUCE CONCURRENT CHEMORADIOTherapy-INDUCED ESPHAGAsITIS IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCer

Cheng-Yu Chang1, Jui-Chi Hung2, Yi-Chun LA3, Shih-Chieh Chang4

Background and Aims: Complications related to concurrent chemoradiotherapy (CCRT) such as acute radiation-induced esophagitis (ARIIE) may cause significant morbidity and unplanned treatment delays in patients with advanced non-small cell lung cancer (NSCLC). We designed a prospective randomized study to assess the impact of Glutamine supplementation in preventing CCRT-induced toxicities of advanced NSCLC patients.

Methods: From January 2014 to December 2015, sixty patients diagnosed with NSCLC were included in the study. Thirty patients (50%) received prophylactic powdered GLN orally at a dose of 10g/8h. The prescribed radiation dose to the planning target volume was 30 Gy in 2-Gy fractions. The endpoints were radiation-induced esophagitis, mucositis, body weight loss, overall survival and progress free survival.

Results: The 60 patients with NSCLC included 42 men and 18 women with a mean age ± standard deviation of 60.3 years ± 18.2 (range, 44-78 years). At a median follow-up of 26.4 months (range 10.4-32.2), all patients tolerated GLN well. In multivariate analysis, administration of GLN was associated with a decrease in the incidence of grade 2 or 3 ARIE (6.7% vs. 53.4% for GLN+ vs. GLN-; p=0.004). GLN supplementation appeared to significantly delay ARIIE onset for 5 days (18 days vs.12 days; p=0.027) and reduced incidence of weight loss (20% vs. 73.3%; p=0.01).

Conclusions: Our study suggests a beneficial effect of oral glutamine supplementation for the prevention from radiation-induced injury and body weight loss in advanced NSCLC patients who receiving CCRT.

THE EFFECT OF FORCED EXPIRATORY VOLUME IN ONE SECOND ON THE TREATMENT RESPONSE OF SMALL CELL LUNG CANCER

Kangwon Cho1, Hye Seon Kang1, Sang HaaK Lee2

Background and Aim: The impact of chronic obstructive pulmonary disease (COPD) and pulmonary function on the treatment response of small cell lung cancer (SCLC) has not been studied. The objective of this study was to compare the clinical characteristics and treatment response of SCLC patients with and without COPD and investigate predictors related with pulmonary function of mortality in patients with SCLC.

Methods: This was a retrospective multicenter study performed between January 2011 and December 2015. In all, 147 SCLC patients treated with chemotherapy and had pulmonary function test were enrolled. Patients were divided into the COPD group and the non-COPD group. The overall survival (OS) and progression free survival (PFS) were compared, and predictors of worse OS were analyzed using Cox regression analysis.

Results: COPD was present in 54.4% of all SCLC patients. There were no differences in clinical characteristics except pulmonary function test between COPD and non-COPD group. OS and PFS (log-rank test, p = 0.165 and p = 0.071, respectively) were not different between COPD and non-COPD groups. In a multivariate analysis using Cox regression model, extensive disease (hazard ratio [HR] = 2.59, 95% CI: 1.60-4.19) and the low forced expiratory volume in one second (FEV1 <80%) (HR = 1.85, 95% CI: 1.15-2.96) were independent risk factors for shorter survival.

Conclusion: COPD was no impact on the treatment response of SCLC, but low FEV1 was a predicting factor for poor clinical outcome.
COMBINED SMALL CELL AND LARGE CELL CARCINOMA: A RARE FORM OF LUNG CARCINOMA
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1Makati Medical Center, Makati City, Philippines

Background and Aims: Combined small cell lung carcinoma (C-SCLC) is a rare, multiphasic form of lung cancer under the subset of Neuroendocrine Tumors. Currently, very little is known about the clinical characteristics and response to therapy of these tumors. In this paper we aim to present the unique challenges in diagnosing and treating patients with Combined small cell lung carcinoma.

Methods: This is a case report of a 76 year-old female, 90 pack year smoker presenting with chronic cough, weight loss, anorexia, with on and off headaches.

Results: A right upper lobe pulmonary mass was seen on chest computed tomography scan, biopsy results showed Chronic Granulomatous Inflammation, initially treated as Pulmonary Tuberculosis. Despite anti-koch’s treatment, there was progression of pulmonary lesions on repeat CT imaging, repeat biopsy revealed Small Cell Carcinoma. Further metastatic work-up showed Extensive Stage Disease. Chemotherapy with 6 cycles of Carboplatin+ Etoposide was given with 10 sessions of Thoracic Radiation. Surprisingly, after the course of both chemotherapy and radiation therapy, there was a new growth of a right anterior chest wall mass, excision biopsy was done with histopathologic result of Metastatic Non-Small Cell Carcinoma, Poorly Differentiated Adenocarcinoma in a known Small Cell Carcinoma. Further, immunohistochemical staining revealed positive for TTF-1, CK5/6.

Conclusions: Knowledge in the diagnosis and treatment of Combined small cell lung carcinoma is still lacking, we need to be aware of its existence and do further research for us to better understand this clinical entity.

SYNCHRONOUS MULTIPLE BONE METASTASES FROM A LARGE-CELL NEUROENDOCRINE CARCINOMA WITH RAPID PROGRESSION OF BONE-RELATED EVENTS
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A 74-year-old man presented with multiple tumor shadows in the left lung on chest computed tomography (CT) 2 years previously. Diagnostic thoracoscopic surgery led to the diagnosis of a large-cell neuroendocrine carcinoma (LCNEC). After surgery, he received 6 cycles of chemotherapy with etoposide and cisplatin. At follow-up, tumor marker levels were elevated and chest CT revealed tumor regrowth; as progression of disease was considered, he was admitted for further examination and treatment. Although bone scintigraphy did not reveal any abnormal uptake 4 months previously, he had complained of right shoulder pain since admission. Magnetic resonance imaging (MRI) revealed a metastatic fracture of the right humerus, for which invasive reduction and plate fixation were performed. Bone scintigraphy and MRI of the left femur, performed in the same period, also revealed metastatic bone tumors. Radiotherapy and chemotherapy with amrubicin were initiated for the tumors in the right humerus and left femur. The patient is currently treated as an outpatient. Accordingly, when patients complain of bone-related events during the treatment of a LCNEC even for a short period, they should be reexamined for possible bone metastasis.

LARGE CELL NEUROENDOCRINE CARCINOMA IN THREE SITES- LUNG, STOMACH AND BRAIN: A CASE REPORT
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Background and Aims: Large cell neuroendocrine carcinoma (LCNEC) is a rare pulmonary tumor, grouped with the pulmonary neuroendocrine carcinomas in the 2015 WHO classification. Primary LCNECs tend to be located peripherally and is more aggressive and has a poorer prognosis.

Results: 55/F came in due to incidental finding of left lower lung mass in CXR. Chest CT scan and lung biopsy revealed chronic granulomatous disease and she was treated for PTB. After 2 months, repeat CXR showed doubling in size of the mass. Anti-Koch’s was discontinued and repeat biopsy was done twice revealing inconclusive results. The mass further increased in size but patient is still asymptomatic. She was scheduled for lobectomy to remove mass and adequately get a specimen and diagnosis, but pre-op, there was note of anemia. She underwent colonoscopy where only a small polyp was seen which was biopsied. Two days after biopsy, the patient experienced hematochezia. Results of previous lung biopsy staining and colonic polyp came in revealing neuroendocrine tumor. A possible gastric mass was seen in CT angio and she underwent exploratory laparotomy. Intra-operative finding was a 4cm duodenal mass which turned out to be high-grade neuroendocrine tumor. All previous lung biopsy specimens were collected and read by one pathologist. Neuroendocrine tumor. Chemotherapy was started but then she subsequently had episodes of seizures and persistent of abdominal pain, repeat CT scans were done which revealed increasing size of lung mass and duodenal mass and a new growth on the brain. Radiotherapy was started but she had decrease in sensorium and eventually expired.

Conclusions: Accurate differentiation of LCNEC from other types of NSCLC is important because it identifies those patients at highest risk for developing recurrent disease. Efforts to identify effective adjuvant therapies are needed to improve treatment outcomes with this aggressive type of lung cancer.

Critical Care Medicine

COMPLAINTS TO THE INTENSIVE CARE MEDICINE: APPLICATION OF THE HEALTHCARE COMPLAINT ANALYSIS TOOL (HCAT) TO EXPLORE IMPROVEMENT OPPORTUNITIES
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Background and Aim: There were limited reports regarding classification and analysis of healthcare complaints to the critical care setting.

Methods: We retrospectively analyzed the records of healthcare complaints to the intensive care units (ICUs) from 2008 to 2016 from the database of the Center for Quality management of the institution. The complaints were typed according to the Healthcare Complaint Analysis Tool (HCAT) 1.

Results: We identified 356 complaints during the study period. Most (94.7%) of them came from the family members, and feedback sheets accounted the major channel (59.2%). The numbers of complaints based on the categories of HCAT included quality (15.2%), safety (3.7%),...
Background and Aims: Tracheal stenosis is a life-threatening condition. It can be an inevitable iatrogenic result for patients requiring artificial airway assist such as tracheal intubation and tracheostomy. There are many treatment options to treat tracheal stenosis such as tracheal resection with reconstruction, laser surgery, tracheobronchial airway stent, and transient tracheostomy for delayed operation. However, clinicians should be aware of the possibility that some of above options could be ineffective to treat tracheal stenosis.

Case: A 38-yr-old female patient was suffered from dyspnea with respect of tracheal stenosis in general ward. The tracheal stenosis was caused by prolonged tracheal intubation status for 2X days. Until tracheostomy was planned after several failures of trials of tracheal intubation, her lungs were well ventilated with a tracheal tube impinged just above the proximal site of tracheal stenosis. However, manual bagging through an inserted cannula became more difficult after tracheostomy even if confirmation of successful making of stoma and adequate insertion of the cannula. Eventually, respiratory arrest occurred and cardiopulmonary resuscitation began promptly. However, she died unfortunately.

Conclusion: Tracheostomy is one option of treatment for tracheal stenosis, even if it could be a temporary expedient. However, clinicians should be aware of the possibility that tracheostomy cannot be effective to treat tracheal stenosis. Outcome can end in a disaster even though a cannula is completely inserted after completion of making stoma site, because tracheostomy site is same or lower level compared with stenotic site.
bronchoscopy and chest computerized tomography revealed disrupted anterior wall of trachea and endotracheal tube displacement, which created a false track into the mass. (Figure 2) Tumor necrosis was thought to be the cause of this perforation and tube malposition. The tube was repositioned by bronchoscopic guidance. Unfortunately, the disrupted trachea could not be reconstructed. Palliative care was consequently provided, and the patient finally passed away a week after the catastrophic event.

Conclusions: This report demonstrates clinical presentation, chest imaging and bronchoscopic findings of tracheal perforation, which is a rare complication following the treatment of lymphoma.

Figure 1. Chest radiography and CT at admission (1A) Chest radiography shows narrow tracheal lumen and anterior mediastinal mass. (1B) Chest CT shows an infiltrative homogeneous neck mass with an enhancing hypodensity lesion which extends to the superior and anterior mediastinum, and encases the brachiocephalic and subclavian vessels.

Figure 2. Chest radiography, chest CT, bronchoscopic findings and ventilator graphics at the critical event (2A) Chest radiography shows the displaced ETT. (2B) Chest CT shows malposition of ETT. The ETT anteriorly penetrates disrupted tracheal wall to the mass in superior mediastinum. (2C) Ventilator graphics reveal high peak airway pressure from increased airway resistance with low minute ventilation and bronchoscopic findings show granulation-like tissue at the tip of ETT.
CLINICAL FEATURES OF TAKOTSUBO CARDIOMYOPATHY EXPERIENCED IN RESPIRATORY DEPARTMENT.  
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Background: Takotsubo cardiomyopathy is an acute cardiomyopathy characterized by transient left ventricular systolic dysfunction induced by emotional or physical stress, including respiratory failure.

Aim: The aim of this study was to analyze the clinical features of patients who developed takotsubo cardiomyopathy in a respiratory department.

Methods: We retrospectively evaluated the characteristics, causes, and outcomes of takotsubo cardiomyopathy experienced in our respiratory department from January 2011 to December 2016.

Results: Of 14 patients, 35% were women over 50 years of age. The most frequent trigger was bronchoscropy. Laryngeal reflex in response to irritation of the trachea results in elevation of catecholamine levels, thereby inducing takotsubo cardiomyopathy. At onset, more than half of the patients did not show typical symptoms such as chest discomfort. 57.1% of cases showed type 2 respiratory failure and 42.9% showed acidosis which might related to elevation of catecholamine level as well. 50.0% of patients had comorbidities of chronic obstructive pulmonary disease (COPD) or asthma, treated regularly with β2-stimulant. Since there are abundant β2-stimulant receptors in apical myocardium, repeated treatment with β2-stimulant may have contributed to the disease onset. Some cases complicated with heart failure, but all patients improved.

Conclusions: In respiratory department, it is necessary to be aware of takotsubo cardiomyopathy especially when conducting procedures including tracheal manipulation, when using repetitive β2-stimulant, and when a patient shows exacerbation of respiratory failure with hypercapnia, even without any chest complaints.

SAPS II OR APACHE II IS BETTER TO PREDICT MORTALITY IN MEDICAL ICU PATIENTS

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Background and Aims: Selecting patients to admit at the ICU is crucial. The SAPS II and APACHE II scores have been used to choose appropriate patients to the ICU particularly in resource limited setting. However, the best predictor score is still debating.

Methods: The study was conducted retrospectively at Khon Kaen Hospital between Jan 1, 2015 to Jan 1, 2016. The inclusion criteria were consecutive adult patients who admitted and treated at the ICU. Those patients who admitted at the ICU for procedures such as hemodialysis were excluded. Clinical factors including SAPS II and APACHE II were study. The primary outcome was death at the ICU. Independent factors associated with mortality were analyzed by multivariate logistic regression analysis. For significant scores to predict mortality, a receiver operating characteristic (ROC) curve was executed to calculate diagnostic properties of each cut off points.

Results: During the study period, there were 201 eligible patients. Of those, 98 patients (48.76%) died. Those who died had higher average SAPS II score and APACHE II score than those who were survived significantly (49.76 vs 30.61; p value < 0.001; 23.88 vs 20.62; p value 0.0157). There were three independent factors associated with mortality including SAPS II score, male sex, and sepsis with adjusted odds ratio (95% CI) of 1.04 (1.02, 1.07), 2.10 (1.08, 4.06), and 2.33 (1.09, 4.97), respectively. The SAPS II score of more than 42 gave sensitivity of 78.57%, specificity of 63.11%, and the area under ROC curve of 73.18%.

Conclusion: The SAPS II score was better than the APACHE II score to predict medical ICU mortality.

Key words: death; predictor; sensitivity; specificity

EVALUATION OF HYDROCORTISONE THERAPY FOR SEPTIC SHOCK PATIENTS IN REAL LIFE PRACTICE

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Background and Aim: Septic shock is common in critical illness. The evidence of NF-κB overactivity and adrenal insufficiency in septic patients suggested a possible role of glucocorticosteroid therapy. Nowadays, hydrocortisone is recommended for septic shock patients who do not respond to adequate fluid resuscitation and vasopressors. However, the definition of adequate resuscitation or vasopressor therapy was not mentioned in a current guideline. Therefore, we conducted a retrospective cohort study to evaluate guideline usage compliance of hydrocortisone therapy in septic shock patients and to evaluate the effect of hydrocortisone therapy.

Methods: Admitted septic shock patients between January 2016 and December 2016 were screened. Eligible patients had to receive hydrocortisone injection. Data, including gender, age, dose of norepinephrine before and after hydrocortisone injection, incidence of hyperglycemia, incidence of secondary infection and mortality, were collected.

Results: Eighty-three septic shock patients were enrolled. Shock reversal was reported in 55 patients (66.3%). ICU death was reported in 34 patients (41.0%). Forty-seven patients (56.6%) were prescribed hydrocortisone despite inadequate vasopressor therapy and 26 patients (31.3%) of them had a history of previous corticosteroids treatment. The hazard ratio for shock reversal in patients with rapid reduction of vasopressor within 12 hours after hydrocortisone injection, as compared with patients requiring vasopressor that could not be tapered within 12 hour, was 4.3 (95% confidence interval, 2.5-7.5, p<0.001). Early hydrocortisone prescription and intravenous bolus of hydrocortisone could shorten shock reversal and survival.

Conclusion: In real life practice, a half of septic shock patients were prescribed hydrocortisone despite inadequate vasopressor therapy. Early prescription of hydrocortisone could not show any benefit. Rapid reduction of vasopressor after hydrocortisone therapy was a good predictor for shock reversal and survival.
CLINICAL APPLICATION OF THE QUICK SEPSIS-RELATED ORGAN FAILURE ASSESSMENT IN INTENSIVE CARE UNIT PATIENTS WITH BACTEREMIA: A SINGLE-CENTER STUDY IN KOREA
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Background and Aims: According to the new international sepsis guidelines (Sepsis-3), patients with a quick Sepsis-related Organ Failure Assessment (qSOFA) score of greater than or equal to 2 are more likely to have a poor outcome. Our study evaluated the clinical usefulness of the qSOFA score in patients with bacteremia at the time of intensive care unit (ICU) admission.

Methods: We retrospectively analyzed clinical data from the medical records of 158 patients with infectious diseases who had a positive blood culture within 3 days after ICU admission in a tertiary care hospital between March 2011 and February 2015.

Results: The patients’ median age was 69 years, and 61.4% were male. Of the 158 patients, 83 (52.5%) had altered mentality, 76 (48.1%) had a respiratory rate of ≥22/min or greater and 95 (60.1%) had a systolic blood pressure of 100 mmHg or less. Of the patients, 87 (55.1%) had a qSOFA score of 2 or more points. The patients with a qSOFA score of 2 or more had a significantly higher APACHE II score at admission (median 27 vs. 24, p = 0.001). In addition, patients with a qSOFA of 2 or more had a higher incidence of pneumonia as a cause of sepsis (49.4 vs. 25.4%, p = 0.003), neutropenic state at diagnosis of sepsis (12.6 vs. 2.8%, p = 0.039), Gram-negative bacteremia (46.0 vs. 29.6%, p = 0.048), and candidemia (17.2 vs. 5.6%, p = 0.028). Univariate logistic regression analysis showed that a qSOFA score of 2 or more was associated with 28-day mortality in our cohort (odds ratio = 2.820, p = 0.002).

Conclusions: In our study, a qSOFA score of 2 or more was associated with greater disease severity and a higher 28-day mortality rate. Also, patients with a qSOFA score of 2 or more had a higher incidence of pneumonia, neutropenia, Gram-negative bacteremia, and candidemia.

DYNAMIC CHANGES IN ESOPHAGEAL DOPPLER DERIVED PARAMETERS BY ELEVATION OF PEEP, PREDICT FLUID RESPONSIVENESS IN PATIENTS WITH SEPTIC SHOCK
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Background: Optimization of preload is important in septic shock. Esophageal Doppler monitoring (EDM) provide measurements of noninvasive and real-time hemodynamic parameters. These EDM-derived parameters may be valuable as a surrogate of fluid responsiveness.

Aims: We aimed to assess changes of EDM-derived parameters after increased in PEEP could predict fluid responsiveness in patients with septic shock.

Methods: We performed a prospective study in 20 patients with septic shock who were mechanically ventilated. EDM-derived parameters were measured while the patients were mechanically ventilated with 5 cmH2O of PEEP, 15 cmH2O of PEEP, and immediately after 500 mL of fluid bolus with 5 cmH2O of PEEP. The patients then were categorized into fluid responder (increased in SV ≥15% after fluid bolus) and fluid non-responder (increased in SV <15% after fluid bolus). Percent changes in corrected flow time, peak velocity, stroke volume and cardiac output (%ΔFTc, %ΔPV, %ΔSV and %ΔCO) following increased in PEEP from 5 to 15 cmH2O were measured and analyzed.

Results: There were 11 fluid responders and 9 fluid non-responders. Before fluid infusion, %ΔPV, %ΔSV, %ΔCO were significantly higher in fluid responder than fluid non-responders (10.7 vs. 1.3%, 19.2 vs. 8.1%, and 23.6 vs. 2.9%, respectively). There were significant correlation between these parameters and changes in SV after fluid bolus (RF = 0.37, 0.26, 0.65). Using ROC analysis, we found that %ΔCO ≥15.6% can predict fluid responsiveness with a sensitivity of 82% and specificity of 89% (AUC 0.88, 95% CI 0.72-1.00, p = 0.004).

Conclusions: Changes in EDM-derived hemodynamic parameters after increased in PEEP can predict fluid responsiveness in patients with septic shock.
ASSESSMENTS AND RE-EVALUATION FOR LONG-TERM OXYGEN THERAPY (LTOT) IN A CONJOINT CLINIC

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Background: Oxygen therapy is commonly prescribed to patients, but subsequent monitoring may be suboptimal.

Aims: To evaluate the usefulness of an Oxygen Therapy Assessment Clinic (OTAC) this is run by respiratory nurses and physiotherapists.

Methods: A prospective study in patients who were referred to OTAC was carried out from October 2014 to October 2015. The patients are either on oxygen therapy or referred for LTOT consideration. Transcutaneous carbon dioxide (TCO2), pulse oximetry saturation level (SpO2), dyspnea level (visual analogue scale: 1-10) and perceived exertion level ( Borg scale 6-20) are measured. The following would also be measured if necessary: (a) arterial blood gas or venous blood for pH and HCO3; (b) Exercise test with 6-minute walk by physiotherapist; (c) Nocturnal SpO2 saturation. Pre-and post-educational questionnaire assessments were carried out with at least more than one month's interval.

Results: Thirty-two subjects (mean age 72) were included with 68.7% were already on LTOT. 59.4% were COPD and 50.1% could manage one flight of stairs while 15.6% couldn’t because of dyspnea or wheelchair bound. The initial dyspnea level (1-3) and perceived exertion level (6-11) were mild for 46.9% and 50% respectively. Oxygen concentration was adjusted for 96.9%: titrated up in 41.9% and down in 45%. Domiciliary oxygen was eventually tailed off in 21.9%. Overnight SpO2 saturation. Pre-and post-educational questionnaire assessments were carried out with at least more than one month's interval.

Conclusion: Home oxygen therapy was often inappropriately used with inadequate monitoring and reassessment after initial prescription. OTAC can be a useful follow-up model in these patients.

OUTCOME PREDICTORS FOR PATIENTS WITH CANDIDEMIA RECEIVING PROLONGED MECHANICAL VENTILATION

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Background and Aims: Recent years have seen advances in critical care, improved prophylactic antifungal agents, mortality and morbidity due to fungal infection remain concerns in ICU (Intensive Care Unit). Prior research has reported role of risk factor identification, molecular diagnosis and new anti-fungal agents, but there are mixed results and gaps in early diagnosis. The aim of this study is to clarify the epidemiology and outcome predictors for candidemia in patients undergoing prolonged mechanical ventilation (PMV).

Methods: Information on 40 candidemia patients undergoing PMV was recorded between 2001 and 2012. The characteristics and outcomes of these patients were determined through a retrospective chart review and evaluated using Student’s t test, chi-square test, and Fisher’s exact test.

Results: Of the 1238 candidemia patients with mechanical ventilation in medical ICU, overall mortality rate was 71%. Data from 40 PMV patients are presented, and a comparison is made between survival and non-survival groups. Mortality rate was 70% which did not reach a statistically significant difference. Patients who developed ARDS before candidemia exhibited higher mortality (8.3% vs. 53.6 %, p =0.02). Sepsis-related ARDS contributes to increased mortality in patients with I-FI (N=12, 80%). High dose corticosteroid (prednisolone 20mg or more for at least 14 days) increase the risk of poor patient outcome. (N=16, 57.1% vs. N=2, 16.7%, P=0.02).

Conclusions: This study investigated the outcome of candidemia in patients undergoing PMV. PMV after sepsis-related ARDS and high-dose corticosteroid use were major risk factors for poor patient outcome. Additional prospective studies are required to identify these risk factors through laboratory method for ensuring timely treatment.
sepsis with fungus colonization in mechanical ventilated patients still be doubted. The study is to identify effectiveness of pre-emptive antifungal agents in patients with severe sepsis and fungus colonization.

Methods: Severe sepsis patients with positive fungus culture and PCR (sputum, urine) in Linkou Chang-Gung Memorial Hospital medical ICU between 2015 and 2017 were randomized into therapeutic (Anidulafungin 100mg /10 days) and control group. The characteristics and outcomes were determined through a prospective controlled study and evaluated using Student’s t test, Chi-square test, and Fisher’s exact test.

Results: Of the 244 severe sepsis patients in medical ICU, 219 cases were excluded due to immunocompromised status and systemic candidiasis. The remaining 25 patients were randomized into therapeutic group (n=12) and control group (n=13). No statistical differences existed between two groups according to underlying conditions, risk factors and disease severity scores. There were no statistical differences in ICU mortality (46.2% vs. 41.7%, p=0.84), hospital mortality (54% vs. 50%, p=0.82), ICU length of stay (21.5 ±9.3 vs. 22.2 ±11.8 ±p=0.89) and ventilator days (20.8 ±11.8 vs. 33.7 ±22.2, p=0.311), but the lactate level decreased after treatment. (13.4 mg/dl vs. 17.8 mg/dl, p=0.04%). Anidulafungin use might decrease fungemia episode (n=2, 15.4 % vs. n=0, p=0.16) and eliminate sputum colonization (n=1, 7.7% vs. n=5, 41.7%, p=0.047) despite a statistically inadequate number of patients in each group.

Conclusions: Although the outcomes didn’t change, the decreasing lactate level and fungemia episodes may suggest some benefit of anidulafungin in mechanical ventilated patients with severe sepsis. Future research is necessary to determine the subgroups who might benefit from preemptive antifungal treatments.

AP101
MONOCYTE CHEMOATTRACTION PROTEIN-1, A POTENTIAL BIOMARKER OF MULTIORGAN FAILURE AND MORTALITY IN VENTILATOR-ASSOCIATED PNEUMONIA
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Background and Aims: Ventilator-associated pneumonia (VAP) increases patient mortality and medical expenditure, and a real-time and reliable method for the rapid diagnosis of VAP may help in reducing the fatal complications. Monocyte chemoattractant protein-1 (MCP-1) plays a role in the pathogenesis of lung inflammation and infection. Therefore, the amount of MCP-1 was assessed and correlated with the clinical course of VAP patients.

Methods: This retrospective observational study recruited 45 healthy volunteers, 12 non-VAP subjects, and 30 VAP patients. The diagnostic criteria for VAP were based on the American Thoracic Society guidelines, and the level of plasma MCP-1 was determined by the ELISA.

Results: Plasma MCP-1 concentration was significantly elevated in the acute stage of VAP patients as compared with that of control (p < 0.0001) and patients non- VAP groups (p = 0.0006). Subsequently, it decreased significantly following antibiotic treatment. Moreover, plasma MCP-1 concentration was positively correlated with the indexes of pulmonary dysfunction, including lung injury score (p = 0.02) and oxygen index (p = 0.02). For the patients of VAP progressing to ARDS, plasma MCP-1 concentration was significantly raised than that of the patients of VAP without ARDS (p = 0.04). On the other hand, plasma MCP-1 level tertiles differed significantly in survival within 28 days of VAP onset (p < 0.0001). As well, plasma MCP-1 concentration was highly correlated among organ failure scores, including SAPS II (p < 0.0001), SOFA (p < 0.0001) and ODINO (p < 0.0001). Our result also demonstrated that plasma MCP-1 was an excellent marker for recognizing VAP when the cutoff level was set to 347.18 ng/ml (AUC = 0.936, 95% CI = 0.863 to 0.977).

Conclusions: MCP-1 not only could be a biological marker related to pulmonary dysfunction, organ failure, and mortality in patient with VAP, and, but could employed to recognize VAP.

AP102
ASSOCIATION OF LUNG ULTRASOUND SCORE WITH LENGTH-OF-STAY AND VENTILATION DAYS IN MECHANICALLY VENTILATED PATIENTS
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Background and Aim: Lung ultrasound is an important part of the evaluation of critically ill patients. It has been shown to predict recruitability in acute respiratory distress syndrome. However, little is known about the application of lung ultrasound in predicting resource utilization (ventilation days and length-of-stay) in mechanically ventilated patients.

AIM: We aimed to investigate the association of lung ultrasound score with ICU/hospital length-of-stay, and with ventilator days.

Methods: Observational study of mechanically ventilated patients admitted to the medical intensive care unit (ICU) of a tertiary hospital (National University Hospital, Singapore) in 2015 and 2016. Only the first ICU admissions of these patients were studied. Lung ultrasound was done at six points per hemithorax and scored according to Soummner (Crit Care Med 2012): normal aeration = 0; multiple, well-defined B lines =1; multiple coalescent B lines = 2; lung consolidation = 3. The Lung Ultrasound (LUS) score was calculated as the sum of points (score range 0-36). We analysed the association of log-transformed LUS score with ICU/hospital length-of-stay, and mechanical ventilation days was analysed using linear regression, adjusted for age and Acute Physiology and Chronic Health Evaluation (APACHE) II score.

Results: 247 patients were included (age 62.0 ± 16.2 years; 89 female [36.0%]; APACHE II 29.7 ± 7.9; 88 sepsis diagnosis [35.6%]). Median (IQR) ICU, hospital length-of-stay and ventilation days were 6 (4-10), 16 (9-37) and 4 (3-8) respectively. LUS score was not associated with log-transformed ICU length-of-stay (β=0.007, 95% CI -0.007 to 0.021), log-transformed hospital length-of-stay (β=0.009, 95% CI -0.009 to 0.028) and log-transformed mechanical ventilation days (β=0.011, 95% CI -0.005 to 0.028), adjusted for age and Acute Physiology and Chronic Health Evaluation (APACHE) II score.

Conclusion: LUS score was not associated with ICU/hospital length-of-stay or ventilation days.
EFFECTIVENESS OF ROUNDS MADE BY RESPIRATION SUPPORT TEAMS ON THE HEAD ELEVATION RATE OF VENTILATED PATIENTS: A RETROSPECTIVE COHORT STUDY

Background and Aims: In Japan, about 60% of the hospitals have respiratory support team (RST). It is reported that lectures to nurses increase head elevation rate of intubated patients. However, we do not know the effect of RST round. The aims of this study is to assess whether head elevation rate of ventilated patient increases with RST round in Japanese tertiary hospital.

Methods: We performed a retrospective chart review of patients undergoing RST round between July 2012 and March 2015. The primary outcome was head elevation ratio.

Results: After selection, 297 patients were enrolled and divided into three groups: year 2012 (between July 2012 and March 2013), year 2013 (between April 2013 and March 2014) and year 2014 (between April 2014 and March 2015). In total, 75, 100 and 122 patients were included in year 2012, 2013 and 2014, respectively. Head elevation rate was achieved in 45 (60%), 65 (65%) and 101 (83%) patients in year 2012, 2013 and 2014, respectively. Heat elevation rate of year 2014 was statistically significant compared with that of year 2012 (risk ratio 1.38, 95% confidence interval 1.12 to 1.69, p-value <0.01). Multivariable analysis showed statistically significant difference of year 2014 (vs. year 2012, odds ratio 3.73, 95% confidence interval 1.81 to 7.68, p-value <0.01). ICU patients (vs. general ward, odds ratio 6.65, 95% CI 2.23 to 19.8, p-value <0.01) and ventilated duration more than 8 days (vs. less than 7 days, odds ratio 2.19, 95% CI 1.09 to 4.37, p-value = 0.027).

Conclusions: Head elevation rate of ventilated patients may improve with continuous RST round in Japanese tertiary hospital.

OUTCOME OF PROTOCOLIZED WEANING FOR PROLONGED MECHANICAL VENTILATION IN A RESPIRATORY CARE CENTER: IMPLICATION TO THE REAL-WORLD PRACTICE OF THE INTEGRATED DELIVERY SYSTEM IN TAIWAN

Background and Aim: The integrated delivery system (IDS) for managing patients with prolonged mechanical ventilation (PMV) had imposed time pressure to the healthcare system. Efficient weaning required a refined protocolized weaning process.

Methods: We retrospectively analyzed the records of tracheostomy patients with PMV treated in the Respiratory Care Center (RCC) of a medical center in Taiwan from July 2014 to December 2016. The three protocols included direct liberation (Step D), stepwised weaning (Step S) and slow/CPAP weaning (Step C) methods. The care team chose the sequence for protocolized weaning based on clinical judgement.

Results: Of the 640 admissions to the RCC during the 30-months period, 118 (18.4%) were extubated without re-intubation, 497 (77.7%) were weaned successfully and 424 (66.3%) had received protocolized weaning. These 424 patients had an average age of 69.3 ± 16.9 years, and 283 (66.7%) were male. The overall weaning success rate for these 424 patients was 78% (65.6%). The success rates, based on the initial protocol after tracheostomy, were 83.1%, 58.7%, and 34.8% for Steps D(n=142), S(n=259), and C(n=23), respectively. For those who failed initial Step D (n=15), the weaning success rate for Step S was 46.7%; for those who failed Step S (n=46), the success rate for Step C was 28.3%.

Conclusion: This study shows that the Steps D-S-C sequential weaning process based on clinical judgement provided optimization of weaning outcome in a real-world practice of weaning in the Integrated Delivery System.

THE EFFECT OF INTRODUCING HOME NPPV IN PATIENTS FOLLOWING ACUTE HYPERCAPNIC RESPIRATORY FAILURE DUE TO CHRONIC RESPIRATORY DISORDER

Background and Aims: Patients with chronic respiratory disorder and hypercapnic respiratory failure have a worse prognosis. The benefit of the home noninvasive positive pressure ventilation (NPPV) has been reported to prevent readmission not only in COPD but other disease including restrictive respiratory disorders. However, the benefit of introducing NPPV in acute phase is not well understood. We evaluated the effect of introducing home NPPV use in patients following acute hypercapnic respiratory failure due to chronic respiratory disorder.

Methods: This retrospective study comprised 47 patients who had treated with NPPV for acute hypercapnic respiratory failure due to chronic respiratory disorder and still had PaCO2 above 45mmHg at the start of weaning process. Comparing the patients with and without home NPPV after discharge, we investigated their clinical outcomes.

Results: 55% of the included patient had restrictive disease, 28% of a total patient had introduced home NPPV following the admission and 30% had home NPPV treatment previously to admission. Compared to patients without home NPPV, home NPPV group demonstrated superior survival although it is not statistically significant (median 206 days (IOR; 60-804) vs 25 (13-352), p=12). They also showed comparative survival to patients who had previous treated with home NPPV (206 days (60-804) vs 341 (33-749), p=0.32).

Conclusions: Home NPPV following acute hypercapnic respiratory failure due to chronic respiratory disorder could improve survival.

THE EFFECTIVENESS OF ROUNDS MADE BY RESPIRATION SUPPORT TEAMS ON THE HEAD ELEVATION RATE OF VENTILATED PATIENTS: A RETROSPECTIVE COHORT STUDY

Background and Aims: In Japan, about 60% of the hospitals have respiratory support team (RST). It is reported that lectures to nurses increase head elevation rate of intubated patients. However, we do not know the effect of RST round. The aims of this study is to assess whether head elevation rate of ventilated patient increases with RST round in Japanese tertiary hospital.

Methods: We performed a retrospective chart review of patients undergoing RST round between July 2012 and March 2015. The primary outcome was head elevation ratio.

Results: After selection, 297 patients were enrolled and divided into three groups: year 2012 (between July 2012 and March 2013), year 2013 (between April 2013 and March 2014) and year 2014 (between April 2014 and March 2015). In total, 75, 100 and 122 patients were included in year 2012, 2013 and 2014, respectively. Head elevation rate was achieved in 45 (60%), 65 (65%) and 101 (83%) patients in year 2012, 2013 and 2014, respectively. Heat elevation rate of year 2014 was statistically significant compared with that of year 2012 (risk ratio 1.38, 95% confidence interval 1.12 to 1.69, p-value <0.01). Multivariable analysis showed statistically significant difference of year 2014 (vs. year 2012, odds ratio 3.73, 95% confidence interval 1.81 to 7.68, p-value <0.01). ICU patients (vs. general ward, odds ratio 6.65, 95% CI 2.23 to 19.8, p-value <0.01) and ventilated duration more than 8 days (vs. less than 7 days, odds ratio 2.19, 95% CI 1.09 to 4.37, p-value = 0.027).

Conclusions: Head elevation rate of ventilated patients may improve with continuous RST round in Japanese tertiary hospital.

OBSTRUCTIVE SLEEP APNEA PREVALENCE AND EXTUBATION OUTCOME IN MEDICAL ICU

Background and Aim: Extubation failure causes prolonged intubation and deleterious consequences. Many factors may contribute to
extubation failure including age, disease severity, and cough strength. Obstructive sleep apnea also has been shown to increase risk of extubation failure. Unfortunately, the presence of obstructive sleep apnea has been overlooked in ICU setting. Screening for OSA with STOP-Bang questionnaire is practically easy and may be recommended in ICU setting.

Aim: To determine the prevalence of obstructive sleep apnea among medical ICU patients and its association with extubation failure.

Methods: Due to no reliable diagnostic tool for diagnosis of OSA in ICU setting and difficulty with conducting polysomnography in ICU setting, STOP-Bang questionnaire was utilized as a screening tool in our study. Obstructive sleep apnea was suspected when STOP-Bang was three or more. Prevalence of OSA was our primary outcome. Secondary outcome was relationship of OSA and extubation failure.

Results: Twenty-nine planned extubation medical ICU patients were enrolled. They were intubated for acute respiratory failure primarily according to pneumonia (58.62%) and sepsis (34.48%). Fifteen patients had three or more of STOP-Bang score so prevalence of OSA was high at 51.72% (Figure 1). STOP-Bang score data of the patients who developed extubation failure are shown in Figure 2. Patients with OSA trended to develop more extubation failure (53.33% VS 28.57%) but the difference did not achieve statistically significant difference (p=0.176).

Conclusion: Obstructive sleep apnea is common and it is overlooked among medical ICU patients. STOP-Bang is a reasonable screening tool for OSA in this setting. The presence of OSA may contribute to extubation failure.

Figure 1. Prevalence of Obstructive sleep apnea among medical ICU patients

Figure 2. STOP-BANG Score and Extubation Failure

THE PREDICTORS OF SURVIVAL OF PNEUMOCYSTIS JIROVECII PNEUMONIA IN NON-HIV CRITICALLY ILL PATIENTS WITH RESPIRATORY FAILURE
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Background and Aims: Pneumocystis jirovecii pneumonia (PCP) in non-HIV patients is more fatal than HIV patients, and typically present with an abrupt onset of respiratory insufficiency. To aim of this study was to evaluate the outcomes and predictors of mortality in PCP in non-HIV patients with respiratory failure.

Methods: This retrospective study enrolled 81 non-HIV patients who were diagnosed and treated PCP with respiratory failure requiring the medical intensive care unit (ICU) care from January, 1, 2013 to December, 12, 2015. The patients were diagnosed through positive polymerase chain reaction (PCR, nested PCR to detection of 260bp, Thermalcycler S1000 (BIO-RAD, USA)) and typical clinical symptoms and radiological findings. PCP PCR was followed up weekly for check the negative conversion.

Results: The ICU overall survival rate of PCP was 35.8% (29/81). Seventy-four patients (91.3%) required mechanical ventilation, and six patients (7.4%) required high-flow nasal oxygen treatment. In total, PCP PCR negative conversion rate is 70.5% (55/81) with a median duration of 10 (7.00-14.00) days. In univariate analysis, APACHE II score (P=0.001), renal failure requiring renal replacement therapy (P=0.04), PCP PCR negative conversion (P=0.003), and PaO2/FiO2 ratio within initial 24 hours (P<0.001) were related to mortality of PCP patients. In multivariate analysis, PCP PCR negative conversion (adjusted OR 7.424; 95% CI 1.957-28.160, p=0.003) and PaO2/FiO2 ratio within initial 24 hours (adjusted OR 0.987; 95% CI 0.979-0.996, p=0.003) were associated with prognosis of PCP in non-HIV patients with respiratory failure.

Conclusions: PCP PCR negative conversion and PaO2/FiO2 ratio within initial 24 hours are prognostic factor of severe PCP in non-HIV patients with respiratory failure. Furthermore, following up PCP PCR negative conversion or not may be predictive factor to failure of initial anti-pneumocystis medication. In conclusion, early diagnosis and prompt treatment are significant to manage with PCP in non-HIV patients.

THE FACTORS RELATED WITH LUNG FUNCTION RECOVERY AT THE FIRST YEAR OF LUNG TRANSPLANTATION
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Background: Post-operative pulmonary function test is one of the most important prognostic factors, commonly used to estimate the graft function or detect graft rejection in early stage. The purpose of this study was to figure out the factors which effect on the FEV1 at the first year of lung transplantation.

Method: We retrospectively reviewed the electric medical records of the lung transplantation patients in our institution between October 2012 and December 2015. The patients who survived for more than one year and performed pulmonary function test more than three times were enrolled for this study. The patients were divided into two groups according as 1 year post-operative FEV1 is more or less than 80%.
operative hospitalization days (median: 4 P P
showed pH of 7.06, pO2=88mmHg, pCO2=89.6mmHg, HCO3=24.3meq/L,
ylline, and antibiotics for infection suspected. Arterial blood gas analysis
non rebreathing mask 10 L/m, intravenous methylprednisolone, aminoph-
ulisation could not be given as the patient was very agitated. We used

Background: Hypercapnic respiratory failure is an advanced compli-
cation of the severe asthma attack that can occur during pregnancy. The
outcome management of respiratory failure in pregnant women is prevent-
ing mother and baby mortalities.

Aims: To manage hypercapnic respiratory failure by using inhaled
long-acting muscarinic antagonists (LAMA).

Methods: A-31-year-old pregnant woman, 28 weeks gestational, with
uncontrolled asthma, was admitted with severe breathlessness. The
patient was disoriented, respiratory rate 36/min, pulse of 136/min, blood
pressure (BP) was 144/79mmHg, pulse oxygen saturation (SpO2) was
91%, and fetal heart rate was 164 pulse/min. Her breath sounds were
wheezes and fi

Results: The patient was conscious after 3 hours observation, RR of
29/min, pulse of 144/min, BP was 120/70mmHg, SpO2 was 96%, and
fetal heart rate was 178pulse/min. Her breath sounds were wheezes and fine crackles at bilateral lung bases. Unfortunately, the rebi-

Conclusions: Immediate postoperative status may be related with
recovery of lung function after lung transplantation.

Keywords: Pulmonary function test, Lung transplantation

CASE REPORT: ADD-ON TIOTROPIUM BROMIDE FOR
HYPERCAPNIC RESPIRATORY FAILURE SECONDARY OF
ASTHMA ATTACK IN PREGNANCY
NANCY SOVIRA

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Background: Hypercapnic respiratory failure is an advanced compli-
cation of the severe asthma attack that can occur during pregnancy. The
outcome management of respiratory failure in pregnant women is prevent-
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Conclusions: Immediate postoperative status may be related with
recovery of lung function after lung transplantation.

Keywords: Pulmonary function test, Lung transplantation

PREDICTORS FOR LUNG COLLAPSE AFTER PEEP
DECREMENT IN RECOVERING ARDS PATIENTS,
PRELIMINARY DATA
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PREDICTING SHORT-TERM PROGNOSIS OF PRIMARY
SPONTANEOUS PNEUMOTHORAX USING CHEST
RADIOGRAPHS
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Iizuka Hospital, Iizuka City, Japan

Background: There are some guidelines for the management of spon-
taneous pneumothorax in each country. In the Japanese guidelin,
intrathoracic pressure measurement has been recommended. We hypothesized that lung movement during respiration on chest X-rays may be useful for predicting the prognosis of primary spontaneous pneumothorax (PSP).

**Aims:** To investigate the utility of respiratory change of lung areas on chest X-ray for predicting the short-term prognosis of PSP.

**Methods:** We retrospectively reviewed 60 patients with PSP (78 pneumothoraces) who underwent both expiratory and inspiratory chest X-rays at Iizuka Hospital between April 2011 and August 2016. The lung and pneumothorax areas on expiratory and inspiratory chest X-rays were measured using an image processing software “Image J”. We examined the relationships between the respiratory changes of those measured areas and the outcome on the third day of the initial treatment.

**Results:** Seventy-eight episodes of PSP were included (63 male and 15 female, mean age was 20.7 year-old). On the third day of the initial treatment, 51 pneumothoraces improved (success group) and 27 pneumothoraces did not (failure group). In univariate analysis, “respiratory change of collapse rate”(1.4±0.7 vs 10.1±4.0, p=0.01) and “ratio of pneumothorax area at inspiration to that at expiration”(1.26±0.18 vs 2.0±0.17, p=0.02) showed statistically significant difference between the two groups. Whereas, there were no significant difference in each AUC (0.657 and 0.668) of the ROC analysis (p=0.76).

**Conclusions:** We conclude that the respiratory change of lung and pneumothorax area on chest X-rays may be useful in the prediction of the third day outcome in the initial treatment of PSP.

**URINOThORAX: AN UNCOMMON CAUSE OF SEVERE RESPIRATORY DISTRESS**

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**Background and Aims:** Urinothorax is a rare condition defined by the accumulation of urine within the pleural cavity, and is usually a result of obstructive uropathy or injury to the urinary system (including iatrogenic post-surgical trauma). The diagnosis of urinothorax depends on the clinical suspicion of transudative pleural effusion especially following surgical procedure.

**Methods** (case report): We present the case of a 52 year-old, Taiwanese woman with history of vaginal hysterectomy one month ago due to development of uterine myoma that presented with cough and dyspnea. Initial chest film showed right-sided pleural effusion, and insertion of an intercostal drainage tube prevented the patient from going in to respiratory failure was done. CT of abdomen and pelvic cavity showed evidence of elevation of the right kidney, minimal fat stranding of the mesentery of abdominal peritoneal cavity, right hydrocele, right hydrome-phrosis, and mild wall thickening of the distal third of right ureter. Right diagnostic ureterorenoscopy revealed disrupted ureter over the lower third portion leading into the peritoneum, with appendix and small intestines seen. Ureteral iatrogenic injury was suspected.

**Results:** Right percutaneous nephrostomy catheter placement was done initially, and reconstruction of injured ureter was done later.

**Conclusions:** The physicians should include urinothorax in the differential diagnosis of transudative pleural effusion, especially in patients underwent abdominal or pelvic surgical procedures.

**ROLE OF MitoCHONDRIAL FORMYLATED PePTIDES IN ALVEOLAR FLUID IMBALANCE IN ACUTE LUNG INJURY**

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**Background and Aims:** Acute respiratory distress syndrome (ARDS) is a critical condition characterized by alveolar fluid accumulation resulting from disruption of the alveolar-capillary barrier and impairment of alveolar fluid clearance (AFC). Current study aimed to investigate the role of mitochondrial formylated peptides (MFP) in ARDS/ALI related alveolar fluid imbalance.

**Methods:** Bronchoalveolar lavage fluid (BALF) levels of NADH-ubiquinone oxidoreductase chain 1 (ND-1) which was a typical MFP and BALF and serum levels of albumin in ARDS patients and healthy volunteers were quantified by enzyme linked immunosorbent assay (ELISA). The ratio of BALF albumin to serum albumin (B/S) was regarded as the positive indicator of capillary permeability. Meanwhile, acute lung injury mouse model was induced by LPS or N-Formyl-Met-Leu-Phe (fMLP, synthetic MFP1 or combination of them, and mouse alveolar fluid clearance rate (AFC) was measured with AlexaFluor488-labeled BSA.

**Results:** BALF ND-1 levels in ARDS patients were much higher than those in healthy volunteers, B/S ratio in ARDS patients was increased when compared with healthy volunteers. Correlation analysis showed that BALF levels of ND-1 were positively related to B/S. In the animal study, LPS alone but not fMLP alone decreased mouse AFC, and fMLP significantly enhanced LPS-induced AFC impairment.
Abstracts

AP114

SODIUM TANSSHINONE IIA SULFONATE ATTENUATES LONG-TERM BEHAVIORAL ALTERATIONS IN MICE INJECTED WITH LIPOPOLYSACCHARIDE VIA INHIBITION OF NLRP3 INFLAMMASOME ACTIVATION

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Background and Aims: Central nervous system might be affected by lipopolysaccharide (LPS) through neuroinflammation, which subsequently leads to brain damage and dysfunction. Nod-like receptor pyrin domain-containing protein 3 (NLRP3) inflammasome activation contributes to long-term behavioral alterations in LPS-exposed mice. In this study, we explored whether sodium tanshinone IIA sulfonate (STS) might attenuate long-term behavioral alterations in mice injected with LPS and the underlying mechanisms.

Methods: Before injected intraperitoneally with LPS (5 mg/kg), the 8-week-old male C57BL/6 mice were treated with saline, and STS (10 mg/kg), respectively, by gavage, once per day for two weeks. At different time points after LPS injection, we assessed locomotor function with a 24-point neurologic deficit scoring system and the rotarod test, and assessed emotional abnormality (anhedonia and behavioral despair) with the tail suspension test, forced swim test, and sucrose preference test. We also assessed protein expression of NLRP3, apoptosis-associated speck-like protein (ASC), caspase-1 p10, and indoleamine 2,3-dioxygenase (IDO) in hippocampus by Western blotting; measured levels of interleukin (IL)-1β, IL-18, and tumor necrosis factor α (TNFα) in hippocampus by ELISA.

Results: We found that LPS-injected mice displayed long-term depression-like behaviors; elevated expression of NLRP3, ASC, and caspase-1 p10; increased levels of IL-1β, IL-18, and TNFα; increased levels of IDO. STS attenuated long-term depression-like behaviors, and downregulated levels of NLRP3, ASC, caspase-1 p10, IL-1β, IL-18, TNFα, and IDO.

Conclusions: These results indicated that STS might become a promising therapeutic candidate for attenuating long-term depression-like behaviors in LPS-exposed mice.

AP115

PREVENTIVE EFFECTS OF CARNOSINE, AN ANTIOXIDANT PEPTIDE ON LIPOPOLYSACCHARIDE-INDUCED LUNG INJURY

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Background and Aim: Acute respiratory distress syndrome (ARDS) is a potentially devastating form of acute lung injury, which involves neutrophil inflammation and pulmonary cell death. Reactive oxygen species (ROS) play important roles in ARDS development. New compounds for inhibiting the onset and progression of ARDS are required. Carnosine (β-alanyl-L-histidine) is a small di-peptide with numerous activities, including antioxidant effects, metal chelation and the inhibition of protein carbonylation and glycoxidation. We have examined the preventive effects of carnosine on tissue injury, edema and inflammation in a murine model for ARDS.

Methods: The severity of the lung injury was assessed based on vascular permeability and histopathological evaluation. The level of ROS was determined by in vivo imaging analysis.

Results: Oral administration of carnosine suppressed lipopolysaccharide (LPS)-induced vascular permeability, tissue injury and inflammation in the lung. In vivo imaging analysis revealed that LPS administration increased the level of ROS and that this increase was inhibited by carnosine treatment. Carnosine also suppressed LPS-induced neutrophilic inflammation (evaluated by activation of myeloperoxidase in the lung and increased extracellular DNA in bronchoalveolar lavage fluid). Furthermore, carnosine treatment suppressed the LPS-induced endoplasmic reticulum stress response in vivo.

Conclusion: These results suggest that the oral administration of carnosine suppresses LPS-induced lung injury via carnosine’s ROS-reducing activity. Therefore, carnosine may be beneficial for suppressing the onset and progression of ARDS.

AP116

THE CHARACTER OF HBO THERAPY ON BLEOMYCIN INDUCED LUNG FIBROSIS ANIMAL MODEL

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Background and Aim of Study: A massive inflammations create a hypoxia environment around injured tissues and cause fibrosis for unknown reason. We hypothesized hyperbaric oxygen (HBO) therapy may attenuate fibrotic response in lung injury disease.

Methods: Set up an animal model of fibrosis by installation the chemotherapy drug - bleomycin into the trachea of mice. Determine the effect of hyperbaric oxygen therapy on bleomycin induced lung fibrosis animal model.

Results: The early treatment group, which were introduced HBO therapy on the first day to the fifth day after bleomycin treatment, has no significant improvement in the results of pathology or cytology. On the contrary, in the late treatment group, which were introduced HBO therapy on day 7 to day 11 after bleomycin treatment, inflammatory cells, mediators in the airways and parenchyma were decreased significantly. The collagen production was also deceased both in the airway and lung tissue, and the healing process even lasted longer until day 21.

Conclusion: On the mice model of Bleomycin induced lung fibrosis, HBO therapy can reduce inflammation and fibrosis on the phase of proliferative stage and the healing effect can last long.

AP117

EXPRESSION OF LACTOFERRIN IN PICHIA PASTORIS INDUCTION BY GLUCOSE IN A MODIFIED G1 PROMOTER SYSTEM AND ITS ANTIMICROBIAL AND ANTITUMOR ACTIVITIES

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Background and Aims: Lactoferrin (LF) is one of the most abundant bioactive iron-binding glycoproteins in milk and it has been exhibited extensive antimicrobial and anticancer activities. But LF’s lager molecular...
weight, the antimicrobial fragments is obstructed in contact with target. Hydrolyzing of LF into small pieces peptides, could enhance antimicrobial activity of lactoferrin hydrolyzate (LFH).

**Methods:** In this study, a modified yeast expression system using G1 promoter (P_{G1}) to drive the pLF gene in Pichia Pastoris was constructed. The expression of pLF was induced by glucose and then the expressed pLF was secreted into the culture media.

**Results:** Current results demonstrated that near 4286 mg/l of pLF was produced by G1 promoter-glucose induction system, higher than 87 mg/l by conventional methanol induction system. The antibacterial activities of pLF against Escherichia coli, Staphylococcus aureus and Candida albicans were subsequently confirmed in this study. Further investigation will be conducted by characterizing the functional short peptides derived from the proteolysis of pLF. Furthermore, 1 mg/L lactoferrin was demonstrated to have inhibitory effect on the growth of several cancer cell line, including human lung cancer cell (A549), human breast cancer cell (MDA-MB-231) and human liver cancer cell (Hep3B).

**Conclusions:** Conclusively, an efficient platform for the production of pLF is established in present study. In perspective, the production of enough pLF with multiple antibacterial activities may provide a novel agent for SDD (selective decontamination of the digestive tract) in critical care medicine.

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**Tuberculosis 1**

**INCIDENCE OF LATENT TUBERCULOSIS INFECTION (LTBI) AMONG HIGH RISK HEALTHCARE WORKERS AT A TERTIARY REFERRAL HOSPITAL IN SOUTH KOREA**

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**Aim:** The aim of the study is to estimate incidence of LTBI among high risk health care workers at a tertiary referral hospital in South Korea.

**Methods:** Records of annual LTBI screening of high risk healthcare workers with frequent exposure to active tuberculosis patients from 2014 to 2016 were retrospectively reviewed. Interferon-γ release assay (IGRA) was used for LTBI screening. Only staffs with initial negative IGRA results were included in the cohort.

**Results:** Total 170 staffs were included and total follow-up was 245 person-years. 11 cases of new LTBI defined as whose IGRA result converted to positive were identified. Incidence rate was 4.49% (person-year).

Departments were classified according to quality of tuberculosis exposure (inpatient/outpatient, usual/during invasive procedure) → 1 Inpatient, usual exposure (pulmonology ward), 2 Outpatient, usual exposure (pulmonology outpatient clinic), 3 Inpatient, exposure during endotracheal intubation (intensive care unit, emergency room), 4 Outpatient, exposure during bronchoscopy (bronchoscopy room), and 5 Exposure to specimens with tuberculosis (laboratory facilities). Contacts with active tuberculosis of co-worker or families living together were surveyed as a confounding factor. In a generalized estimating equation model, working in the laboratory facilities was a significant risk factor for LTBI, when compared with intensive care unit or emergency room (adjusted OR=4.96, p=0.003). Age was also a risk factor for LTBI (adjusted OR=1.08, p= 0.013).

**Conclusions:** Annual incidence of LTBI was 4.49%. Working in the laboratory facilities, old age were significant risk factors for LTBI.

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**PREVALENCE AND RISK FACTORS FOR LATENT TUBERCULOSIS INFECTION AMONG THE HEALTHCARE WORKERS OF RIZAL MEDICAL CENTER**

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**Background and Aim:** The high rate of latent TB infection (LTBI) is one of the factors that make it difficult to achieve global control and eliminate TB. Transmission of M. tuberculosis from patients and healthcare workers (HCW) alike is the greatest. Detecting LTBI through tuberculin skin test (TST) is thus pivotal.

This study aims to determine the prevalence and risk factors for LTBI among HCWs at Rizal Medical Center (RMC), a tertiary government hospital in Pasig City, Philippines.

**Methods:** Two hundred eighty-eight (288) HCWs were included in the study. Each signed informed consent and filled up a questionnaire about LTBI risk factors. BCG vaccine status was assessed through BCG scar inspection. Each underwent chest x-ray and TST administration. The finding of > 8 mm induration indicates positive TST. Statistical analyses were performed using Stata Version 12.

**Results:** Of the 288 participants, 181 (79%) were positive for TST with a mean area of induration diameter of 14.3 mm. The odds of having positive TST among those who employed for 2 to 5 years was three-fold more (OR=3.1) than the odds among those who are employed for less than a year. Age, duration of employment and job description showed no association with TST positivity. The odds of TST positivity among participants with BCG vaccination (OR=10.0; 95% CI: 4.6, 21.7) was shown to be significantly higher (p-value = 0.044) than among those without vaccination (OR=3.4; 95% CI: 1.7, 6.9).

**Conclusion:** This study revealed that the prevalence of LTBI among Filippino HCWs determined through TST was high: 79% of the subjects, a finding seen in related studies. Auxiliary staff and ordelies were shown to have the highest odds of TST positivity. Also, a positive TST result was found out to have an association with the receipt of BCG vaccination, exemplifying TST cross-reactivity with BCG vaccination.

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**CHARACTERISTICS OF CLINICALLY DIAGNOSED DRUG SENSITIVE TB PATIENTS IN A HIGH TB PREVALENCE, LOW HIV INCIDENCE URBAN COMMUNITY**

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*This is part of the UK-MRC Philippine PCHRD Joint Newton Agham TB Project*

**Background and Aims:** The Philippines is a high-TB burden country with a high proportion (64%) of clinically diagnosed (CD) cases in 2016. This study aimed to determine the profile of the CD drug sensitive TB patients and compare them with the bacteriologically confirmed (BC). Method: A review of drug-sensitive tuberculosis (DS) cases randomly selected from a DOTS facility in Cavite with comparative analysis between BC and CD. FGDs were conducted and an expert panel using a modified Delphi technique reviewed the CD's chest x-ray results.
Results: 73% of the 133 cases randomly selected were CD which had higher incidence of malaise, shortness of breath and higher proportion that started treatment beyond one week of sputum examination compared to BC (pvalues <0.05). Only 27.8% received prior antibiotics. 57% of the presumptive TB patients with negative sputum smears were sent to TB Diagnostic Committee (TBDC) for review and 63% were considered active TB. Of all CD cases, 44% of them were diagnosed by the public health physician. An expert panel review of the active TB cases adjudged by the TBDC showed 32.1% were not active TB. In the FGDS, physicians noted that some decisions to treat the smear negatives were influenced by the workers’ requirement for employment considerations.

Conclusions: There is a high percentage of CD cases among registered DSTB patients. Malaise and chest pain are more common in the CDss than the BCs. The high CDs seem to come more from the group consensus (TBDC) than single public physician decisions which is contrary to conventional wisdom. This study shows that there maybe an over-diagnosis with smear negative clinical treatment. There is a need to re-examine of current practice in both public and private sectors.

THE PREVALENCE OF TUBERCULOSIS AMONG LONG-TERM MENTALLY ILL PATIENTS IN STATE RESIDENTIAL CARE: A SINGLE CENTER EXPERIENCE.

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Background and Aim: Sri Lanka has a medium burden of tuberculosis, its co-morbidities and associated factors among a cohort of long-term mentally ill patients of the National Institute for Mental Health in Sri Lanka. This study aimed to determine the prevalence of active and latent tuberculosis, its co-morbidities and associated factors among a cohort of long-term mentally ill patients of the National Institute for Mental Health in Sri Lanka in whom active TB was increasingly observed in the recent past.

Methods: This was a cross sectional, descriptive study of 300 long term mentally ill male (61) and female (239) patients. Patients with a history of tuberculosis or currently on anti-TB treatment were excluded. A structured questionnaire was used to assess socio-demographic factors, duration of hospital stay, current symptoms of TB illness and co-morbidities (HIV infection, intravenous drug use, diabetes mellitus, prolonged corticosteroid therapy, other immunosuppressive therapy and end-stage renal disease).

All the patients were subjected to a chest X-ray and Tuberculin Skin Test.

Results: One hundred and ninety seven (65.9%) patients were tuberculosis positive for active TB, of which 72.9% were females. Non had active TB. In the latent TB group, 78 (29.3%) patients had been in hospital for more than one year. 35 (17.8%) had diabetes mellitus, 25 (12.7%) were underweight, and 22 (11.2%) were smokers. Non had chronic kidney disease nor HIV. Non were on immunosuppressives or intravenous drugs.

Conclusion: The prevalence of latent tuberculosis is high in long term mentally ill patients, hence INAH prophylaxis in them should be discussed.

COST-EFFECTIVENESS ANALYSIS OF TB SCREENING FOR YOUNG FOREIGN-BORN STUDENTS IN JAPAN: A CASE STUDY OF TB SCREENING TARGETING JAPANESE LANGUAGE SCHOOLS IN SHINJUKU CITY, TOKYO

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Background: The number of foreign-born tuberculosis (TB) cases especially in the young age groups has continued to increase in Japan. Shinjuku City Public Health Centre (PHC) has been conducting TB screening for foreign-born students of Japanese language schools.

Aim: To evaluate cost-effectiveness of TB screening for foreign-born students using the results from the experience of Shinjuku City PHC.

Methods: We analyzed the results of a TB screening programme conducted in September 2016, which was targeted at foreign-born students of Japanese language schools in Shinjuku City. TB screening was based on chest X-rays (CXR) and symptom enquiry. Estimates of costs were drawn from the annual report of Shinjuku City. Effectiveness was defined as the number of smear positive pulmonary TB cases prevented by screening.

Results: Of the 11,667 students who participated in the screening, 100 (0.86%) had abnormal CXR findings and were referred for further examination.

A total of 37 TB cases were detected, with the overall TB detection rate of 0.32%. Of the 37 TB cases, 6 (16.2%) was smear positive. Using the TB Surveillance data in Japan, it was estimated that the proportion of smear positive was 52% among foreign-born patients who were diagnosed with pulmonary TB with symptoms within 5 years of entering Japan. Therefore, it was estimated that 13 (37 x 0.52 - 6) smear positive cases were prevented by the screening.

The cost of TB screening was estimated to be 5 USD per participant. It was estimated that 1577 USD was needed to detect one active case, and 4487 USD to prevent one smear positive case.

Conclusions: TB detection rate of screening for foreign-born students was high. Our results suggested that TB screening for foreign-born students is effective and has the potential to reduce the burden of TB in the near future in Japan.

COMPARISON OF CLINICAL MANIFESTATIONS AND TREATMENT OUTCOME ACCORDING TO AGE GROUPS IN ADULT PATIENTS WITH MILIARY TUBERCULOSIS

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Background and Aims: After the introduction of chemotherapy, miliary tuberculosis (TB) has been more prevalent in adults than in children. However, adult patients have a wide age range and may have different characteristics across the age span. Thus, clinical manifestations and treatment outcome may differ according to age groups in adult patients with miliary TB. However, there is limited information regarding this issue. Thus, the present study compared the clinical manifestations, treatment outcome, and cause of death according to age groups in adult patients with miliary TB.

Methods: Adult patients with miliary TB were retrospectively reviewed and were categorized into young (16–40 years), middle-aged (41–64 years), and old adults (≥ 65 years). The clinical manifestations and treatment outcome were compared among the three adult groups.
Results: Of 150 patients, 27, 35, and 88 patients composed the young, middle-aged, and old adult groups, respectively. Overall clinical manifestations were comparable among the three groups. Treatment completion was significantly lower and overall TB deaths were significantly higher in the old group than in the young group. However, deaths in the young and middle-aged groups were all TB-related deaths, whereas deaths in the old group were more attributable to TB-unrelated deaths rather than TB-related deaths. In multivariate analysis, underlying chronic condition, hemoglobin levels, and acute respiratory failure were independent predictors for TB-related deaths in the adult group < 65 years, and albumin levels and acute respiratory failure were those in the adult group ≥ 65 years.

Conclusions: The present study suggests that treatment completion, the cause of death, and risk factors for TB-related deaths may be different according to age groups in adult patients with miliary TB.

DEMOGRAPHICS OF TB PATIENTS SEEN OVER 5 YEARS (2011-2015) AT SINGAPORE GENERAL HOSPITAL, A TERTIARY UNIVERSITY AFFLICTIONED HOSPITAL
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Background and Aims: Tuberculosis (TB), an infectious disease caused by Mycobacterium tuberculosis bacteria, remains to be a global health problem. Singapore, an intermediate TB country, that aims to eliminate TB, has Singapore General Hospital (SGH) treating an approximately 19% of its cases.

We analyse incidences and characteristics of TB patients seen at Singapore General Hospital (SGH) over a period of 5 years (2011-2015).

Methods: We analyse a retrospective view of care records of TB patients seen in SGH between 2011 and 2015 (inclusive).

Results: 2,078 of TB cases were seen in SGH between 2011 and 2015. The patients seen were mostly male (65.9%), Chinese (67.7%), Singapore residents (83.4%) who are more than 65 years old (37.7%). The gender distribution between non-resident women (54%) and non-resident men (46%) were almost equal (Fig. 1). These factors had been similarly reflected over the last 5 years (2006-2010) findings (1).

71.7% of the patients had Human Immunodeficiency Virus (HIV) test done (Fig. 2), of which 3.9% were positive for the virus. The outcome of the treatment resulted in 38.3% completing treatment, 38.5% of being transferred to another institution for the management of their disease, 8.8% died mostly due to other complications of their illness, 7.6% had their TB diagnosis revised and 6.9% leaving Singapore to seek treatment in another country.

Conclusions: The comparison of the 10 year trend shows that TB incidence remains stable and not decreasing. As such, we cannot be complacent to the threat of TB still looming in our country.

REFERENCE

DEALING WITH THE TB EPIDEMIC IN A GEOGRAPHICALLY CHALLENGING CONTEXT: PNG, GULF PROVINCE
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Background and Aims: Tuberculosis (TB) is a major cause of mortality from infectious diseases in Papua New Guinea. Gulf Province (population around 160,000) is located in the Southern Coast of the main island and many areas along the coast are accessible only by open ocean or inland channels. MSF France opened TB project in Gulf in 2014, supporting the NDoH to provide OPD and IPD service in Kerema general hospital and giving support to two basic management units (BMU) at Malalua, Ihu by mobile team.

The aim is to improve medication adherence in remote setting.
**Methods:** Intervention utilized—Treatment supporters (TS) and mobile clinics. Intention to provide daily DOT by TS. At the end of March 2017, 63 TS are assigned for 454 TB patients. Number of patients supported by one TS varies from 1 to 20 according to the ease of location and the amount of patient support required. MSF mobile clinic team consists of health extension officer and community health worker and TB patients are reviewed on monthly basis during their regular visit of Malalua and Ihu clinics. MSF is offering to the patients dinghy and bus transport to these health centers.

**Results:** Since commencing the activity multiple complexities have been noted
- Training and supervision of treatment supporters who are very remote is difficult
- Heavy workload on TS with multiple activities added
- Patient’s acceptance of TS in multicultural context
- Emphasis on TS approach distracted from patient centred approach

**Conclusions:** The geographical difficulties in Gulf has led to using TS for follow up. This approach has shown some limitations. In such a context, to facilitate treatment adherence, an individualized approach accompanied by adequate patient education and counseling may be a more effective approach than TS for all.

**A TRIAGE SYSTEM FOR THE EARLY DETECTION OF CHRONIC COUGH AMONG TB SUSPECTS ATTENDING A HOSPITAL IN BANDA ACEH, INDONESIA**

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**Background and Aims:** One of the main strategies for the early detection of pulmonary tuberculosis (PTB) is through the screening of individuals with symptoms compatible with TB. In the hospital, people with symptoms compatible with TB have an opportunity to get proper diagnosis and treatment. Yet this opportunity is often missed. We hypothesize that a respiratory triage system recommended by WHO for prevention of the spread of respiratory infection at the outpatient department, can be improved to enhance early detection of TB. With this hypothesis an intervention study was conducted at Zainal Abidin Hospital.

The objective of this intervention study was to compare the proportion of patients with cough >2 weeks, offered sputum test and TB case detection rate before versus after a respiratory triage system introduced.

**Methods:** Before-and-after interventional study. Intervention: training of health personnel and setting up a respiratory triage system, to detect patients with >2 weeks cough and offering sputum test for acid-fast bacilli. Data from “exit poll” and central laboratory were compared before vs after the triage set up.

**Results:** After the intervention, sampled patients who visited the hospital were more likely to be asked on >2 weeks cough (85.3% vs 17.9%). In the whole samples (99.2% vs 64.7%) among them have >2 weeks cough patients.

For TB detection, the changes were 39 positive results from 220 AFB tests of 61,871 outpatients to 55 positive from 365 AFB tests among 53,056 outpatients. The rates of sputum testing and TB case detection increased from 3.5 to 6.8 per 1,000 (OR=1.9, 95% CI=1.6-2.3) and 6.3 to 10.4 per 10,000 (OR=1.7, 95% CI=1.1-2.6) respectively.

**Conclusions:** Respiratory triage can significantly increase TB detection rate.

**THE DIFFERENCE OF INTERFERON GAMMA LEVEL IN PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROL IN MEDAN, INDONESIA**

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**Background and Aims:** Interferon gamma is an important cytokine in the immune response against Mycobacterium tuberculosis. Interferon gamma activate macrophage to kill intracellular mycobacterium. The aim of this study is to determine the difference of plasma Interferon gamma level in Pulmonary Tuberculosis (PTB) patients compare to healthy control and factors associated with interferon gamma level.

**Methods:** This is a case control study. Fifty subjects were selected, including 25 PTB patients and 25 healthy control (non TB patients). Interferon gamma concentration was determined by an ELISA technique.

**Results:** Interferon gamma level was significantly different in PTB patients compare to healthy control (p = 0.024). Mean ± SD Interferon gamma level was 317.2 ± 201.97 pg/ml in PTB patients and 213.5 ± 86.43 pg/ml in healthy control. Body Mass Index and age were not associated with Interferon gamma level.

**Conclusions:** Interferon gamma level was significantly higher in PTB patients than healthy control. Body Mass Index and age were not associated with Interferon gamma level.

**Key words:** Pulmonary Tuberculosis, Interferon gamma level, healthy control
OUTCOMES OF ISONIAZID PREVENTIVE THERAPY GUIDED BY T-SPOT TB® TEST AND HISTORY OF RECENT TUBERCULOSIS CONTACT AMONG THAI HEALTH CARE WORKERS

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Background and Aims: Data on the efficacy of T-spot TB® test in diagnosing latent tuberculosis infection and guiding isoniazid preventive therapy (IPT) among healthcare workers (HCWs) from tuberculosis (TB)- endemic settings is limited. HCWs with TB contact within 2 years are likely to have the most benefit from IPT. The aim is to evaluate the efficacy of IPT-guided by the combined T-spot TB® positivity and history of 2-year TB contact among Thai HCWs.

Methods: A prospective study was conducted among HCWs from May 2016 to May 2017. All HCWs underwent T-spot TB® at baseline and were followed for 1 year for incidence of active TB. Only HCWs who had T-spot TB® positivity and 2-year TB contact were offered 9-month IPT.

Results: Of the 140 HCWs, 89% were females, median age was 27 years, 59% were nurses, and 95% reported history of TB contact. None had active TB at baseline based on symptoms and chest radiograph screening. There were 23 T-spot TB®-positive HCWs (16%). Of these 23 HCWs, 14 (61%) had TB contact within 2 years, all of whom accepted IPT. Among these 14 IPT-receiving HCWs, 12 (86%) completed 9-month IPT, 1 (7%) discontinued IPT after 5 months due to grade 3 ALT elevation and 1 (7%) lost follow-up after IPT initiation. Of the 12 HCWs completing IPT, 7 (58%) experienced IPT side effects, most of which were grade 1 and included drowsiness (33%) and elevated AST/ALT (25%). The median number of reported missed IPT dose was 4. One year later, 22 T-spot TB®-positive and 117 T-spot TB®-negative HCWs were evaluable for the outcome and no active-TB case developed in both groups.

Conclusions: The combination of positive T-spot TB® test and TB contact within 2 years could be used as an effective tool to guide IPT among Thai HCWs.

YIELD OF XPERT MTB/RIF IN INDUCED SPUTUM IN PULMONARY TUBERCULOSIS SUSPECTS IN AN UNDER-DEVELOP COUNTRY

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Background and Aims: Pulmonary tuberculosis is endemic in Pakistan with incidence of 281/100000 cases per year. A significant number of patients cannot produce sputum for the proper diagnosis of pulmonary tuberculosis. Induced sputum is a satisfactory method to diagnose PTB. Xpert MTB/RIF is highly sensitive test to diagnose tuberculosis which may be a useful test to diagnose TB in induced sputum.

Methods: We performed a prospective study at chest clinics of Ojha Institute of Chest Diseases. We included patients who were diagnosed as TB suspects on clinical and radiological ground and not expectorating. The included patients were nebulized with 3% saline and encouraged to produce sputum. The expectorated respiratory secretions were then processed using Xpert MTB/RIF.

Results: A total of 370 patients were recruited, out of which 44 (11.5%) patients were AFB smear negative but culture positive. The sensitivity, specificity, positive & negative predictive values for Xpert MTB/RIF in smear negative cases were 65%, 98.4%, 96.6% and 98%.

Conclusions: Xpert MTB/RIF test in induced sputum improve diagnostic yield, in smear negative pulmonary tuberculosis patients. It accelerates treatment in about a quarter of patients.

USEFULNESS OF GENE XPERT MTB/RIF IN THE DIAGNOSIS OF EXTRA-PULMONARY TUBERCULOSIS

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Background and Aims: Diagnosis of extra-pulmonary tuberculosis is often difficult and delayed because of diverse clinical presentations and failure to establish a microbiological diagnosis. This study was designed to evaluate the usefulness of Gene Xpert MTB/RIF in the diagnosis of extra-pulmonary tuberculosis in selected group of Bangladeshi patients.

Methods: This cross-sectional study was done in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital from 2013 to 2016 as part of Bangladesh Diabetic Somitti (BADAS)-USAID-TB Care-II project. Representative samples from 590 clinically suspected extra-pulmonary tuberculosis cases were tested for Gene Xpert MTB/RIF along with conventional methods.

Results: Total patients were 590 with slight male predominance (326, 55.3%) and a mean age of 43.9 (range 1 to 95) years. Most (513, 86.9%) were diabetic and new (574, 97.3%) tuberculosis suspects; while 16 (2.7%) patients had past history of tuberculosis. Common samples were pleural fluid (125, 21.2%), urine (110, 18.6%), cerebrospinal fluid (CSF) (91, 15.4%), pus (82, 13.9%), tracheal aspirates (57, 9.7%), ascitic fluid (45, 7.6%), gastric lavage (31, 5.3%), broncho-alveolar lavage (BAL) (18, 3.1%), lymph nodes (11, 1.9%) and synovial fluid (8, 1.4%). All 590 samples were tested for Gene Xpert MTB/RIF and among them 68 (11.5%) were positive for Mycobacterium tuberculosis. Diagnostic yield was common for lymph nodes (47, 57.1%), pus (25/82, 30.5%), BAL (4/18, 22.2%), tracheal aspirates (8/57, 14.0%), urine (7/110, 6.4%). CSF (6/91, 6.6%) and pleural fluid (7/125, 5.6%). Of the 68 Gene Xpert MTB/RIF positive samples, 52 (76.1%) were rifampicin sensitive, 16 (23.9%) showed intermediate sensitivity and none of the samples was resistant to rifampicin.

Conclusions: Gene Xpert MTB/RIF appeared as useful and time saving tool for diagnosing extra-pulmonary tuberculosis.

ANALYSIS AND COMPARISON OF MANTOUX TEST RESULTS IN PATIENTS WITH EXTRAPULMONARY TUBERCULOSIS AND IN GENERAL POPULATION PRESENTED TO CENTRAL CHEST CLINIC, SRI LANKA

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Background and Aim: Mantoux test is an important ancillary test in diagnosing extra-pulmonary Tuberculosis (EPTB) especially in limited resource settings. The reliability of Mantoux positivity (>10mm) in diagnosing active TB is questionable due to the presence of latent TB. Aim of the study was to assess the validity of Mantoux test comparing the Mantoux results of EPTB patients and the population with no evidence of active TB.
Methods: A descriptive cross sectional study conducted at Central Chest Clinic, Colombo. Mantoux results of patients diagnosed with TB lymphadenitis and TB pleural effusions during 2015 and 2016 with evidence of microbiological positivity, caseation or lymphohytic, exudative pleural aspirations containing Adenosine deaminase level >40IU were studied. Results were compared with the Mantoux values of the general population presented during the same period for screening medical examinations and proven not to have active TB. Children (<12yrs) were excluded from the study.

Results: Mean age of both control group (n=187) & EPTB group (n=153) was 38yrs with a female predominance. Mean Mantoux value of the control group was 10.7mm with 63% positivity while it was 17.5mm with 95% positivity in the EPTB group. Mean difference was statistically significant (p value<0.05).

Mean Mantoux value of patients with TB pleural effusions was 16mm while it was 19mm in patients with TB lymphadenitis. Mean Mantoux value of true positives was 19.8mm.

The sensitivity and specificity of the test were 95% and 37% respectively and the rates were 76% and 67% respectively when the cut off level of 15mm applied. Positive predictive value increased from 56% to 66% with the higher cut off level.

Conclusion: Patients with TB lymphadenitis demonstrate a high mean Mantoux value compared to TB pleural effusions. As the mean mantoux value was >10mm in the group without active TB a higher cut off value would be more appropriate for EPTB diagnosis.

Microbiologic Correlation with Radiographic Activities on Chest Computed Tomography in Suspected Pulmonary Tuberculosis

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Background and Aims: Chest computed tomography (CT) has the great role in the diagnosis of pulmonary tuberculosis (PTB). However, little is known about microbiologic correlation with radiographic activities based on CT in suspected PTB. The aim of this study was to investigate microbiologic correlation with radiographic activities on chest CT, with a focus on relative frequencies of culture-positive of Mycobacterium tuberculosis (MTB) according to radiographic grades of CT.

Methods: We conducted this study to evaluate the microbiologic yield of MTB correlated with categorized radiographic grade on chest CT via bronchoscopy in presumptive PTB patients. CT findings were categorized into 4 groups as radiographic activities from highest to lowest grade, based on previously published criteria: definitely active, probably active, indeterminate activity, and probably inactive.

Results: Of 653 patients included, 316 had culture-confirmed PTB. There were 371 (56.8%) males with a median age of 57.0 (IQR 41.0–71.0) years. Of these with suspected PTB, 188 (28.8%), 301 (46.1%), 93 (14.2%), and 71 (10.9%) were classified as de

Conclusions: The radiographic activities based on chest CT showed good correlation with microbiological yield of MTB and prediction of PTB. Thus, it can be used easily in the clinical practice.

Mixed Infection of Mycobacterium Tuberculosis and Nontuberculous Mycobacteria in Sputum Culture at a Single Tertiary Hospital

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Background and Aims: Incidence and prevalence of pulmonary infection by NTM species have increased in worldwide. A rapid diagnosis of Mycobacterium tuberculosis (MTB) and nontuberculous mycobacteria (NTM) infection and reliable identification of mycobacterial species are important for proper treatment.

The aim of this study was to analyze the extent of co-infection of MTB and NTM and to determine its significance on treatment.

Methods: We collected ninety nine patients’ sputum Acid-Fast Bacilli (AFB) culture positive specimens from 2016 August to 2017 January in Inha University Hospital, Incheon, South Korea.

Results: Mixed cultures of MTB and NTM were four patients (4%). NTMs were more frequently isolated in eighty one patients (82%) and MTBs were in fourteen patients (14%). Three of four mixed infection consisted of M. tuberculosis and M. intracellulare. The other was M. tuberculosis, M. abscessus and M.massilense. The commonly detected NTM species were Mycobacterium intracellulare (31%) and M. avium (28%).

Conclusions: AFB drug susceptibility testing was performed in all four confirmed cases of mixed infections, but the results of MTB could not be obtained and only the susceptibility of NTM could be done. Therefore, MTB treatment was done by standard regimen.

Clinical Evaluation of Activity of Tuberculosis Infection Using the Supernatant of QFT-IT

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Background and Aims: We previously reported that IL-2 was the least effective among several biomarkers including IFN-γ using the supernatant of QFT-IT for the diagnosis of active tuberculosis (TB) disease. The aim of this study was to evaluate the use of IL-2, IFN-γ, and TNF-α levels for the differential diagnosis of active TB disease, healed TB disease, and latent TB infection (LTBI).

Methods: The subjects consisted of 33 patients with active TB disease, 23 with healed TB disease, and 8 with LTBI. We measured IFN-γ, IL-2, and TNF-α levels using the supernatant of QFT-IT. The transitional change of these biomarkers was also measured before and after antituberculous treatment in seven patients with active TB disease.

Results: Among the three groups, the IFN-γ level was significantly high-
est in patients with active TB disease, and TNF-α was also highest, although not significantly. However, IL-2 showed similar levels between patients with LTBI and those with active TB disease. Concerning the transitional change of several biomarkers in patients with active TB disease, while IFN-γ showed
THE INCIDENCE OF TUBERCULOSIS IN DIABETICS IN COMPARISON WITH NON-DIABETIC HYPERTENSIVE PATIENTS
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Background and Aim: Diabetes mellitus is a well-known risk factor for tuberculosis, but there are no long-term studies that investigated the trend of incidence with time. This study was planned to compare the incidence of tuberculosis development in diabetes patients with that in non-diabetic hypertensive patients over a 12-year follow-up period.

Methods: In this retrospective cohort study, the diabetes cohort consisted of diabetes patients who visited a secondary referral hospital from January 2004 to April 2004. The development of tuberculosis was assessed in comparison with non-diabetic hypertensive patients on a yearly basis.

Results: There were 2,535 patients in the diabetes cohort and 1,905 in the hypertension cohort, and after 12 years, 1,056 patients (41.7%) and 697 patients (36.6%) remained uncensored, respectively. Forty-five patients developed tuberculosis in the diabetes cohort, compared to 13 in the hypertension cohort; the estimated annual incidence was 227.3 and 98.2 per 100,000 persons, respectively (P = 0.005). Multivariate analysis showed the risk for tuberculosis was higher in the diabetes than in the hypertension cohort (hazard ratio, 2.34; 95% confidence interval, 1.287–4.249; P = 0.005).

Conclusion: Diabetes was associated with an increased risk for developing tuberculosis, compared to non-diabetic hypertensive patients. The increased risk persisted for more than 10 years.

IMPACT ON DIABETES MELLITUS ON INDETERMINATE RESULTS OF THE QUANTIFERON TB GOLD IN-TUBE TEST: A PROPENSITY SCORE MATCHING ANALYSIS
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Background and Aims: The sensitivity of interferon-gamma release assays (IGRAs) in the detection of Mycobacterium tuberculosis infection could be affected by conditions of immune dysregulation. For this reason, diabetes mellitus (DM) may increase the frequency of indeterminate results of IGRA. However, there have been inconsistent reports of role of DM on indeterminate IGRA results.

Methods: We retrospectively reviewed all patients who underwent Quantiferon-TB Gold In-Tube testing (QFT-GIT) at Chonnam National University Hospital. We collected the clinical and laboratory data of these patients.

Results: Of all 3,391 subjects, 1,265 (37.3%) had a positive QFT-GIT result, 266 (7.8%) had an indeterminate result, and 1,860 (54.9%) had a negative result. The mean age was 54.8 ± 18.1 years and 55.0% of the patients were male. There were 512 (15.1%) patients with DM. Multivariate analysis revealed that systemic corticosteroid use, tuberculosis, lymphocytopenia, low serum albumin, and high serum C-reactive protein (CRP) levels were significantly associated with indeterminate QFT-GIT results. However, DM was not associated with indeterminate QFT-GIT results (odds ratio [OR], 0.98; 95% confidence interval [CI], 0.92–1.67; P = 0.932). After propensity score matching, DM still did not increase the incidence of indeterminate QFT-GIT results compared with the determinate group (adjusted OR, 1.09; 94% CI 0.68–1.75; P = 0.697).

Conclusion: In this large cohort study, DM does not affect the incidence of indeterminate results of QFT-GIT.

PERITONEAL TUBERCULOSIS MIMICKING OVARIAN CYST TO PULMONARY TB PATIENT: A CASE REPORT
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Background and Aim: Tuberculosis usually manifest to the lung but also can manifest to other organs or organs system, one of the is peritoneal tuberculosis. Incidence of Peritoneal tuberculosis approximately 0.1%-3.5% above active pulmonary TB patient, 4-10% came from extrapulmonary TB. Peritoneal TB can be mimicking ovarian cyst because from clinically, radiology and laboratories, both have same representation. Similarly between them that is pain and abdominal distention, lost of body weight, abdominal tumor cystic or solid, ascites also increase of Ca 125 in blood.

Case: Presenting a case of 28-years-old female, with chief complain enlarged of abdomen, menstrual irregularities, had exploration laparotomy with suspected of ovarian cyst. Intraoperative diagnosed with peritoneal tuberculosis. There is no intraepithelial lesions or malignancy. Abdominal ultrasonography we find ascites with mass diameter 3 cm at pelvis, thick wall irregularly have content fluid that possibility came from ovarian. Chest X-Ray minimal pleural effusion sinistra. Tumor marker increase of CA-125 406 IU/ml. Intraoperative we find adhesive of bowel and omentum with multiple nodule at peritoneal surface and internal genitalia organ that impress peritoneal tuberculosis. Biopsy we find focus necrosis around implicoplastik cells and epitheloid histiosid and langhans giant cell. We conclude with chronic granumatism inflammation with tuberculosis.
Abstracts

Conclusion: This case illustrates that peritoneal tuberculosis and ovarian cyst have a similarity from clinical findings, radiology and laboratory.

Keywords: tuberculosis peritoneal, ovarian cyst

SILICOTUBERCULOSIS WITH COMPLICATION SPONTANEOUS PNEUMOTHORAX SECUNDER SINISTRA VINODIN MERINDA1, WINARIANI KOEOEMOPRODO1
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Background and Aim: Silicosis is a lung disease caused by inhaled respirable crystalline silica, often occurs in mining gold, iron, tin, granite, sandstone, slate, foundries, cement, ceramics and glass workers. The risk of silicosis develop to lung tuberculosis (TB) is higher than patients without silicosis and called as silicotuberculosis. Pneumothorax is a complication of silicotuberculosis

Case Presentation: A 45 years old man with a history of working as a brickstone for 5 years with chief complaints is shortness of breath since three days prior to admission, chest pain in right hemithorax, and cough more than 4 months. Patients on ATD therapy. From radiographic imaging, there is collapse line in the right hemithorax, fibroinfiltrat with multiple cavities on both hemithorax. Patients then got chest physiotherapy and chest tube insertion, but from evaluation for 5 weeks, the lung has not expanded.

Conclusion: A 45 years old man with a history of working as a brickstone for 5 years with chief complaints is shortness of breath since three days prior to admission, chest pain in right hemithorax, and cough more than 4 months. Patients on ATD therapy. Diagnosed as spontaneous secondary pneumothorax as a complication of silicotuberculosis There is no specific treatment for silicosis, it is aimed to the complications of silicotuberculosis e.g pneumothorax and tuberculosis. Prevention is the main action especially in working environment with silicosis risk. The evaluation 6 months after ATD therapy, the lung is fully expanded.

Keywords: Silicotuberculosis, pneumothorax

A FILIPINO WITH MULTIPLE SACULAR ANEURYSMS CAUSED BY MYCOBACTERIUM TUBERCULOSIS OMOHAIRE DILANGALEN1, T DE GUIA1
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Background and Aims: Tuberculous aortitis is an unusual presentation of a common disease in the Philippines. The majority of tuberculous aortic aneurysms are sacular (98%) and false (88%) with abdominal and descending aorta as preferential sites. We report a case infectious aortitis with no previous history of pulmonary tuberculosis.

Case Report: A 58-year-old Filipino male presented with severe abdominal pain. There was no cough, hemoptysis or afternoon fever. His past history was negative for connective tissue diseases, tuberculosis or vasculitis. CT aortography revealed an atheromatous aorta with a partially thrombosed sacular aneurysm arising from the aberrant right subclavian artery (figure 1) and segmental partially thrombosed dissections at the distal abdominal aorta (figure 2). He was referred to thoraco-cardiovascular surgery service and underwent total arch replacement. Surgeon noted aortitis with external inflammatory granulomatous aortitis and showed acid-fast bacilli on staining. Patient was started with fixed dose anti-tuberculous therapy.

Discussion: Tuberculous aortitis is a very rare form of extra-pulmonary tuberculosis. Mycobacterium infection of the aorta usually occurs as a result of direct extension from an adjacent focus or via hemogenous spread. A primary tuberculous infection in the lung spreads into the periaortic structures subsequently invading the aortic wall. Clinically, a patient with a tuberculous aeurysm may initially present pain related to the location of the aneurysm. Medical treatment is not sufficient, and once tuberculous aortic aneurysm is suspected, surgery should not be delayed because of the high probability of aneurysmal rupture. Tuberculous aortitis, albeit rare, should be suspected in any patient presenting with aortic aneurysm. A combination of surgical treatment and long term anti-tuberculous therapy is the best treatment option.

Figure 1. Saccular aneurysm from aberrant abdominal aorta

Figure 2. Aneurysm at the distal right subclavian artery

This abstract has been withdrawn

CENTRAL VENOUS THROMBOSIS IN PULMONARY TUBERCULOSIS: A RARE CO-MORBIDITY OF COMMON DISEASE NAJMA KORI1, TIDI HASSAN1, ANDREA YU-LIN BAN1, FAISAL ABDUL HAMID1 1UKMMC, Respiratory Unit, Department of Internal Medicine, Hospital Canelor Tunku Muhriz, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur Malaysia

Background and Aim: Tuberculosis (TB) is a common life threatening disease, but its occurrence in association with venous thromboembolism (VTE) is considered uncommon. Hemostatic abnormalities such as impaired fibrinolysis, causing high level of plasma fibrinogen, reduced protein C and antithrombin III activities were postulated to be responsible for the hypercoagulable state promoting the development of thrombosis in TB. Most data collected reported pulmonary TB in association with venous thromboembolism occurs in lower limb DVT and pulmonary embolism. Here, we present a case of venous thromboembolism that complicates severe pulmonary TB at a rare site.

Results: A 55-year-old man with diabetic history was diagnosed with smear positive pulmonary tuberculosis with superimposed community acquired pneumonia complicated with septicemic shock and TB adrenalitis. Chest radiograph showed right pleural thickening at right upper zone, right lower zone hydropneumothorax and collapse of the right lung. Computed tomography (CT) scan of the thorax showed multifocal empyema, right hydropneumothorax, right bronchopleural fistula and incidental finding of thrombosis involving the right brachiocephalic vein, extending into the right internal jugular, subclavian and axillary veins. Warfarin was instituted for the thromboses along with antituberculous (anti-TB) therapy. 6 months later, at the completion of anti-TB
medications, a repeat CT showed complete resolution of the venous thromboses.

**Conclusion:** Patients with severe tuberculosis are at risk of developing VTE, and in this case, highlights how it may occur in rare site such as the upper extremity.

**Figure 1.** Coronal view of CT thorax of the patient. Filling defect seen in superior vena cava (yellow arrow), and right subclavian vein (red arrow).

**ULNAR NERVE TUBERCULOMA**
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Tuberculoma as a rule occurs as a solitary space-occupying lesion and is caused by hematogenous spread of the tuberculosis bacillus. The most common central nervous system site for tuberculosis is the cerebellum. Tuberculoma involving a peripheral nerve is very rare, with only 3 cases reported in the literature. From literature review, there was six cases of peripheral tuberculomas (from 1964 – 2013).

A 25 years old woman was consulted from Orthopedic Outpatient Department, presented with 2 years history of paraesthesia and numbness of her right hand. She also presented weakness and wasting of her right hand and forearm in last 6 months. These symptoms made her difficult to writing. There was a gradually increasing swelling in the postero-medial aspect of her right arm just above the elbow joint for last six months. No history of trauma. The patient does not have past history of tuberculosis, weight loss or appetite nor fever. No history of contact with pulmonary tuberculosis. She has performed peripheral nerve decompression 3 weeks before she consulted to our department. On local examination there was a postoperative scar over the postero-medial aspect of her right arm just above the elbow joint in the ulnar nerve distribution. There was paresthesias along the ulnar nerve distribution. There were no skin changes, lymphadenopathy, or restriction of movement at the elbow joint. Neurological examination revealed loss of pain, temperature, touch, and vibration sensations along the distribution of the right ulnar nerve. There was wasting of the hypothenar muscles present. The chest radiograph did not reveal any abnormality. Histopathological examination of the specimen (after peripheral nerve decompression ) revealed extensive areas of caseous necrosis, epithelioid granulomas, and Langhans giant cells. She is getting better after received adequate antituberculosis treatment and physiotherapy.

**Conclusion:** We are presented with a case with hemodynamically stable but repeated embolisms. It is crucial to have a high index of suspicion in order to diagnose early and treat accordingly.

**Pulmonary Circulation**

**MASSIVE PULMONARY EMBOLISM AND TRIPLE INTRACRANIAL EMBOLI IN AN OBSCURE MALIGNANCY: A CASE REPORT**
MICHELLE ANGELA TAN-REYES1,2,3
1Asian Hospital and Medical Center, Muntinlupa, Philippines, 2Rizal Medical Center, Pasig, Philippines, and 3Cardinal Santos and Medical Center, San Juan, Philippines

**Background and Aims:** Pulmonary embolism remains to be one of the most problematic diagnostic dilemmas in admitted patients. The clinical presentation of PE can vary widely from one patient to another, is often nonspecific making the diagnosis challenging.

**Results:** A 55/F admitted with chief complaint of left sided weakness. Known diabetic and hypertensive, s/p CVD cerebellar infarct a year prior. Cranial MRI revealed multiple acute infarcts. She is started on Enoxaparin 0.6cc OD. On her 10th hospital day, patient suddenly developed hypoxemia as low as 83%. She claimed having occasional shortness of breath that day, no cough/fever. Chest x-ray now revealed bilateral lower lobe pneumonia compared to one done on admission. Desaturation persisted despite oxygen support, and pulmonary embolism was considered. D-dimer was 28,000. CT angiogram revealed massive pulmonary embolism, with bilateral atelectasis and pleural effusion; DVT, left leg. Enoxaparin was increased to 0.6cc twice daily. At this time she was only on high flow oxygenation and is improving clinically but there is a nagging pain on her hypogastric and lumbosacral areas. Ten days after, repeat CT angiogram showed significant clearing of the pulmonary embolism. Repeat duplex scan of lower extremities showed partial recanalization of the left common femoral and popliteal veins. Enoxaparin was shifted to Rivaroxiban and patient was sent home but was re-admitted due to persistent hypogastric and lumbosacral pain. Repeat trans-vaginal ultrasound (4th total) showed a thickened endometrium, biopsy revealed endometrial adenocarcinoma. She was scheduled for chemo once soluble. While undergoing pain management and physical therapy, she had changes in sensorium. Repeat scan revealed cranial hemorrhage, and she deteriorated until she expired.

**Conclusion:** We are presented with a case with hemodynamically stable but repeated embolisms. It is crucial to have a high index of suspicion in order to diagnose early and treat accordingly.

**SYSTEMIC HYPERTENSION-INDUCED LEFT ATRIAL PRESSURE ELEVATION ACCOUNTS FOR THE PATHOGENESIS OF NEUROGENIC PULMONARY EDEMA IN ANESTHETIZED RATS**
TOSHIHIGE SHIBAMOTO1, MOFEI WANG1,2, MAMORU TANIDA1, YUHICHI KUDA1, TAO ZHANG1,2, WEI YANG1,4, YASUTAKA KURATA1
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**Background and Aims:** Neurogenic pulmonary edema (NPE) observed in patients with severe brain injuries is sometimes fatal, but its pathogenesis remains unsettled.

**Conclusion:** Neurogenic pulmonary edema (NPE) observed in patients with severe brain injuries is sometimes fatal, but its pathogenesis remains unsettled.

**Systemic Hypertension-Induced Left Atrial Pressure Elevation Accounts for the Pathogenesis of Neurogenic Pulmonary Edema in Anesthetized Rats**

**AP143**

**Massive Pulmonary Embolism and Triple Intracranial Emboli in an Oblique Malignancy: A Case Report**

**AP144**

**Systemic Hypertension-Induced Left Atrial Pressure Elevation Accounts for the Pathogenesis of Neurogenic Pulmonary Edema in Anesthetized Rats**

**Respirology** [2017] 22 (Suppl. 3), 88–278
Aims: We determined whether NPE could be produced only by high pulmonary vascular pressure due to systemic hypertension-induced left atrial pressure elevation in open-chest anesthetized rats.

Methods: The pulmonary arterial pressure (PAP), left atrial pressure (LAP), and aortic blood flow (ABF) were directly and continuously measured. The rats were assigned to 1) NPE, 2) LAP elevation and 3) control groups. NPE was induced by intra-cisternal injections of thrombin and fibrinogen, with resultant transient increases in SAP, LAP and PAP. In the LAP elevation group, LAP was forcibly elevated in a manner similar to the NPE group by occluding the aorta with a polyethylene tubing placed between the brachiocephalic artery and the left carotid artery.

Results: In the NPE group, following an intra-cisternal injection, marked systemic vasoconstriction occurred, as reflected by an increase in SAP to 195±3 mmHg along with increases in LAP and PAP. In the LAP elevation group, LAP was increased in the same way as the NPE group, with the same peak values of LAP and PAP of 47±2 and 46±2 mmHg, respectively. The lung wet-to-dry weight ratio of either group was similar and not significantly different from each other (5.5±0.3 and 5.3±0.6, NPE and LAP elevation, respectively), while it was significantly larger than that of the control group (3.2±0.1). Plasma levels of syndecan-1, a component of endothelial glycocalyx, showed similarly higher values of 1.2±0.3 and 1.2±0.5 ng/mL in the NPE and the LAP elevation groups, respectively, than that in the control group (0.3±0.3 ng/mL).

Conclusions: The pathogenesis of neurogenic pulmonary edema could be explained by marked increase in pulmonary microvascular pressure due to systemic hypertension-induced left atrial pressure elevation in anesthetized rats.

AP145

THE INFRARED THERMAL IMAGING PRESENTATION AND DISTRIBUTION CHARACTERISTICS OF RABBITS DVT MODELS INDUCED BY LIGATION AND THROMBIN FANGGE DENG1, HUIZHI GUO1, LIN LIN1, TAO LI1, MEI JIANG1
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Background and Aim: To investigate infrared thermal imaging (IRTI) presentation and distribution characteristics of rabbits DVT models induced by ligation and thrombin.

Methods: Rabbit DVT models were respectively prepared by thrombin (experimental group) and extracorporeal ligation (control group) performed on right femoral vein, and the left side served as sham operation control side. Detecting IRTI respectively at three time points: T1 (pre-operation), T2 (2 hours after operation) and T3 (48 hours after operation), then determined IRTI presentation and distribution characteristics as qualitative analysis. Furthermore utilizing IRTI system to extract highest temperature (Thi), lowest temperature (Tli) and average temperature (Tav) of region of interesting (ROIs) for quantitative analysis.

Results: In comparison with control side, a little swelling was found in the experiment side. IRTI qualitative analysis showed that there was relative symmetric distribution on both sides at T1 in both groups. At T2, the infrared temperature of both sides had decreased both in both groups, but the distribution was asymmetry, with experiment side’s temperature was higher than that of control side in ligation DVT, whereas it was lower in thrombin DVT. The results of both groups at T3 were similar, in that, the bilateral side were continue asymmetry, and the experiment side presented abnormal high temperature while the temperature of the control side was recover to the level of temperature of T1. The quantitative analysis displayed that there were statistical difference between experiment side and control side at T3 on both DVT groups (p<0.05). Repeated measure and multiple comparisons of temperature differences (TD) between experimental side and control side showed that there were significant differences on ligation DVT (TDTh and TDti) and thrombin DVT (TDTh and TDti).

Conclusion: IRTI has significant presentation and distribution characteristics in both rabbits DVT group, which is closely related to the pathophysiological basis of model preparation.

AP146

SAFETY OF DIAGNOSTIC BRONCHOSCOPY IN JAPANESE PATIENTS WITH PULMONARY HYPERTENSION TSUKASA ISHIWATA1, H KASAI1, S SAKAO1, N TANABE1, K TATSUMI1
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Background and Aim: Flexible bronchoscopy (FB) is one of the most important diagnostic tools performed by pulmonologists. Safety of FB in patients with pulmonary hypertension (PH) is controversial. To investigate whether Japanese patients with PH who undergo FB are at greater risk for complications compared to patients without PH.

Methods: We conducted a retrospective analysis of patients who underwent FB at Chiba university hospital between 2004 and 2016, and whose estimated pulmonary artery pressure (PAP) were >40 mmHg estimated by Doppler echocardiography within three months from the day of the diagnostic FB procedures. Controls were selected among patients without PH who underwent FB with matching variables: age, sex and types of FB procedures.

Results: A total of 225 patients, PH group (N=45) and controls (N=180; 1:4 matching) were included. The mean PAP in PH group was 49.8±11.6 mmHg; 28 (62.2%) mild (40-50 mmHg), 11 (24.4%) moderate (51-60) and 6 (13.3%) severe (≥61). The proportion of patients with congestive heart failure, obstructive airway disease, chronic kidney disease, liver disease and use of anticoagulant drugs were higher in PH group. The proportion of procedures was similar between the groups: transbronchial biopsies (62.2 vs. 57.5 %), transbronchial needle aspiration (13.3 vs. 13.3 %). Incidence of bleeding due to FB procedures was similar in both groups (17.8 vs. 13.3 %, p=0.445). None of the patients had significant bleeding. There was no statistically significant difference in noninvasive hemodynamics between the groups before and after FB procedures. There was no procedure-related mortality in this cohort.

Conclusion: Our study provides additional support that diagnostic FB procedures can be performed safely in patients with PH. Transbronchial biopsies and transbronchial needle aspirations are not associated with an increased risk of bleeding.
ADHERENCE TO EUROPEAN SOCIETY OF CARDIOLOGY GUIDELINE IN THE MANAGEMENT OF PULMONARY EMBOLISM AT WAIKATO HOSPITAL

TAE YOUNG YOON 1, QI HAO ONG 1, HENRY GALLAGHER 1, ESKANDARAIN SHAFUDDIN 1

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Background: Acute pulmonary embolism is associated with poor outcomes. The 2014 European Society of Cardiology (ESC) guideline recommends risk stratification to identify and manage patients at increased risk of early mortality.

Aim: To characterise the investigation, management and outcome of patients admitted to Waikato Hospital with acute pulmonary embolism according to the ESC risk stratification.

Methods: This was a retrospective study of 67 patients admitted with imaging-diagnosed acute pulmonary embolism between March 2015 and March 2016. Patient demographic, clinical, laboratory and imaging data were used to group patients according to ESC risk stratification (table 1).

We evaluated the investigations, management, treatment complications, and 30-day all-cause mortality according to risk group.

Results: Diagnosis was made on computerised-tomography pulmonary angiography in 62 patients (91%) and ventilation-perfusion scan in 6 patients (9%). The median Pulmonary Embolism Severity Index (PESI) class and simplified PESI were 2 and 1, respectively (table 2). 52 patients (78%) were risk stratified (figure 1). 15 patients (22%) had unclassifiable risk group: all had imaging assessment of right ventricular function but not cardiac biomarkers. 12 patients (86%) with intermediate-high risk were not admitted to high-dependency unit for close monitoring. Only 2 patients received thrombolysis from high risk and intermediate-high risk groups without complications (table 3). All patients received initial treatment with anticoagulation: 6 patients (9%) suffered non-intracranial haemorrhage. 4 patients (6%) died at 30 days: 3 from unclassifiable risk group (figure 2).

Table 1. Risk stratification of patients with acute pulmonary embolism

<table>
<thead>
<tr>
<th>Early mortality risk group</th>
<th>Shock or hypotension (systolic BP &lt;90mmHg)</th>
<th>PESI class</th>
<th>RV dysfunction on imaging (CTPA or echocardiogram)</th>
<th>Cardiac biomarkers (NT-proBNP &gt;71 pmo/L or Troponin T &gt;14 ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Absent</td>
<td>Absent</td>
<td>Optional or both normal</td>
<td>Either raised (overrides normal PESI/sPESI)</td>
</tr>
<tr>
<td>Intermediate-low</td>
<td>Absent</td>
<td>Present</td>
<td>Both raised (overrides normal PESI/sPESI)</td>
<td>RV dysfunction present. Biomarkers are optional</td>
</tr>
<tr>
<td>Intermediate-high</td>
<td>Present</td>
<td>Optional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
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</table>

SD = standard deviation, VTE = venous thromboembolism, BP = blood pressure, PESI = pulmonary embolism severity index, sPESI = simplified pulmonary embolism severity index, CTPA = computed tomography pulmonary angiography, V/Q = ventilation perfusion
Background and Aim: Patients presenting with an unprovoked PE have an increased incidence of occult malignancy. The optimum strategy for workup of these patients isn’t well established. Our aim is to assess the prevalence of occult malignancy in patients presenting with unprovoked PE, and to identify certain risk factors that may predict a higher likelihood of occult malignancy in this population.

Methods: We performed a retrospective analysis of patients presenting to a tertiary hospital with PE from 2012. Variables that may predict a higher risk of occult cancer were assessed, including age, gender, pre-existing conditions, and biochemical abnormalities at presentation.

Results: One hundred and sixty-nine patients were considered for the study and 67 (34%) had unprovoked PEs and only these patients were evaluated for further analysis. Mean (±SD) age of the cohort was 69±14 years and 33 (49%) patients were female. No occult malignancy screening was scheduled for 26 (54%) patients, standard age/gender specific screening was performed in 21 (31%) patients and extensive screening was performed in 8 (11%) patients. Subsequently malignancy was diagnosed in 4 patients (6%) and the mean time to diagnosis from the PE related hospital admission was 26 weeks. Of the variables evaluated (age, gender, PE severity index, haemoglobin, platelets and malignancy screening evaluated, only malignancy screening (p<0.001) was associated with a diagnosis of an occult malignancy on follow-up.

Conclusion: Unprovoked PE is associated with a high risk of subsequent cancer diagnosis. The prevalence of occult malignancy in our study population was similar to that of other recent studies. Further study is needed to determine which additional variables may predict a higher risk of occult malignancy.
Table 2. Simplified Pulmonary Embolism Severity Index (sPESI) components and clinically significant investigations showing right heart strain in high risk patients who were discharged early from hospital

<table>
<thead>
<tr>
<th>sPESI component, n (%)</th>
<th>Signs of right heart strain present, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of high-risk patients discharged early</td>
<td></td>
</tr>
<tr>
<td>Age &gt;80</td>
<td>5 (18.5)</td>
</tr>
</tbody>
</table>

Note: One patient showed right heart strain on both CTPA and ECG, while another had cardiopulmonary disease and right heart strain on ECG.

83 on Warfarin. 173 patients received at least one therapeutic dose of Enoxaparin during admission. Investigations included 192 ECG, 132 Troponin, 28 Transthoracic echocardiography and 0 Brain natriuretic peptide. 190 patients were referred to General Practice, 127 to Respiratory clinics and 37 to Haematology clinics.

Conclusion: Patients diagnosed with acute pulmonary embolism are being appropriately risk stratified by the sPESI and evidence of right ventricular strain. However, 20.45% of high-risk patients were discharged inappropriately. With evidence showing substantial mortality in high-risk patients who are discharged early, this presents an area for further focus.

Figure 1. Discharge and admission decisions stratified by a risk profile based on the 2014 European Society of Cardiology guidelines.

PULMONARY HYPERTENSION IN THE EASTERN PART OF LIBYA: A NEWLY STARTED SERVICE

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Background and Aim: Pulmonary hypertension (PH) is a rare disease with high rate of morbidity and mortality. Multi-disciplinary coordinated service is essential in patient management. We wanted to describe a 5 years data of a newly started PH service (2011 - 16) in the Eastern part of Libya.

Method: In liaison with cardiology team, patients with echocardiography suspected PH at Benghazi Medical Centre were referred to a newly started pulmonary hypertension clinic. They underwent clinical, laboratory, and radiological assessment for suspected PH as per international guidelines. Diagnosis of PH required confirmation by right side cardiac catheterization (RCC) measurement of pulmonary pressure. Pulmonary pressure of >25 mmHg was considered abnormal.

Results: Sixty patients attended PH clinic for assessment. 39 patients completed full workup. 27 out of 39 patients (69%) were females and the mean age was 44 years. 34 out of 39 patients (87%) had RCC pulmonary pressure (more than 25 mmHg) while 5 patients had normal study. The mean pulmonary pressure was 56.4 mmHg (25-118 mmHg). 11 patients (32%) had primary PH, 9 patients (26%) had connective tissue disease, 4 patients (11%) had congenital heart disease, 3 patients (8%) had haematological diseases.

At presentation to PH clinic and based on NYHA classification, 6 patients (18%) were class I, 10 patients (29%) class II, 11 patients (33%) and 7 patients (20%) class IV. 25 patients were on mono-therapy, 4 patients were on combined therapy and 5 patients were not on treatment. The commonest drug used was endothelin receptor antagonist. 9 patients out of 34 (26%) died over five years follow up period.

Conclusion: In the Eastern part of Libya (2 million populations) 34 patients had right cardiac catheterization confirmed PH with 4 to 1 female predominance. Up to our knowledge this is the first service of PH in Libya.
CHANGES IN PULMONARY FUNCTION AND PULMONARY ARTERY PRESSURE IN COMBINED PULMONARY FIBROSIS AND EMPHYSEMA: FOLLOW-UP EXAMINATION

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Background and Aims: Combined pulmonary fibrosis and emphysema (CPFE) is recognized as smoking related interstitial pneumonia characterized by upper-lobe emphysema and lower-lobe fibrosis, and its unique clinical features have been reported in comparison with chronic obstructive pulmonary disease (COPD). As to pulmonary function, lung volume is preserved and capacity of gas exchange is severely impaired. As to pulmonary circulation, CPFE is frequently complicated by pulmonary hypertension. However, correlation of dynamic change of pulmonary function and pulmonary artery pressure compared with COPD has not sufficiently been reported.

This study was performed to investigate dynamic change and correlation of pulmonary function and pulmonary artery pressure of CPFE compared with those of COPD.

Methods: Stable 5 CPFE patients and 11 COPD patients who had undergone pulmonary function test and right heart catheterization at the same time more than twice during follow-up period of over half a year were chosen for our study. We compared the result of annual changes of pulmonary function and right heart catheterization of CPFE with those of COPD.

Results: There were no significant differences between annual changes of lung function and mean pulmonary artery pressure (mPAP) of CPFE and those of COPD. However, there were significant differences between annual changes of pulmonary vascular resistance (PVR) and cardiac output (CO) of CPFE and those of COPD (PVR: 95 vs -57.38 dynes/sec/cm5; p=0.021, CO: -2.4 vs 0.6L/min/m2; p=0.0047). CO: -2.4 vs 0.6L/min/m2; p=0.0047. CO: -2.4 vs 0.6L/min/m2; p=0.0047.

Conclusions: In our study, CPFE is more likely to decline annual change of PVR and CO than COPD. Incidentally, the number of subject will increase until the presentation and the result and conclusion can change.

EFFECTS OF IMATINIB ON PULMONARY VASCULATURE IN AN ANIMAL MODEL OF OBSTRUCTIVE SLEEP APNEA

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Background: Obstructive sleep apnea (OSA) has been demonstrated to develop pulmonary hypertension (PH), on the pathological basis of chronic intermittent hypoxia (CIH). Platelet-derived growth factor (PDGF) signaling pathway was demonstrated to be involved in the development of pulmonary arterial hypertension (PAH), whereas its role in CIH-associated PH has not been documented.

Aims: To examine the effects of imatinib mesylate, PDGF receptor inhibitor, on overall aspects of pulmonary vasculature in an OSA/CIH-associated PH rat model.

Materials & Methods: Fifteen Sprague Dawley rats were randomly divided into three groups (5 rats/group), including one control-group and two CIH-groups. Rats in CIH-group were exposed to alternating 30-second-cycle of normoxia (21%O2)-hypoxia (10%O2), repeated continuously for 8 hours/day during the light phase for 28 days. Imatinib was given to one CIH-group throughout the study. At the end of study, hemodynamics and histopathological studies were completely executed.

Results: Hemodynamic studies revealed significant reduction in mPAP in imatinib-treated CIH-group, compared with those in untreated CIH-group (38.7±2.7, 48.3±5.8 mmHg respectively; p=0.009). The mPAPs in both CIH-groups were significantly higher than that in control-group (18.2±1.9 mmHg, p<0.05). Histopathological studies revealed significant difference in percent wall thickness of pulmonary arteriole (50-100μ) among control-group, untreated CIH-group and imatinib-treated CIH-group (24.4±3.3 %, 32.0±3.0 %, 27.6±3.3 %, respectively; p=0.003).

Right ventricular hypertrophy (RVH) were found in untreated and imatinib-treated CIH-group, compared with that seen in control-group (mean of right ventricle to left ventricle plus septum weight ratio were 0.21±0.02, 0.21±0.02, 0.17±0.03 respectively; p=0.05).

Figure 1. Effect of imatinib on hemodynamic study in CIH-associated PH rat model

Figure 2. Effect of imatinib on histopathological study in CIH-associated PH rat model.
Conclusions: This is the first translational research aimed to focus on other contributing pathway, PDGF signaling pathway, in the pathogenesis of OSA/CIH-associated PH. As the results, CIH induces increased mean PAP, pulmonary vascular remodeling and RVH. Moreover, PDGF signaling pathway may be associated with the development of OSA/CIH-associated PH proven by beneficial effects of imatinib on pulmonary hemodynamics and pulmonary vascular remodelling.

AP153

CHRONIC LUNG DISEASE AND THE PULMONARY HEMODYNAMICS: A SINGLE CENTER RETROSPECTIVE STUDY

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Background and Aims: Once chronic lung disease (CLD) patients develop pulmonary hypertension (PH), their prognosis worsen. To investigate the tendency of pulmonary hemodynamics in CLD, we conducted a single center retrospective observational study.

Methods: From March 2014 to December 2016, CLD patients who had characteristic symptoms of PH such as dyspnea on exertion underwent transthoracic echocardiography (TTE). We performed right heart catheterization (RHC) to those with high estimated right ventricular pressure (eRVP) to measure mean pulmonary artery pressure (PAPm) and analyzed the correlation with other indexes; arterial blood gas (ABG) parameters and radiographic findings.

Results: Twenty four patients were enrolled (median age; 70.5 year-old, male; 58%). Median eRVP was 38mmHg (29-100mmHg) and median PAPm was 20.5mmHg. Patient distribution by PAPm was as follows: ≥25mmHg, 16%, 20-24mmHg, 33% and <20mmHg, 50%. There were high correlation between eRVP and PAPm. Radiographic findings; diameter of right descending pulmonary artery (PA), abrupt tapering of the peripheral vessels in chest X-ray and diameter of PA and PA/aorta diameter ratio in chest computer tomography and ABG: PaO2, PaCO2 and HCO3 parameters showed middle to strong correlations with PAPm.

Conclusions: In this study, patients who met the criteria of PH were limited to 13%. However, there were 50% patients showing PAPm≥20mmHg. Since previous studies showed poor prognosis for patients with PAPm ≥20mmHg, we should concern early intervention for this certain amount of population. In our patients, not only eRVP but other indexes showed correlation with PAPm. Along with TTE, radiographic and ABG findings may be simple daily objective parameters of PH in CLD patients.

AP154

RELATIONSHIP BETWEEN CD4 COUNT WITH TROPONIN I (CTNI) LEVEL IN HIV/AIDS PATIENTS

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Background: Several studies have shown that an increasing incidence of cardiovascular disease in HIV patients associated with traditional risk factors for cardiovascular disease, antiviral treatment, low HDL levels, and HIV-inflammatory status itself. CD4 lymphocytes are the main target of HIV infection because the virus has an affinity for the CD4 surface molecule. Cardiac troponin (cTnI) has been used generally as a sensitive and specific marker in the detection of myocardial injury.

The aim of this study is to evaluate relationship between CD4 count and troponin I levels in HIV / AIDS patients.

Methods: This research is a descriptive analytical research with cross sectional method. The study was conducted in Inpatient, Outpatient institution and Pathology Laboratory Clinic of Dr. dr. Wahidin Sudirohusodo Hospital Makassar starting from March 2017 until sufficient number of samples.

Results: During the sampling period from March 2017 to April 2017, the number of samples fulfilled the inclusion criteria was 43 patients. Groups with elevated troponin had lower CD4 levels than those with normal troponin (144.9 ± 118.3 vs. 293.9 ± 111.3, p <0.001). In this study found a significant relationship between CD4 count with troponin I levels, where the direction of the relationship is reversed (p <0.005). The most common cardiac abnormality found by echocardiography is ventricular diastolic dysfunction (72.2%). Groups with cardiac abnormalities had lower CD4 counts compared with those without cardiac abnormalities. In addition, there is a relationship between the two, where the greater the CD4 count, the less likely to find cardiac abnormalities (OR 0.99, p <0.034).

Conclusion: There is relationship between CD4 count and troponin I levels in HIV / AIDS patients.

Respiratory Neurobiology Sleep

AP155

AWARENESS AND KNOWLEDGE OF OBSTRUCTIVE SLEEP APNEA AMONG THE GENERAL POPULATION

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Background and Aims: Obstructive sleep apnea (OSA) is an increasingly prevalent condition that remains largely undiagnosed. Strategies to optimize diagnosis and treatment of OSA are dependent on public awareness of the disease.

Methods: We aimed to assess the level of awareness and knowledge of OSA among the general population. The Singapore Health 2 was a population-based study that comprised interview and health screening components. Out of 2,720 subjects who completed the interview component, 2080 subjects gave consent for further health surveys. We contacted these subjects and conducted a structured telephone interview.

Results: We completed 1306 telephone interviews (response rate 62.8%). The mean age (standard deviation) of the respondents was 47.1 (14.8) years and 567 (43.4%) were males. Two hundred and eighty-one (21.5%) respondents were aware of OSA, but only 170 (13.0%) respondents could define OSA correctly. A total of 77 (5.9%), 158 (12.1%), 150 (11.5%) and 110 (8.4%) respondents were able to correctly list at least one risk factor, symptom, health consequence and treatment options for OSA, respectively. The most common sources of information about OSA were traditional media such as newspapers (42.0%), internet (14.2%) or relatives and friends (14.6%). On multivariate analysis, respondents were more likely to define OSA correctly if they were older (≥61years), (odds ratio of 2.99, 95% Confidence Interval [CI]: 1.66-5.41), were Chinese as compared to Indians (odds ratio 2.63, 95% CI: 1.66-4.72), had higher levels of income (odds ratio 2.18, 95% CI 1.16-4.10) and post-secondary education (odds ratio 2.87, 95% CI: 1.28-6.45).
HIGH PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH ASTHMA

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Background and Aim: Previous reports regarding sleep disorder in allergic diseases including asthma are limited. Sleep disorder is known to cause fatigue and daytime sleepiness and may worsen asthma control and quality of life. Moreover, it increases the risk of various diseases such as hypertension, diabetes and cardiovascular disease. Although sleep disorder is considered one of high risk factor for systemic inflammation, the association of sleep disorder with asthma is not fully clarified. Both asthma and obstructive sleep apnea (OSA) are common diseases and therefore may often coexist. However, the prevalence of OSA in asthmatics is not well established. In this investigation, we focused on the association between asthma and OSA utilizing screening questionnaires.

Methods: Study participants enrolled in this study consist of asthma patients(n=89) who regularly visited Saitama medical university hospital. Screening questionnaires included a physique, Asthma Control Test (ACT), Pittsburgh Sleep Quality Index (PSQI), Berlin questionnaire, Epworth Sleepiness Scale (ESS), and Hospital Anxiety and Depression scale (HADS). Sleep study was carried out in asthma patients suspicious of OSA by these questionnaires.

Results: A total of 89 patients with asthma were divided into 2 groups: 39 were suspicious OSA, 50 were not suspicious. Twenty four of 39 asthma patients with suspicious OSA carried out sleep study, and 16 of them were diagnosed as OSA. Finally, 10 of 16 patients treated with CPAP.

Conclusion: Although it is reported OSA prevalence is 3 to 7% in general population, the prevalence of OSA with asthma showed quite high: approximately 18% in the present study. These findings suggest a certain relationship among not only asthma control and/or asthma medication, but also various factors causing systemic inflammatory conditions, such as obesity, sleep disorders, depression, anxiety and so on.

CLINICAL AUDIT OF ADHERENCE TO CONTINUOUS POSITIVE AIRWAYS PRESSURE (CPAP) IN OBSTRUCTIVE SLEEP APNOEA (OSA)

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Background and Aims: Benefits of CPAP in treating OSA are well established. CPAP adherence improves with reinforcement and follow-up. Prior to the availability of telemonitoring, sleep services in the UK generally had a policy of discharging most patients, except lorry drivers. Several variables have been implicated in non-adherence, however study results have been inconsistent. We aimed to identify reliable predictors of CPAP adherence, including the apnoea-hypopnoea index (AHI) and co-morbidities, in order to improve follow-up protocol. Subsequently, this would allow us to explore the application of telemonitoring to optimise outcomes.

Methods: Data from 248 patients completing annual follow-up after initiation of CPAP for OSA by 31st December 2014 was collected retrospectively. CPAP usage per day was averaged over the preceding year. AHI at diagnosis was used as a marker of OSA severity. The association between usage and initial AHI (data available for 207 patients) was analysed by linear regression. The severity of co-morbidities was assessed using the Adult Co-morbidity Evaluation-27 (ACE-27) score, which was analysed against usage by ANOVA.

Results: Initial AHI against CPAP usage was statistically significant (p=0.00126, fitted equation: Adherence= 4.161+0.024xAHI). There was no significant difference in CPAP usage between different ACE-27 groups. However, analysis of individual co-morbidities revealed significance in three sub-categories: cardiac arrhythmia (p=0.031), coronary artery disease (p=0.006) and congestive heart failure (p=0.045).

Conclusions: AHI at diagnosis remains a strong determinant of CPAP adherence at 1 year. In light of this, we recommend that those with moderate severity of OSA (AHI 15-29) and/or those with cardiac co-morbidities are also monitored more regularly to ensure sustained adherence to CPAP. The advent of telemonitoring in CPAP adherence and remote adjustment opens new avenues of CPAP follow-up, for which we have now set up a pilot that will be re-audited as part of our quality improvement project.
This abstract has been withdrawn

**AP157**

**Methods:** A review of medical reports of patients who did a sleep study at National University Hospital, Singapore, between January 2014 and March 2017 was carried out. SA severity (x) was defined as Total number of Apneic events/ Total Sleep Time (in hours); Pure Obstructive events was defined as Total number of Obstructive Apneic events/ Total Sleep Time (in hours), with the ranges coded as Normal: x<5; Mild 5≤x<15; Moderate 15≤x<30; Severe x≥30.

**Results:** A total of 1616 patients were studied, after excluding 5 patients with incomplete data. There were 7.1% (108/1513) of patients who were diagnosed with SA, but had no symptoms of snoring. Interestingly, this also held true, for 2.9% (20/692) of patients, when only pure obstructive events were considered in the numerator; indicating that even in extreme cases, snoring is not a definite symptom.

**Conclusion:** The absence of snoring does not exclude the diagnosis of SA; and all symptomatic patients should be evaluated for SA, even in the absence of snoring.

**AP159**

**Effect of Sleep Time Versus Bed Time Denominators on the Classification of Sleep Apnea Severity**

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**Background and Aim:** Sleep apnea that results in intermittent hypoxia is associated with increased cardiovascular risk and greater morbidity and mortality. Traditionally, the indicator of severity (X) is expressed as the number of apneic events per hour of sleep, using total sleep time as the denominator. A meta-analysis of previous studies reports that portable studies may underestimate sleep apnea severity, but did not discern the cause. No studies to date have analysed how severity may be affected by the determination of sleep.

This study aims to analyse the effect of different denominators on the classification of sleep apnea severity, and hence the importance of electroencephalogram (EEG) determination of sleep.

**Methods:** A review of laboratory sleep studies done at National University Hospital, Singapore, between January 2014 and March 2017 was carried out. Sleep apnea events included obstructive, mixed, central and hypopnea events unless otherwise stated. Sleep apnea severity was coded as Normal(0) X<5; Mild(1) 5≤X<15; Moderate(2) 15≤X<30; Severe (3) X≥30. The use of total sleep time as a denominator was compared to that of total bed time.

**Results:** A total of 1616 patients were studied, after excluding 5 patients with incomplete data. Using bed time rather than sleep time as the denominator lead to 10.4% (32/308) of patients with mild sleep apnea being classified as normal. 2.5% (21/843) of patients with severe sleep apnea, were likewise classified as normal/mild when bed time was used. 27.5% (39/142) of patients classified as normal using bed time as the denominator, actually had mild/moderate/severe sleep apnea.

**Conclusion:** Sleep apnea severity can be significantly underestimated if bed time rather than sleep time as the denominator lead to 10.4% (32/308) of patients with mild sleep apnea being classified as normal. 2.5% (21/843) of patients with severe sleep apnea, were likewise classified as normal/mild when bed time was used. 27.5% (39/142) of patients classified as normal using bed time as the denominator, actually had mild/moderate/severe sleep apnea.

**Conclusion:** The absence of snoring does not exclude the diagnosis of SA; and all symptomatic patients should be evaluated for SA, even in the absence of snoring.
ASSOCIATION BETWEEN RISK OF OBSTRUCTIVE SLEEP APNEA AND DEGREE OF EXCESSIVE DAYTIME SLEEPINESS AMONG ADMINISTRATION STAFF OF UNIVERSITAS INDONESIA

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Background: Obstructive sleep apnea (OSA) is one of sleep-related breathing disorders in which there are repeated obstructions in the upper airway during night-time sleep. OSA can cause fragmentation of sleep that leads to excessive daytime sleepiness. When someone is sleepy, there is a slight reduction of perception and change of emotion, negatively affecting work productivity. 

Methods: A total population-based sample of administration staff of Universitas Indonesia were asked to fill in the Epworth Sleepiness Scale (ESS) questionnaire to grade daytime sleepiness and the STOPBANG questionnaire to predict the risk of OSA.

Results: More than half of the subjects who were at high risk of OSA experienced excessive daytime sleepiness. However, no correlation was found between the degree of daytime sleepiness and the risk of OSA in administration staff of Universitas Indonesia.

Conclusion: There was no association between degree of daytime sleepiness and risk of OSA in administration staff of Universitas Indonesia. In addition, there was no association between risk factors of OSA, such as gender, age, BMI, and smoking habit with excessive daytime sleepiness. Further research is needed to understand the other causes of excessive daytime sleepiness in administration staff of Universitas Indonesia.

PREDICTION OF OBSTRUCTIVE SLEEP APNEA (OSA) AND ITS CORRELATED FACTORS TO RISK OF OSA ON ADMINISTRATION STAFF OF UNIVERSITAS INDONESIA USING STOP-BANG QUESTIONNAIRES

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Background and Aim: Obstructive sleep apnea (OSA) is a respiratory disorder arising from obstruction in the upper respiratory tract, disturbing sleep cycle. Patients with OSA could not sleep well and experience arousal during effortful breathing. Employees with OSA were expected to have a decrease in fitness and an increase in sleepiness and fatigue, implicating performance at work and quality of life.

Methods: Data collection was held twice; once to each respondent based on cross-sectional method. As many as 191 administration staff of Universitas Indonesia, majority of whom were female, filled STOP-Bang questionnaires and underwent weight, height, and blood pressure examination to determine the risk prevalence and its relation to blood pressure, BMI, age, neck circumference, sex, and smoking.

Results: Among them, 158 (82.7%) respondents were classified as low risk, 14 (7.3%) moderate risk, and 19 (9.9%) high risk. OSA was found to be significantly related to age, sex, and smoking (p<0.01), related to blood pressure by bidirectional relationship; insignificantly related to BMI (p=0.306) and neck circumference (p=0.153). It was found only 5 respondents in each group with BMI >35 kg/m2 and neck circumference ≥41 cm or 43 cm.

Conclusion: Risk of OSA is statistically related to all risk factors proposed in this study, but BMI and neck circumference, due to unequal sample sizes within each study group. The majority of respondents with moderate and high risk were known to have more than one risk factor.
THE EFFECT OF EDUCATION ABOUT LIFESTYLE ON KNOWLEDGE AND ATTITUDE CHANGES AMONG OBESITY EMPLOYEES IN UNIVERSITAS INDONESIA

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Background and Aim: One of the risk factors of sleep disordered breathing is obesity. It is believed that unhealthy lifestyle, stemming from poor knowledge-attitude, plays a big role in the pathogenesis of obesity. Therefore, if people have good knowledge-attitude towards lifestyle, the risk of getting obesity and sleep disordered breathing could be reduced. This research aims to enhance the knowledge and attitude of employees in Universitas Indonesia who had body mass index of more than 23 (n=52).

Methods: The author used intervention method in the form of mass counseling which conducted on August 2016. Questionnaire was given before and after education as an instrument to measure changes in knowledge-attitude towards lifestyle. There are 3 tests that were used to analyze the data. First, paired T test and Wilcoxon test were performed to see whether there was a significant change in knowledge-attitude before and after counseling. Afterwards, Fisher test was done to see the relationship between knowledge-attitude changes and respondents’ sociodemographical factors.

Results: Statistical analyses showed significant difference between knowledge-attitude before education and knowledge-attitude after education (p<0.001). Mean of knowledge score before education was 13.29 (+/- 3.99) and after education was 16.40 (+/- 4.10). Meanwhile, mean of attitude score before education was 31.69 (+/- 2.23) and after education was 36.90 (+/- 4.49). Age and gender have significant relationship with attitude changes (p=0.007 and p=0.034).

Conclusion: In conclusion, education in the form of mass counseling enhances knowledge-attitude changes significantly. This could encourage better behavior; especially in lifestyle hence it would decrease risk of getting obesity and sleep disordered breathing.

Acknowledgement: First, I would like to express my gratitude to my mentor, Prof. dr. Menaldi Rasmid and Dr. dr. Saptawati Bardosono who gave me great opportunity to do this research project. Second, to my beloved parents, grandmother, and friends who have helped and supported me in finishing this project.

DIFFERENCES IN PREDICTED THERAPEUTIC OUTCOME AND OPTIMAL PROTRUSION POSITION OF ORAL APPLIANCE DETERMINED DURING REMOTELY CONTROLLED MANDIBULAR POSITION BETWEEN CANADIAN AND CHINESE OSA PATIENTS

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Background and Aims: In-lab mandibular protrusive titration using a Remotely Controlled Mandibular Positioner (RCMP, MATRix, Zephyr sleep technologies, Canada, CDN) has been found to predict the success rate of oral appliance (OA) in obstructive sleep apnea (OSA) and reliably determine the Optimal Protrusive Position (OPP) for participants predicted to be therapeutically successful with oral appliance therapy in these patients. The aim of this prospective pilot study was to compare OA success rate and OPP using in-lab RCMP titration performed in Canadian (Quebec, Canada) and Chinese (Shenyang, China) OSA patients.

Methods: 23 untreated Canadian and 16 Chinese OSA patients were recruited (inclusion criteria: age: 20-75 years, AHI:15-50/hr, BMI < 40 kg/m2). In each center, manual RCMP titration was performed during an in-lab sleep study using a same procedure that had been previously reported.

Results: Anthropometric features and OSA severity didn’t differ between Canadian and Chinese subjects. The habitual occlusal position of lower mandible (determined by the scales on RCMP trays) was lower in Chinese patients than in Canadians (3.91 ± 1.95 mm vs. 9.76 ± 2.22 mm, p < 0.01, independent T-test), with similar maximal mandibular advancement level (17.24 ± 1.51 vs. 17.14 ± 1.55, p = 0.05). The predicted success rate according to the RCMP titration tend to be lower in Canadians (41%) than its rate in Chinese (78%) (p = 0.07, chi-square test). Among patients with predicted success, the mean OPP was 16.24 ± 2.02 mm (94.6 % ± 11% of maximal protrusion) in Canadians, which tended to be higher than its value in Chinese subjects (14.03 ± 2.86 mm, 81.1% ± 13% of maximal protrusion, p = 0.08).

Conclusions: According to in-lab RCMP titration, Chinese OSA patients appear to be more prone to benefit from OA treatment than Canadians, with lower level of optimal mandibular advancement.

PREDICTORS OF CPAP THERAPY ADHERENCE FOR OBSTRUCTIVE SLEEP APNEA

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Background and Aims: Obstructive Sleep Apnea (OSA) has serious adverse health social and community effects arising from disturbed breathing during sleep. Continuous Positive Airway Pressure (CPAP) which acts as a pneumatic splint to the upper airway is the most common and effective treatment for OSA. When applied during sleep, CPAP effectively reduces or eliminates most sleep-disordered breathing events; thereby increasing consolidated sleep and improving sleep architecture. However, CPAP is known to have problems with adherence, with many patients eventually abandoning the device. Therefore, this study aimed to determine the potential and quantifiable factors affecting CPAP adherence.

Methods: A retrospective study was performed 27 patients who received both polysomnography (PSG) and CPAP titration were included from July 2013 to May 2016. Twenty seven patients divided into two groups from CPAP usage which downloaded to obtain the data. These two groups were examined by comparing the polysomnographic parameters between diagnostic and titration.

Results: Twenty seven patients with OSA aged 54.5±11.9 years old with a BMI 29.3±6.0 kg/m2 with excessive daytime sleepiness, habitual snoring and the patients include 19 males and 8 females. Seventeen patients were classified as “adequate adherence group” as they used CPAP on average over 4 hours per night since CPAP therapy was initiated. Ten patients who did not use CPAP at all were indicated as the “inadequate adherence group”.

Conclusions: These findings may demonstrate that characteristics of sleep architecture, between diagnostic PSG and CPAP titration PSG, predict some of the variance in CPAP adherence. Furthermore, better impression after sleep on the first titration night might be related to better CPAP adherence.
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Background and Aims: Obstructive sleep apnea (OSA) is associated with worse cardiovascular outcomes and a high prevalence of anxiety and depression. This study investigated the effects of CPAP on the severity of anxiety and depression in OSA patients with or without CAD, and on the rate of cardio- and cerebrovascular events in those with OSA and CAD.

Methods: This prospective study included patients with moderate-to-severe OSA, with or without a recent diagnosis of CAD, all were started on CPAP (S8; ResMed). Patients completed Chinese versions of the Beck Anxiety Inventory (BAI) and Beck Depression Inventory-II (BDI-II) at baseline and after 6 months. Occurrence of major adverse cardiac and cerebrovascular events (MACCE) was assessed every 3 months up to 1 year.

Results: In patients with good CPAP compliance, BAI scores decreased from 8.5±8.4 at baseline to 5.4±6.9 at 6 months (OSA; p<0.05) and from 20.7±14.9 to 16.1±14.5 (OSA/CAD). Corresponding values for BDI-II scores were 11.1±10.7 to 6.6±9.5 (OSA; p<0.05) and 20.4±14.3 to 15.9±7.3 (OSA/CAD). Besides, there was large effect size of BAI and BDI in 6-month CPAP treatment of OSA/CAD and large effect size in those with OSA under CPAP treatment. Those with OSA/CAD compliant to CPAP had significant lower MACCE than non-compliant with 1 year follow up (11% in CPAP compliant and 50% in non-compliant, p<0.05).

Conclusions: CPAP improved anxiety and depression in patients with OSA and OSA/CAD, and decreased the 1-year rate of MACCE in patients with OSA and CAD.

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HOME MECHANICAL VENTILATION FOR PATIENTS WITH CHRONIC RESPIRATORY FAILURE: A REGIONAL HOSPITAL EXPERIENCE

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Background and Aim: Home mechanical ventilation (HMV) is an established treatment for Chronic respiratory failure (CRF) which improves survival and quality of life particularly in selected patients with chest wall or neuromuscular disorders. Due to the special expertise required in the management of HMV patients, most care is provided and co-ordinated by tertiary metropolitan hospitals. Recently there has been a trend to de-centralise care of HMV patients. However it is not known if the resource utilisation and patterns of HMV usage in regional hospitals is different compared to metropolitan hospitals.

Methods: We retrospectively evaluated patients who were prescribed HMV at Gold Coast Hospital and Health Service (GCHHS) between the years 2010 to 2017. Patients’ demographic data, diagnosis, indication of HMV, duration of therapy, treatment adherence, interface and machine settings, and overall survival were analysed. We also compared the pattern of HMV usage at our institution with previously published literature.

Results: Clinical data was available for sixty-one patients. 35 (57%) patients were female and mean (±SD) age was 58±18 years. The most common indications for HMV were obesity hypoventilation syndrome (26%), motor neurone disease (MND) (26%), muscular dystrophy (23%) and COPD (16%). Patients underwent a mean (±SD) of 1.6±1.2 polysomnograms and 84% of these studies were performed as in-patient studies. After commencement of HMV patients had a mean (±SD) 5.4±2.8 number of out-patient clinic reviews. During the study period, 23 (38%) patients had died and the mean (±SD) overall survival of the study cohort was 24±20 months since commencement of HMV.

Conclusion: Our study describes the prevalence of HMV usage at GCHHS and these findings can assist in local HMV service planning and provision. The patterns of HMV prescription are broadly consistent with previously published literature. Future research will focus on comparing patient outcomes between our institution and metropolitan hospitals.

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These pores, together with overt fissures in alveolar walls, allowed leakage of plasma components into alveoli. These findings appear to be important features of RPE development.

**AP169**

**COMPARISON OF BRONCHODILATION TEST IN RECURRENT WHEEZING INFANTS WITH ATOPY OR WITHOUT ATOPY**

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**Background:** Wheezing is a common symptom of respiratory disease in infants, and asthma is a major cause of chronic respiratory disease in children. Airway responsiveness test is the most important method of asthma diagnosis and evaluation in older children, especially the bronchial dilation test, which can reflect airway reversibility objectively. But it is unknown whether bronchial dilation test can identify infants from different wheezing phenotypes.

**Objective:** To explore the change of ventilation function and airway resistance after inhaled bronchodilators in recurrent wheezing infants with or without atopy, and assess the application value of the bronchial dilation test in different phenotypes of wheezing.

**Methods:** Tidal pulmonary function test, single occlusion test and plethysmography were performed in 30 recurrent wheezing infants with atopy and 28 wheezing infants without atopy before and after salbutamol inhalation. To compare their changes of lung function parameters before and after inhalation of bronchodilators.

**Results:** Lung function parameters in recurrent wheezing infants with atopy after inhalation bronchodilators: TV/Kg, RR, TPTEF/TE, VPEF/VE, Reff were improved significantly (5.74±7.22)%,- (4.88±6.70)%, (9.86±16.30)%, (11.84±15.57)%, (-10.51±41.41)%, respectively, p<0.05). In control group after inhalation bronchodilators: RR, VPEF/VE were also improved significantly (3.71±8.05), (7.18±12.04), respectively, p<0.05), while the changes of TV/Kg, TPTEF/TE, Reff have no statistically significant difference.

**Conclusion:** The tidal pulmonary function bronchodilation test is difficult to identify from recurrent wheezing infants with atopy to whom without atopy. Airway resistance decreased in atopy group after bronchodilation test but not in control group. Moreover, the airway reversibility in recurrent wheezing infants with atopy was higher than whom without atopy.

**Key words:** Recurrent Wheezing; Atopy; Plethysmography; Bronchodilation test; Airway resistance (Reff)

**AP170**

**PROFILING OF PEFR RANGE IN TIBETAN YOUTH POPULATION LIVING IN INDIA - AN INTERVENTIONAL STUDY**

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**Introduction:** The scale that we use for PEFR is borrowed from European standards and there are no Indian standards. Individuals living in high altitudes have better lung function when compared to their counterparts in lower altitude. This study was conducted to study the PEFR values in Tibetians who relocated from higher altitude to lower altitude.

**Methods:** After receiving an ethical approval, a prospective intervention Study was conducted inside a university campus in south India. The study duration was seven months. Healthy adults aged between 18 to 30 years and non-smokers, were included. Demographic data, anthropometric measurements and PEFR values were recorded.

**Results:** A total of 55 students were included in the study of which 16 were males and 39 were females. The mean PEFR values obtained were 582.49 (±69.84) for males and 324.98 (±53.34) for females. Mean height of the participant was 161.98 ± 9.078, chest circumference 33.675 ± 3.246 and mean age 21.381 ± 1.545. The data below show PEFR as a function of height of the participant. The coefficient of determination was (r²) was 0.666. The chart illustrates the PEFR data

**Conclusion:** PEFR positively correlates with height, weight and chest circumference. Height had a significant influence on the PEFR value (66%).

**AP171**

**USE OF THE FORCED OSCILLATION TECHNIQUE TO ESTIMATE SPIROMETRY VALUES**

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**Background and Aims:** Spirometry is sometimes difficult to perform in elderly patients and in those with severe respiratory distress. The forced oscillation technique (FOT) is a simple and noninvasive method of measuring respiratory impedance. The aim of this study was to determine if FOT data reflect spirometric indices.

**Methods:** Patients underwent both FOT and spirometry procedures prior to inclusion in development (n=1089) and validation (n=552) studies. Multivariate linear regression analysis was performed to identify FOT parameters predictive of vital capacity (VC), forced vital capacity (FVC), and forced expiratory volume in 1 second (FEV1). A regression equation was used to calculate the estimated VC, FVC, and FEV1. We then determined whether the estimated data reflected spirometric indices.
Abstracts

**Results:** Significant correlations were observed between actual and estimated VC, FVC, and FEV₁₀ values (all r>0.6 and P<0.001). These results were deemed robust by a separate validation study (all r>0.8 and P<0.001). However, the bias between the estimated data and the actual data for VC, FVC, and FEV₁₀ in the validation study was -0.201 L, -0.267 L, and -0.174 L, respectively, suggesting that the estimated data in the validation study did not have high accuracy.

**Conclusions:** Further studies are needed to generate more accurate regression equations for spirometric indices based on FOT measurements.

**THE BASIC INTERPRETATION OF THE IMPEDANCE OF RESPIRATORY SYSTEM MEASURED BY FORCED OSCILLATION TECHNIQUE**

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**Background and Aims:** Although the Forced Oscillation Technique (FOT) was widely utilized in the clinical evaluation of airway disease, there were few reports for basically understanding for the meanings of the impedance of respiratory system (Zrs, respiratory resistance (Rrs) and respiratory reactance (Xrs)).

We assessed the fundamental meanings of the components of Zrs using a phantom model.

**Methods:** We measured Zrs of a 3.0-L metallic syringe, which was connected to the outlet of a commercially available FOT device (MostGraph-01, Ver.1.70R, CHEST MI. Inc., Tokyo, Japan).

Model 1: We measured Zrs when the air capacity of the syringe was set at 2.0, 2.5, 3.0-L. Each measurement was performed during 10 seconds with impulse signals generated.

Model 2: To imitate the tidal breath, Zrs was consecutively measured all the while the piston of the syringe was shuttled from the position of 2.0-L to that of 3.0-L in 2 seconds cycle. We simultaneously measured the flow velocity and calculated its acceleration.

**Results:** Model 1: The magnitude of Rrs of 5Hz (R5) was 2.04, 1.97, 1.59 cmH2O/L/sec at 2.0-, 2.5-, 3.0-L, respectively. The magnitude of Xrs of 5Hz (X5) was -7.70, -5.73, -4.97 cmH2O/L/sec at 2.0-, 2.5-, 3.0-L, respectively. The magnitude of Xrs of 5Hz (X5) was -7.70, -5.73, -4.97 cmH2O/L/sec at 2.0-, 2.5-, 3.0-L, respectively. The magnitude of Xrs of 5Hz (X5) was -7.70, -5.73, -4.97 cmH2O/L/sec at 2.0-, 2.5-, 3.0-L, respectively.

Model 2: Because Rrs showed positive prominent change synchronously with flow, the three-dimensional graphic pattern of Rrs was showed as the bimodal pattern. The mean magnitude of Rrs during mimic respiratory cycle was 6.71 cmH2O/L/sec. At the position of 2.0-, 3.0-L, the flow velocity was zero, but the magnitude of acceleration was detected (0.69, -0.45 L/sec, respectively). The value of R5 (2.20, 2.28 cmH2O/L/sec at 2.0-, 3.0-L, respectively) was higher than that in Model1.

**Conclusions:** Our data suggested that it was necessary to consider the involvement of lunge volume, respiratory flow velocity and its acceleration when we interpreted the clinical data of Zrs measured by FOT.

**HOW DO THE PROXIMAL AND PERIPHERAL ASTHOMATIC AIRWAYS RESPOND WHEN PROVOKED DIRECTLY AND INDIRECTLY?**

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**Background and Aim:** Bronchoconstriction is a typical response when the asthmatic airways are provoked. However, little is known about how other physiological features of the airways change in parallel, specifically in the proximal and peripheral airways. This study aims to determine how airway resistance (AR), ventilation heterogeneity (VH) and nitric oxide activity (NO) changes in the same proximal and peripheral airways when provoked by direct and indirect means.

**Methods:** Newly diagnosed (untreated) patients with atopic Asthma were recruited for the study (n=9). All subjects demonstrated a clinically positive test based on Spirometry to both direct (Methacholine) and indirect (Mannitol) provocation tests on separate visits, ~7-days apart. On another visit, a placebo provocation was also performed. Before and immediately after each provocation test, the following measures were made; AR using the Forced Oscillation Technique, VH using the Multiple Breath Nitrogen Washout technique and NO using the Multiple Exhalation Flow technique.

**Results:** There was no significant change (p>0.05) in lung volumes measures (FRC, RV and TLC) from the washout technique after any of the provocation tests. All other changes are tabulated below (mean ± SEM).

**Conclusions:** In asthma, when the proximal airways were provoked directly and indirectly, both AR and VH increased in response. However, NO decreased only when the airways were provoked indirectly. When the peripheral airways were provoked directly and indirectly, VH remained unchanged while AR increased in response. However, NO decreased only when the airways were provoked indirectly. Overall, provoking the airways resulted in more physiological changes in the proximal airways than the peripheral airways. All these physiological changes were demonstrated in the absence of any change in lung volumes or gas trapping.

**Support:** Australia and New Zealand Society of Respiratory Science.

**Variability of Forced Expiratory Manoeuvre in Patients with Advanced Neuromuscular Diseases**

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**Background and Aim:** Using Forced Expiratory Manoeuvres in patients with advanced Neuromuscular diseases is commonly performed to determine the respiratory function. However, the variability of these measures is not well established. The aim of this study was to establish the variability of Forced Expiratory Manoeuvres in patients with advanced Neuromuscular diseases.

**Methods:** The study was approved by the Ethics Committee of the Alfred Hospital. Patients with advanced Neuromuscular diseases were recruited (n=9). All subjects demonstrated a positive test based on Spirometry to both direct (Methacholine) and indirect (Mannitol) provocation tests on separate visits, ~7-days apart. On another visit, a placebo provocation was also performed. Before and immediately after each provocation test, the following measures were made; AR using the Forced Oscillation Technique, VH using the Multiple Breath Nitrogen Washout technique and NO using the Multiple Exhalation Flow technique.

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**Conclusions:** In asthma, when the proximal airways were provoked directly and indirectly, both AR and VH increased in response. However, NO decreased only when the airways were provoked indirectly. When the peripheral airways were provoked directly and indirectly, VH remained unchanged while AR increased in response. However, NO decreased only when the airways were provoked indirectly. Overall, provoking the airways resulted in more physiological changes in the proximal airways than the peripheral airways. All these physiological changes were demonstrated in the absence of any change in lung volumes or gas trapping.

**Support:** Australia and New Zealand Society of Respiratory Science.

<table>
<thead>
<tr>
<th>Measures</th>
<th>Units</th>
<th>Prox.</th>
<th>VH</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td>R₁₀</td>
<td>hPa/(L/sec)</td>
<td>-0.094±0.156</td>
<td>+0.990±0.266*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.003±0.003</td>
<td>+0.02±0.006*</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-0.394±0.097</td>
<td>-0.65±0.193</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+0.261±0.166</td>
<td>+2.70±0.506*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+0.013±0.013</td>
<td>+0.041±0.008</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>+1.225±0.842</td>
<td>-0.94±0.342</td>
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</tbody>
</table>

Background and Aim: Assessment of ventilatory capacity via forced expiratory manoeuvre (FEM) in patients with neuromuscular weakness is important during consideration for home mechanical ventilation (HMV) but the variability of FEM is not well-described. We aim to study the variability of FEM in these patients.

Methods: Retrospectively, 98 consecutive patients with neuromuscular disease referred for evaluation of HMV from 2008 to 2015 were screened. 50 patients who had baseline spirometry were identified and divided into motor neurone disease (MND) (33, 66%) and non-MND (17, 34%) group for analysis. All spirometry were performed at the Respiratory Function Laboratory, Tan Tock Seng Hospital on calibrated equipment. All FEMs were individually reviewed. The coefficient of variation (COV) of 3 best trials of each patient were calculated.

Results: MND patients were older, similar in gender distribution, body mass index and HMV use compared to non-MND patients (see Table 1). Median (interquartile range, IQR) FVC was 39 (24-59) %predicted in MND and 38 (26-68) %predicted in non-MND. More MND patients (23, 70%) failed to meet spirometry standards than non-MND patients (4, 24%) (p<0.01, Fisher’s exact test); most of these were due to inability to meet within-manoeuvre end of test criteria (16 in MND, 4 in non-MND).

Only 2 patients in each group were unable to demonstrate repeatable FVC (within 150mLs difference). FEV1 in non-MND patients were significantly less variable than MND patients (COV 1.7, IQR 1.5-3.3 versus 4.7, IQR 2.5-7.5%; p<0.01, Mann-Whitney U test for continuous data; Mann-Whitney U test for categorical data; see Table 1). Differences for intra- and inter-network connectivity between normal and effort breathing were investigated using FMRIB Software Library (FSL) tools (Melodic ICA, dual regression, FSL Nets).

Table 2. Spirometry abnormality and variability. *Mann-Whitney U test. MND = Motor neurone disease. IQR = Interquartile range. FEV1 = Forced expiratory volume 1 second. FVC = Forced vital capacity. PEFR = Peak expiratory flow rate. COV = Coefficient of variation.

<table>
<thead>
<tr>
<th></th>
<th>MND (n=33)</th>
<th>Non-MND (n=17)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of trials</td>
<td>8</td>
<td>6-8</td>
<td>6-4-8</td>
</tr>
<tr>
<td>FEV1, L (%)</td>
<td>1.1 (43)</td>
<td>0.6-1.6</td>
<td>1.0 (38)</td>
</tr>
<tr>
<td>predicted</td>
<td>(27-65)</td>
<td>(33-38)</td>
<td>(0.94)</td>
</tr>
<tr>
<td>FEV1 COV, %</td>
<td>4.7</td>
<td>2.5-7.5</td>
<td>1.7</td>
</tr>
<tr>
<td>FVC, L (%)</td>
<td>1.2 (39)</td>
<td>0.7-1.6</td>
<td>1.1 (38)</td>
</tr>
<tr>
<td>predicted</td>
<td>(24-59)</td>
<td>(26-68)</td>
<td>(0.69)</td>
</tr>
<tr>
<td>FVC COV, %</td>
<td>4.7</td>
<td>2.8-9.0</td>
<td>3.2</td>
</tr>
<tr>
<td>PEFR, L/s (%)</td>
<td>3.1 (43)</td>
<td>1.6-4.3</td>
<td>3.3 (51)</td>
</tr>
<tr>
<td>predicted</td>
<td>(32-64)</td>
<td>(40-75)</td>
<td>(0.29)</td>
</tr>
<tr>
<td>PEFR COV, %</td>
<td>5.4</td>
<td>2.7-9.5</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Conclusion: In advanced neuromuscular diseases, a significant proportion of patients, especially in MND, was unable to perform FEMs that meet acceptability criteria. Between-manoeuvre variability of FEV1, FVC and PEFR were acceptable when best FEM trials were selected.

Table 1. Baseline demographics. *Fisher’s exact test for categorical data; Mann-Whitney U test for continuous data. MND = Motor neurone disease. BMI = Body mass index. HMV = Home mechanical ventilation. ATS = American Thoracic Society.

<table>
<thead>
<tr>
<th></th>
<th>MND (n=33)</th>
<th>Non-MND (n=17)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62 (53-67)</td>
<td>46 (33-55)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male, %</td>
<td>55</td>
<td>47</td>
<td>0.77</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>18.4</td>
<td>18.3</td>
<td>0.56</td>
</tr>
<tr>
<td>(16.9-23.4)</td>
<td>(15.1-21.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMV, %</td>
<td>76</td>
<td>88</td>
<td>0.46</td>
</tr>
<tr>
<td>Failed to meet ATS criteria, %</td>
<td>70</td>
<td>24</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

AN OPTIMIZED MEASUREMENT OF EFFORT BREATH BY FUNCTIONAL MRI

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Background and Aims: Several studies have mapped brain regions associated with acute dyspnea perception. However, the effect breath on central nerve networks is still unknown. Our objective was to determine the resting state networks during dyspnea.

Methods: Resting-state functional magnetic resonance imaging (rsfMRI) data was collected for 16 healthy control with or without effort breath devices.

Differences for intra- and inter-network connectivity between normal and effort breathing were investigated using FMRIB Software Library (FSL) tools (Melodic ICA, dual regression, FSL Nets).

Results: Eighteen ICA maps were identified as components of neuronal origin. For intra-network connectivity changes, effort breathing caused significant connectivity increase within the cerebellum and the anterior insular-anterior cingulate cortex network. There was decreased connectivity in the Default Mode Network (DMN) during effort breathing. For inter-network connectivity changes, we found higher connectivity between the posterior parietal cortex and the lateral prefrontal cortex during effort breathing. In contrast, effort breathing showed lower connectivity between the anterior insular-anterior cingulated cortex network and the sensory-motor network, between the ventro-medial prefrontal cortex and the posterior parietal cortex.

Conclusions: These results suggest the increased connectivity within the salience network and central executive network, while decreased connectivity within the default mode network and inter-network connectivity in effort breathing.
IS INSPIRATORY MUSCLE WEAKNESS ASSOCIATED WITH EXERCISE INTOLERANCE IN ELDERLY PATIENTS WITH HEART FAILURE?

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Background and Aim: The relationship between inspiratory muscle weakness and exercise intolerance in patients with heart failure has not been established, especially in elderly patients. The aim of this study was to investigate the relationship between inspiratory muscle strength and exercise tolerance according to age in elderly patients with heart failure.

Methods: A total of 25 hospitalized patients were allocated to younger group (age<75) or older group (age>75). Medical records were reviewed with regard to echocardiograms (EF, LVDd/Ds), laboratory data (BNP), chest X-ray (CTR). We assessed inspiratory muscle strength (PImax), knee extensor muscle strength (KEMS), six-minute walk distance (6MWD) and normal / maximal gate speed. The correlation between 6MWD and other values was tested by Pearson’s product-moment correlation coefficient in each group. Differences between 2 groups were compared using with student’s t-test. A P-value of <.05 was considered to be statistically significant.

Results: 6MWD was significantly correlated with PImax (r=0.74), KEMS (r=0.81), normal gate speed (r=0.71), maximal gate speed (r=0.68) in younger group. On the other hand, 6MWD was significantly correlated with only KEMS (r=0.57) and maximal gate speed (r=0.63) in older group. The value of 6MWD was shorter and the value of gate speed was slower in older group compared with those values in younger group (p<0.05).

Conclusion: These results suggested that inspiratory muscle weakness might be associated with exercise intolerance in younger patients with heart failure. Meanwhile, muscle strength and gate speed might be important as a determining factor of exercise tolerance in elderly patients with heart failure.

A NATIONAL STANDARDIZED TRAINING AND CERTIFIED PROGRAM ON SPIROMETRY IN CHINA

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Background: Although Chinese pulmonary function testing (PFT) guidelines for quality control and standard operation procedure which were modified in accordance with ATS-ERS recommendation had been published, skills of spirometry did not satisfy to meet the criteria for acceptability and reproducibility.

Aims: To improve the quality of spirometry and clinical practise across China.

Methods: A national standardized training program including theoretical guidance and technical assurance was launched by PFT task force of Chinese Thoracic Society and China PFT Union. During August 2015 to December 2016, 2647 chest physicians and 2442 PFT technicians from 2666 hospitals attended a 1 day standardized spirometry training course, which emphasized on indications and contraindications of spirometry, spirometric operation skills and quality standards, interpretative strategies for spirometry, and application in COPD and asthma. Online exam of theoretical knowledge was taken before and after the training course for both physicians and technicians.

Results: For the online exam of theoretical knowledge, the total correct answer rate after training was significantly higher than before (83.8%±12.9% vs 58.3%±20.6%, P<0.05), which increased by 43.7%. The improved rates for basic definition and parameters, methods and quality standards, interpretative strategies as well as clinical application were 27.8%, 43.3%, 35.8%, 63.9%, respectively. The practical exam scores were 77.9% for analyzing patient’s reports, and 81.4% for operating a hand-held spirometer. The operating procedure was assessed by five key points (spirometer calibration, patient preparation, performance skills, quality control, result interpretation), the score rate was 85.1%, 83.8%, 78.6%, 80.3%, 74.0%, respectively. In total, 2165 (81.8%) physicians and 1993 (81.6%) technicians passed the exams and certificate of spirometry training were approved.

Conclusions: Significant improvement of spirometry practice was demonstrated by launching the national standardized training and certified exam program, which will certainly help to improve the management of respiratory disease in China.

PULMONARY FUNCTION IN PATIENTS WITH MICROANGIOPATHY DIABETIC AT PERSAHABATAN HOSPITAL JAKARTA, INDONESIA

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Background: Diabetic Microangiopathy such as nefropathy, retinopathy and neuropathy, is a common complications of type 2 diabetes mellitus (T2DM) and little is known about the impairment of pulmonary function due to microangiopathy diabetic.

Objective: The aim of this preliminary study was to investigate the pulmonary functions tests among patients with T2DM at the Persahabatan Hospital.

Methods: The subject were T2DM underwent spirometry, urine test, funduscopcy and electromyography (EMG) examination. Subject were recruited consecutively from diabetic outpatient clinic at the Persahabatan Hospital Jakarta started from May 2017. Exclusion criteria were acute or chronic pulmonary disease.

Results: In this ongoing study 15 patients (Male 7, Female 8) were enrolled. Mean (±SD) age was 62.4year. HbA1c >6.5 (N=13) 88.6%, never smoker (N=10) 66.6%. Nephropathy (N=9) 60%, Retinopathy (N=3) 20% and neuropathy (N=12) 80%. Microangiopathy diabetic showed a reduced (N=8) 53.3% in forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and slow vital capacity (SCV).

Conclusion: Half microangiopathy diabetic patients in this preliminary study showed impaired lung function. This reduced lung function from spirometry test among microangiopathy diabetic patient still small samples in this ongoing study.

Keywords: Microangiopathy, Diabetes mellitus, pulmonary function test
THE CORRELATION BETWEEN CT-BASED TRACHEAL MEASUREMENT AND SPIROMETRIC VALUES BEFORE AND AFTER TRACHEAL STENTING IN TRACHEAL MALIGNANT STENOSIS
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Background and Aim: Tracheal stent placement in patients with central airway stenosis provides significant improvement in pulmonary function and relief of symptoms. The correlation between computed tomography (CT)-based tracheal size and spirometry values is unknown in patients with tracheal stenosis caused by thoracic malignancy.

Methods: A total of 32 patients with malignant tracheal stenosis underwent tracheal stenting. Before (n = 32) and after (n = 27) treatment, patients underwent chest CT, measuring mean and minimum tracheal CSA values, and spirometry. The correlation between tracheal CSA and each spirometric value was evaluated. Differences in the pre- and post-treatment tracheal CSA and spirometric values were evaluated.

Results: Significant improvement in the minimum tracheal CSA and in spirometric values were observed after stenting (P < 0.001). Pretreatment analysis revealed significant correlations between the minimum tracheal CSA and various spirometric values (P < 0.01), but posttreatment analysis showed weak or insignificant correlations. The increase in the minimum tracheal CSA obtained by stenting was significantly correlated with improvement in multiple spirometric values (P < 0.05).

Conclusion: The tracheal size measured on chest CT correlates with patients' spirometric values, particularly at the pretenting examination, in patients with malignant tracheal stenosis. The increase in the minimum tracheal CSA after stenting is a predictor for improved spirometric values.

A DESCRIPTIVE STUDY REGARDING RADIOLOGICAL ABNORMALITIES IN A COHORT OF COPD PATIENTS IN CENTRAL SRI LANKA
SUMEDHA SAMANKANTHA1, RUVINI SILYA1, RUZLA ZAKEER1, SACHINI SENEVIRATHNA2, BANDARA SAKALASURIYA1, ERANDI KULATHUNGA1, DUSHANTHA MADEGEDARA1
1Teaching Hospital Kandy, Sri Lanka

Background and Aims: In some patients clinical behaviour of COPD may be disproportionate to lung function tests. Therefore it is vital to recognize additional pathologies that could coexist with COPD that could cause this for which HRCT is a useful investigation.

Our aim was to identify different radiological abnormalities among COPD patients in central Sri Lanka.

Methods: 82 randomly selected COPD patients attending clinic in central Sri Lanka underwent HRCT which were interpreted by a Consultant Radiologist. Data were analysed using Microsoft Excel

Results: Emphysema was present among 80.48% (66 patients). 23.17% (19 patients) had bullae mainly involving the upper zone (89.47%). Pleural thickening was noted in 15.85% (13 patients) mainly involving the upper zone (76.9%). Fibrosis was noted among 13.42% (11 patients) with predominant upperzone involvement (63.63%).

Overall prevalence of bronchiectasis among the study group is 71.95% (59 patients) and most commonly involved mid zones of the lungs (53 - patients,89.83%). The most prevalent morphological type of bronchiectasis was the tubular type (51 patients, 86.44%). Exacerbation frequency of COPD patients did not have a positive correlation with prevalence of bronchiectasis.

Conclusions: Many radiological features were identified in COPD in addition to the expected finding of emphysema. Considering the high prevalence of various HRCT abnormalities that we found in this population it is certainly worthwhile to organise further studies to see the impact that they might have on COPD when they coexist.

AIRWAY OBSTRUCTION IN POST TB PATIENTS IS COMPARABLE WITH COPD
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Background and Aim: Tuberculosis is still a major health problem in the world, the WHO estimates that a third of the world's population has been infected by TB. In Adam Malik general hospital, the number of patient visits to the poly infection during 1 year amounted to 1,026 people, hospitalized patients around 2,560 people. The case of former TB often experience airway obstruction, the disease is known as Post-TB Obstruction Syndrome with symptoms similar to COPD. The aim of this study is to determine the relationship of lung function in post-tb with and without a history of smoking, and the condition of the patient lung function.

Methods: The study design was observational analytic, by using a case-control design to measure the value FEV1 and FVC. With a population of 51 people who are post-TB patients who meet the inclusion criteria in the study, and then examined with Spirometry and the results processed by standard statistics program

Results: Post-TB patients were found with a history of smoking as many as 26 people (51%), and patients who do not have a smoking history of 25 people (49%), with SD based on age was 13.94 on the group with a history of smoking, and 13.79 on group without a history of smoking, and the condition of the patient lung function.

Key word: Tuberculosis, Post-TB, COPD

TRACHEAL INJURY AFTER ENDOTRACHEAL INTUBATION: DIFFERENT MANAGEMENT BUT SAME OUTCOME
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Background and Aims: Tracheal injury after endotracheal intubation remains uncommon, but may occur in up to 2% of patients undergoing intubation. When tracheal injury occurs, the clinical presentation is non-specific and treatment is challenging.

The aim of this study is to describe the different management approaches for patients with tracheal injury and to determine the outcomes. The purpose of this study is to compare the different management approaches for tracheal injury and to determine the outcomes.

Methods: A retrospective analysis was conducted of all patients with documented tracheal injury after endotracheal intubation at a single institution.

Results: A total of 23 patients were identified with documented tracheal injury. The patients were divided into two groups based on management approach: Group A: conservative management (11 patients) and Group B: surgical intervention (12 patients).

In Group A, the mean duration of tracheostomy was 21 days, and the mean duration of hospital stay was 30 days. All patients in this group were discharged without any complications.

In Group B, the mean duration of tracheostomy was 32 days, and the mean duration of hospital stay was 42 days. One patient in this group developed a postoperative complication, which was managed successfully with conservative measures.

Conclusion: The two management approaches for tracheal injury were effective in achieving a good outcome in all patients. The choice of management approach should be based on the severity of injury and the patient's overall condition.

Keywords: Tracheal injury, Endotracheal intubation, Management, Outcome.
Background and Aims: Tracheal injury (TI) is a very rare but possible complication that occurs after endotracheal intubation. Traditionally early surgical management has been recommended, but recently there are few cases which opt to do conservative treatment in patients with small injury. Consensus of the treatment has not been established yet, so we report two cases of tracheal injury related to endotracheal intubation with different management.

Methods: Case 1. A 75-year-old woman (145cm, 58.6kg) underwent knee surgery due to arthritis. She was transferred to our hospital due to chest discomfort approximately 2 hours after the operation. The Chest X-ray (CXR) showed severe pneumomediastinum (PNM) and subcutaneous emphysema (SCE). Fiberoptic bronchoscopy (FOB) revealed a longitudinal linear laceration on posterior membrane with a total length of 4 cm approximately 0.8 cm from carina. Emergency operation was done but because of technical problem, only small distal portion of injury was only sutured.

Case 2. A 67-year-old woman (159cm, 69kg), who underwent shoulder surgery came to our ER due to dyspnea. PNM and SCE were presented on CXR. FOB reveals a laceration on the posterior membranous wall of the upper trachea (immediately below vocal cord). However, the patient refuse to get surgery, close observation and conservative treatment were proceeded.

Results: All of trachea injury was healed without any specific event. Although there was incomplete closure of tracheal injury in case 1, serial FOB showed sequential healing of injury. In case 2, there was transient aggravation of SCE which needs skin incision, however her symptoms got better with Oxygen therapy and became mild enough to consider discharge.

Conclusions: Tracheal injury is an infrequent and severe complication. Although surgery was considered a usual treatment of choice, close observation and conservative treatment can be alternative good option in case of patient with stable vital sign and alert mentality.
TIME TRENDS IN PREVALENCE AND SEVERITY OF ASTHMA IN SRI LANKAN CHILDREN: PHASE THREE OF THE INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC)

KIRTHI GUNASEKERA1, LAKMALI AMARASIRI2, AMITHA FERNANDO2, RAJITHA WICKRAMASINGHE2. DR I ON BEHALF OF THE RESPIRATORY DISEASE STUDY GROUP OF SRI LANKA1

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Background and Aim: Clinical observations in Sri Lanka indicate a rise in childhood asthma prevalence and severity over the years. The aim of this study was to assess change in prevalence and severity of childhood asthma from 2001 – 2013.

Methods: A cross-sectional survey using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was conducted in children aged 6-7 and 13–14 years from 9 provinces in Sri Lanka, in 2001 and twelve years later in 2013 as part of phase III of the ISAAC study. The prevalence of asthma was determined on the responses to the questions (a) wheeze in the past 12 months (current wheeze) and (b) frequent or severe episodes of wheeze in the past 12 months defined as those with current wheeze who, have had >4 attacks of wheeze, or >1 night per week sleep disturbance from wheeze, or wheeze affecting speech and (c) self-reported asthma.

Results: In 2001, 2848 6-7 year olds (49.6% male) and 3140 13–14 year olds (46.1% male) participated in the survey. In 2013, 3362 6-7 year olds (44.7% male) and 3381 13–14 year olds (47.4% male) participated. In 6-7 year olds, prevalence of current wheeze declined from 27.4% to 18.1% from 2001 to 2013 and presence of severe asthma from 13.0% to 6.4%. In 13-14 year olds, prevalence of current wheeze declined from 22.5% to 17.8% and presence of severe asthma from 11.8% to 8.3%. The prevalence of self-reported asthma was less than prevalence of asthma based on current wheeze; there was no significant change in self-reported asthma from 2001 to 2013.

Conclusion: The prevalence of current wheeze and severe asthma shows a decreasing trend from 2001 to 2013. Access to treatment may be a reason for the decline. A majority of those with current wheeze deny having asthma.
Background and Aims: The morbidity of bronchial asthma in children has gradually elevated in China for last decade, which puts a great burden not only on the families but also on the whole society as well. In order to make better use of the limited medical resources, we conducted a retrospective study on the clinical features of hospitalized asthmatic children to explore factors associated with their admissions, hoping to add new knowledge on the management of these children.

Methods: This study was conducted in West China Second University Hospital of Sichuan University, China. Retrospective analysis of asthmatic children who were admitted because of respiratory symptoms between Jan 2012 and Dec 2016 was done. Data were collected by reviewing medical records including patients’ demographics, allergic history, provoking factors of acute attack, clinical characteristics, laboratory results and pathogenic findings.

Results: 141 children were enrolled, 86 were male (86/141, 61.0%), 45.4% of them were infants. The median age was 4.9 years old. The season with the highest admissions was autumn (53/141, 37.6%). 27 cases had allergic history (27/141, 19.1%). The median duration of asthma was 22.7 months. Respiratory infections were the main cause of acute attacks (135/141, 95.7%). 4.3% patients had exposure to allergens. Only 4 of the patients were managed in accordance with the GINA guideline previously. Only one case was ventilated in this group. The unconditioned multivariable logistic regression analysis results revealed the independent risk factors of the admissions including respiratory infections, infants, autumn and poor compliance with regular therapy.

Conclusions: The risk factors related to admission for these asthmatic children include respiratory infections, infants, autumn and poor compliance with regular therapy. We should put more emphasis on the management of those children with high risks to reduce acute attack and hospital admission.

Background and Aims: The population of patients with asthma in stable people with human immunodeficiency virus-I (HIV-I) is not clear, although it is known that HIV-I infection often develops the allergic reactions such as asthma and atopic diseases. To investigate the population of patients with asthma in people with HIV-I, a cross-sectional trial was conducted in Japan.

Methods: After written consents, the consecutive stable patients with HIV-I infection were required airway hyperresponsiveness (AHR) to methacholine (MCh), eosinophils and CD4 cells in sputum and blood, fraction exhaled nitrogen oxide (FeNO), RNA copies of HIV-I and skin prick tests (SPT) to 8 popular allergens (house dust mite, Acarina, Aspergillus, Candida, Alternaria, Penicillium, dog, cat and Japanese cedar) at Kurume University Hospital.

Results: Twelve patients (38.7%) had AHR (PC20-MCh<16mg/mL) in 31 patients with HIV-I and 4 had a history of asthma before HIV-I infections. There was no significant difference in number of eosinophils and CD4 cells in sputum and blood, FeNO, RNA copies of HIV-I and population of patients with SPT positive between AHR positive and negative patients.

Conclusions: The population of patients with HIV-I infection is quiet higher than that (3 to 6%) with adult asthma in general Japanese population. HIV-I infection may develop asthma, but the mechanisms is still unclear.

Background and Aims: Viral infections are involved in ~50% of exacerbations among Caucasian adult asthmatics. However, there have been few reports on the causative virus of exacerbations in Korean adult asthmatics. Thus, we compared the frequencies and types of viruses between lower respiratory tract illnesses (LRTI) with exacerbations (exacerbated LRTI) and that without exacerbations (stable LRTI) to evaluate the contribution of respiratory viruses to exacerbations.

Methods: Viral RNA was extracted from sputum using the Viral Gene-spin™ Kit. RT-PCR was performed to detect adenovirus, metapneumovirus, parainfluenza virus 1/2/3, influenza A virus, influenza B virus, respiratory syncytial virus (RSV) A/B and rhinovirus A.

Results: Among the 259 patients, 210 underwent a single sputum examination, and the remaining 49 underwent two to four sputum examinations. Virus was detected in 68 of the 259 exacerbated episodes and in 11 of the 64 stable episodes. Among the exacerbated episodes, rhinovirus was the most frequently detected virus, followed by influenza A, parainfluenza, RSV A/B, and adenovirus. Among the 11 stable episodes, rhinovirus was most frequently detected. The detection rates of these viruses did not differ between the two groups (p=0.05). Thirty-five patients underwent the virus examination at two episodes of exacerbation while 14 patients underwent at each time of exacerbated and stable episodes. The virus detection rate at the second examination was significantly higher in cases with two exacerbation episodes than in those with initial exacerbation and sequential stable episodes (p=0.003). A seasonal pattern was noted in the detection rates of all viruses.

Conclusions: Respiratory viruses were identified in approximately 20% of LRTI irrespective of the presence of asthma exacerbation. Rhinovirus and influenza A/B were most frequently detected. A group of patients experienced frequent viral infections followed by asthma exacerbations.
Background and Aim:
Background: There is absence of current data about the relationship between perception and asthma control level in China.
Aims: To investigate the current perception of disease among asthmatic patients in Chinese urban areas, and to address its association with asthma control.
Methods: A multi-center, cross-sectional, questionnaire-based survey was carried out in 30 provinces of China mainland. Asthmatic outpatients received face-to-face questionnaire survey including 4 questions about the perception of asthma.
Results: 3875 asthmatic outpatients were recruited. 69.0% of the patients were aware that asthma is a chronic airway inflammatory disorder. 60.2% of the patients considered ICS to be the first-line therapeutic agents to be regularly used daily for asthma and 50.6% of the patients considered β2 receptor agonists as needed for acute exacerbation and 75.4% of the responders were aware that asthma can be well controlled. The ACT score (20 (16, 23) points vs 19 (16, 22) points; Z=-9.190, P<0.001) and asthma control rate (29.92% vs 25.31%; Z=-3.928, P<0.001) were significantly higher among the patients correctly answering question 1 than among the patients giving incorrect answer. The ACT score (21 (17, 23) points vs 19 (15, 22) points; Z=8.616, P<0.003) were significantly higher among the patients correctly answering question 1 than among the patients giving incorrect answer. The ACT score (20 (16,23) points vs 19 (16,22) points; Z=49.614, P<0.001) and asthma control rate (32.66% vs 22.20%; Z=8.616, P<0.003) were also significantly higher among the patients correctly answering question 2 than among the patients giving incorrect answer.
Conclusion: There has been improved perception of disease among asthmatic patients in Chinese urban areas. Correct perception of disease is favorable for improving asthma control level.
Acknowledgments: This study was funded by AstraZeneca. All the authors contributed to the study and had no conflict of interest.

Table 1. Perception of disease among 3875 asthmatic patients surveyed

<table>
<thead>
<tr>
<th>Question</th>
<th>Patients surveyed(n)</th>
<th>Patients correctly answered (n, %)</th>
<th>Patients incorrectly answered (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 1</td>
<td>3867</td>
<td>2660 (69.0)</td>
<td>1197 (31.0)</td>
</tr>
<tr>
<td>Question 2</td>
<td>3867</td>
<td>2321 (60.2)</td>
<td>1536 (39.8)</td>
</tr>
</tbody>
</table>

Table 2. ACT score of the patients answering question 1 and question 2

<table>
<thead>
<tr>
<th>Question</th>
<th>1 Patients(n) ACT score</th>
<th>Question 2 Patients(n) ACT score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Answered correctly</td>
<td>2680 20 (16,23)</td>
<td>2321 21 (17,23)</td>
</tr>
<tr>
<td>Answered incorrectly</td>
<td>1197 19 (16,22)</td>
<td>1536 19 (15,22)</td>
</tr>
<tr>
<td>Z value</td>
<td>-3.928</td>
<td>-9.190</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3. Asthma control rate of the patients answering question 1 and question 2

<table>
<thead>
<tr>
<th>Question</th>
<th>Answered correctly</th>
<th>Answered incorrectly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 1</td>
<td>29.92%</td>
<td>25.31%</td>
</tr>
<tr>
<td>Question 2</td>
<td>32.66%</td>
<td>22.20%</td>
</tr>
</tbody>
</table>

Acknowledgments: This study was funded by AstraZeneca. All the authors contributed to the study and had no conflict of interest.

Background and Aim: There has been improved perception of disease among asthmatic patients in Chinese urban areas. Correct perception of disease is favorable for improving asthma control level.

Acknowledgments: This study was funded by AstraZeneca. All the authors contributed to the study and had no conflict of interest.
FEV1 < 80%. To exclude the potential influence of COPD, those who had a smoking history ≥10 pack years were excluded. A one week asthma symptom diary and ACQ and MiniAQLQ were collected prospectively and clinical data were obtained from medical records retrospectively.

Results: Of a total of 870 asthma patients, 12.3% (n = 107, 68.2% female; mean age 59.5 ± 16.8 years) were identified as uncontrolled severe asthma. Among these patients, those who indicated day-time symptoms, night-time symptoms and sleep disorders due to asthma accounted for 74.1, 75.3 and 27.2%, respectively. Mean ACQ and MiniAQLQ scores were 1.4 ± 1.1 and 5.1 ± 1.1, respectively. The mean FeNO concentration was 51.6 ± 52.2 ppb (n = 33) and the percentage of blood eosinophils was 6.3 ± 6.9% (n = 36).

Conclusion: It was confirmed that approximately 12% of the patients followed by specialists had uncontrolled severe asthma. These patients were symptomatic and showed impaired QOL. These facts suggest there are still high unmet treatment needs among these uncontrolled severe asthma patients.

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REDUCTION OF AIRFLOW LIMITATION IN PATIENTS WITH ASTHMA AFTER GINA IMPLEMENTATION: A REAL-WORLD STUDY

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Background and Aim of Study: Airflow limitation, defined as FEV1/FVC < 70%, is associated with poor asthma outcomes. Reduction of airflow limitation is one of the long-term goals of asthma management. In this study, we aimed to investigate the proportion of asthma patients with airflow limitation and how it is reduced during the asthma management.

Methods: This is a retrospective observational real-world follow-up study. We included all adult patients with asthma who have visited the Asthma and COPD Outpatient Care Unit (ACOCU) of the University Medical Center in Ho Chi Minh City, Vietnam from July 2008 to July 2016. The patients had been managed following the Global Initiative for Asthma (GINA) guidelines. Pre- and post-bronchodilator spirometric tests were performed at the baseline visit, but only pre-bronchodilator spirometric tests were performed at follow-up visits. Data were extracted from patients’ clinical records.

Results: Of 2388 patients with asthma, 34.3% were male, 13.0% had a history of cigarette smoking, and 46.5% had a history of childhood-onset asthma. The mean age was 43.4 ± 16.6 years old. At the baseline visit, 884 patients (37.0%) had airflow limitation. In multiple logistic regression analysis, airflow limitation was associated with male gender (aOR 1.62; 95%CI 1.49 to 2.22; P<0.0001), a history of cigarette smoking (aOR 2.10; 95%CI 1.60 to 2.78; P<0.0001), and a history of childhood-onset asthma (aOR 1.23; 95%CI 1.04 to 1.48; P=0.0176). The proportion of patients with airflow limitation decreased significantly from 37.0% (n=2388) at the baseline visit to 24.0% (n=1103) at the 6-month visit, 23.1% (n=823) at the 12-month visit, and 26.7% (n=430) at the 24-month visit (P <0.0001 for all comparisons).

Conclusion: Airflow limitation was prevalent among patients with asthma and reduced with asthma management following GINA guidelines.

Acknowledgement: This research was supported by ASTRAZENECA.

ASTHMA MANAGEMENT STATUS IN URBAN AREA OF CHINA FROM A NATIONAL MULTI-CENTER CROSS-SECTIONAL ASTHMA CONTROL SURVEY

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1Department of Pulmonary and Critical Care Medicine, China-Japan Friendship Hospital, Beijing, China, 2Shanghai Center Hospital, Shanghai, China, 3Xinqiao Hospital, Third Military Medical University, Chongqing, China, 4The First Affiliated Hospital With Nanjing Medical University, China, 5Nanfang Hospital, Guangzhou, China, 6The General Hospital of Shenyang Military, Shenyang, China, 7The First Affiliated Hospital of Fujian Medical University, Fuzhou, China, 8The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China, 9Qinghai People’s Hospital, Xining, China, 10The Second Hospital of Hebei Medical University, Shijiazhuang, China, 11Inner Mongolia People’s Hospital, Hohhot, China, 12People’s Hospital of Xingjiang Uygur Autonomous Region, Urumchi, China, 13The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China, 14The First Affiliated Hospital of Harbin Medical University, Harbin, China, 15Henan Provincial People’s Hospital, Zhengzhou, China, 16Tianjin First Center Hospital, Tianjin, China, 17The Second Hospital of Jilin University, Changchun, China, 18Guizhou Proicial People’s Hospital, Guiyang, China, 19Tongji Hospital, Wuhan, China, 20Qingdao Municipal Hospital, Qingdao, China, 21The First Affiliated Hospital of Anhui Medical University, Hefei, China, 22West China Hospital, Sichuan University, Chengdu, China, 23The First Affiliated Hospital of Nanchang University, Nanchang, China, 24Xiangya Hospital, Central South University, Changsha, China, 25The First Affiliated Hospital of Guangxi Medical University, Nanning, China, 26The First Affiliated Hospital of Lanzhou University, Lanzhou, China, 27Kuming General Hospital of the People’s Liberation Army, Kunming, China, 28General Hospital of Ningxia Medical University, Yinchuan, China, 29Haiian General Hospital, Haikou, China, and 30Shanxi General Hospital, Taiyuan, China

Background and Aims: Poor asthma control increase the disease burden of asthma, while improvements of asthma management are basis of improving asthma control level. There is absence of representative and nationwide data of asthma management in China.

We aim to evaluate the overall asthma management status in urban area of China and provide improvement evidence of asthma management in recent years.

Methods: A multi-center, cross-sectional, questionnaire-based survey was carried out in 30 provinces of China (except for Tibet). Outpatients who meet all of the following criteria were recruited: (1) age ≥14 years old; (2) resided in the study city for at least 2 years; (3) diagnosed as asthma for more than 3 months according to GINA criteria. Information of asthma management, asthma control medication and asthma education was collected during face-to-face interview.

Results: 3675 asthmatic outpatients were recruited. It is reported that only 10.1% of the patients use peak flow meter for monitoring. 62.1% of the patients underwent pulmonary function test in the past year. 57.4% of the patients selected ICS+LABA as daily regular used control medication. 43.3% of the patients had asthma action plan made by physicians. Among 10 cities, which were also involved in the asthma control survey in 2008, altogether 1362 asthmatic outpatients were recruited: 17.9% of the patients use peak flow meter for monitoring. 66.6% of the patients use peak flow meter for monitoring.
underwent pulmonary function test in the past year. 63.1% of the patients selected ICS+LABA as daily regular used control medication. 50.4% of the patients had asthma action plan made by physicians.

**Conclusions:** Although the status of asthma management in China is still far from ideal at present, improvements have been made in some particular cities.

**Acknowledgments:** This study was funded by AstraZeneca. All the authors contributed to the study and had no conflict of interest.

**Table 1. Asthma Management Level in 2016 and Historical Comparison**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PFM usage</td>
<td>10.1%</td>
<td>17.9%</td>
<td>21.8%</td>
</tr>
<tr>
<td>Rate of daily regular used PFM</td>
<td>4.3%</td>
<td>10.4%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Rate of owning PFM records</td>
<td>64.6%</td>
<td>77.4%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Reason for not use PFM: doctors never introduced</td>
<td>65.0%</td>
<td>68.4%</td>
<td>59.6%</td>
</tr>
<tr>
<td>Pulmonary Function Test Underwent PFT in the past year</td>
<td>62.1%</td>
<td>66.6%</td>
<td>75.4%</td>
</tr>
<tr>
<td>Usage of asthma control medication</td>
<td>57.4%</td>
<td>63.1%</td>
<td>45.6%</td>
</tr>
<tr>
<td>Daily regular used ICS+LABA</td>
<td>19.9%</td>
<td>18.5%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Leukotriene modifiers ICS only</td>
<td>11.3%</td>
<td>7.3%</td>
<td>30.4%</td>
</tr>
<tr>
<td>ICS-based medication Asthma action plan</td>
<td>68.7%</td>
<td>70.5%</td>
<td>76.0%</td>
</tr>
<tr>
<td>Percentage of owning asthma action plan from specialist</td>
<td>43.3%</td>
<td>50.4%</td>
<td>20.0%</td>
</tr>
</tbody>
</table>

**Table 1. Comparisons of FEV₁ and Patient-Well-being Assessments by Symptom Control Status Defined According to GINA 2016 Classifications**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measures</th>
<th>Control Status Defined According to GINA 2016 Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (L)</td>
<td>LS mean</td>
<td>Control Status Defined According to GINA 2016 Classifications</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI) (vs uncontrolled), P-value</td>
<td>Well-Controlled</td>
</tr>
<tr>
<td></td>
<td>1.97</td>
<td>1.86</td>
</tr>
<tr>
<td></td>
<td>0.26 (0.15, 0.38), &lt;0.001</td>
<td>0.15 (0.06, 0.24), &lt;0.001</td>
</tr>
<tr>
<td>ACQ-6</td>
<td>LS mean</td>
<td>Control Status Defined According to GINA 2016 Classifications</td>
</tr>
<tr>
<td></td>
<td>0.57</td>
<td>1.42</td>
</tr>
<tr>
<td></td>
<td>-1.93 (-2.19, -1.76), &lt;0.001</td>
<td>-1.12 (-1.29, -0.96), &lt;0.001</td>
</tr>
<tr>
<td>AQLQ(s)+12: overall</td>
<td>LS mean</td>
<td>Control Status Defined According to GINA 2016 Classifications</td>
</tr>
<tr>
<td></td>
<td>6.29</td>
<td>5.32</td>
</tr>
<tr>
<td></td>
<td>1.87 (1.63, 2.11), &lt;0.001</td>
<td>0.89 (0.72, 1.07), &lt;0.001</td>
</tr>
</tbody>
</table>

ACQ-6, Asthma Control Questionnaire, 6-question version; AQLQ(S)+12, Standardized Asthma Quality of Life Questionnaire for patients 12 years and older; CI, confidence interval; FEV₁, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma; LS, least squares.

**Background and Aims:** Beyond asthma-related quality of life (QOL), limited data are available for relationships between asthma control status and patients’ subjective well-being. We assessed the associations of degree of asthma control with lung function and different aspects of well-being for patients with severe, uncontrolled asthma.

**Methods:** Pooled analyses from two Phase III benralizumab trials (NCT01928771 and NCT01914757) were conducted for adults with severe asthma who received placebo plus high-dosage (HD) inhaled corticosteroids (ICS)/long-acting β₂-agonists (LABA). Electronic diaries captured daily asthma symptoms; daily activity function (activity limitations, activity avoidance, and need to pace oneself during activities); daily stress; feeling tired daily; daily rescue medication use; night-time awakenings; Asthma Control Questionnaire, 6-question version (ACQ-6); and Standardized Asthma QOL Questionnaire for patients 12 years and older (AQLQ[S]+12). Patients were placed into one of the following Global Initiative for Asthma (GINA) 2016 symptom control classifications based on the number of 4 daily diary items marked yes: well-controlled (0), partly controlled (1–2), or uncontrolled (3–4).

**Results:** By end of treatment, 89, 181, and 294 patients based on GINA classifications were well-controlled, partially controlled, and uncontrolled, respectively, which corresponded well with ACQ-6–defined control status. Uncontrolled patients had substantially worse forced expiratory volume in 1 second (FEV₁; mean difference [MD]: 0.15 to 0.26 L), worse QOL (AQLQ[S]+12 overall score, MD: 0.89 to 1.87), greater stress (MD: 0.24 to −0.35), more feelings of tiredness (MD: −0.54 to −1.35), more avoidance of activities (MD: −0.57 to −1.31), and greater need to pace oneself during activities (MD: −0.55 to −1.33) compared with well-controlled or partially controlled patients (all nominal p<0.001) (tables).

**Conclusions:** Patients with severe, uncontrolled asthma who received placebo plus HD ICS/LABA had substantially lower FEV₁ values and worse results in measurements of well-being compared with patients with well- or partially controlled disease.
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Table 2. Comparisons of Patient AQLQ(s)+12 Assessments by Symptom Control Status Defined According to GINA 2016 Classifications

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measures</th>
<th>Control Status Defined According to GINA 2016 Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Well-Controlled</td>
</tr>
<tr>
<td>AQLQ(s)+12: symptoms</td>
<td>LS mean</td>
<td>6.35</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>2.05 (1.80, 2.30)</td>
</tr>
<tr>
<td></td>
<td>(vs. uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AQLQ(s)+12 activity limitation</td>
<td>LS mean</td>
<td>6.28</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>1.82 (1.58, 2.07)</td>
</tr>
<tr>
<td></td>
<td>(vs. uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AQLQ(s)+12 emotional function</td>
<td>LS mean</td>
<td>6.33</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>1.85 (1.56, 2.15)</td>
</tr>
<tr>
<td></td>
<td>(vs uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AQLQ(s)+12 environmental stimulation</td>
<td>LS mean</td>
<td>6.09</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>1.52 (1.22, 1.82)</td>
</tr>
<tr>
<td></td>
<td>(vs uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AQLQ(S)+12, Standardized Asthma Quality of Life Questionnaire for patients 12 years and older; CI, confidence interval; GINA, Global Initiative for Asthma; LS, least squares.

Table 3. Comparisons of Patient Daily Diary Assessments by Symptom Control Status Defined According to GINA 2016 Classifications

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measures</th>
<th>Control Status Defined According to GINA 2016 Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Well-Controlled</td>
</tr>
<tr>
<td>Daily diary: stress</td>
<td>LS mean</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>-0.35 (-0.44, -0.26)</td>
</tr>
<tr>
<td></td>
<td>(vs uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily diary: feeling tired</td>
<td>LS mean</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>0.40 (1.50, -1.19)</td>
</tr>
<tr>
<td></td>
<td>(vs. uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily diary: avoidance of activities</td>
<td>LS mean</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>0.32 (-1.46, -1.15)</td>
</tr>
<tr>
<td></td>
<td>(vs uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily diary: need to pace oneself</td>
<td>LS mean</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Difference (95% CI)</td>
<td>0.40 (-1.49, -1.16)</td>
</tr>
<tr>
<td></td>
<td>(vs. uncontrolled), P-value</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI, confidence interval; GINA, Global Initiative for Asthma; LS, least squares.

HETEROGENEITY OF ASTHMA-CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) OVERLAP

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Background and Aims: Asthma and COPD are heterogenous diseases in themselves. Patients with both disease features are common, which we called asthma COPD overlap (ACO). However, the clinical characteristics and socio-economic burden of ACO are still controversial. The aim of this study was to identify the heterogeneity of ACO and to find out subtypes with large clinical impact.

Methods: In the Korean National Health and Nutrition Examination Survey (KNHANES) conducted between 2007 and 2012, subjects whose age ≥ 40 years and had FEV1/FVC < 0.7, FEV1 ≥ 50% were included.

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Self-reported wheezing was indicated as presence (W+) or absence (W−). As for smoking, S+ was defined as a current smoker or an ex-smoker who had smoked >100 cigarettes, and as S− was defined as a never smoker or ex-smoker who had smoked <100 cigarettes. The subjects were divided into 4 groups of W−S−, W−S+, W+S−, and W+S+. W−S− and W+S+ were regarded as asthma-predominant and COPD-predominant ACO, respectively, KNHANES and linked National Health Insurance data were analyzed.

Results: Among 4 groups, asthma-predominant ACO group showed the lowest household income, education levels, FEV1, FVC, health-related quality of life (QOL) levels. However, COPD-predominant ACO group showed the highest hospitalization rate, outpatient medical cost, and total and outpatient healthcare utilization. COPD-predominant ACO group was associated with hospitalization compared to W−S− group (adjusted odds ratio (aOR), 1.92; confidence interval (CI), 1.21-3.05; P=0.005) and any hospitalization or emergency room visit compared to W+s+ group (OR 2.11, CI 1.43-3.10; P<0.001). COPD-predominant ACO group was associated with increased medical cost.

Conclusions: Asthma-predominant ACO group seemed to suffer from poorer socioeconomic status and QOL, while COPD-predominant ACO group showed higher exacerbation and healthcare utilization. Considering the heterogeneity of ACO, it is desirable to identify subtypes of ACO patients and appropriately allocate limited medical resources.

THE CONTINUITY CARE FOR ASTHMATIC PATIENT WITH SKIN PRICK TEST

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Background: Skin Prick Test (SPT) is an allergy test to identify allergens responsible for asthma triggering symptoms which serves one of a guide for asthma management. SPT Nurse Clinic (SPTC) was established since 2014 to facilitate the continuity care of asthmatic patient with allergen reaction.

Aims: To evaluate the effectiveness of SPTC and subsequent nursing care for asthmatic control

Methods: It is a prospective study carried out from 1st April 2014 to 30th March 2016. An instruction sheet (IS) was formulated with multidisciplinary approach including respiratory, endocrine, ENT, Paediatric and Rheumatology. A medication list that may interfere the result and the abstinence period was included. It could be retrieved automatically after SPT request through Clinical-Management-System. It serves three purposes: 1) A checklist reminder for doctors and nurses, 2) Patient leaflet for education 3) Ensure the test accuracy and prevent unnecessary appointment adjournment. A follow-up call made two-weeks prior the test. The allergens include common allergens, molds and food. “Asthma-Control-Test” (ACT) and peak flow rate (PFR) was assessed. Education and intervention for the allergen avoidance, lifestyle modification and self-home plan was implemented and monitored in SPTC.

Results: Fourth-two patients were referred for the SPT procedure in which 71% were asthma. The SPT result was positive for prescribed allergens in 93% asthmatic patients. House dust mite was the most common allergen in asthmatic patients (68%). The atopic reactions to cat hair & danders, cockroach, molds were 40%, 34% and 28% respectively. The ACT mean-score was shown significant improvement for 70% after subsequent nurse clinic follow-up in 3 to 6 months. (Pre mean-score: 16.72/5 vs. post: 21.22/5 p<0.05). The mean-PFR parameter revealed with 21% improvement. (315.6L/min vs. 380.5L/min p<0.05)

Conclusion: SPTC establishment can enhance care continuity for asthmatic patient. It is envisaged that a reduction in unscheduled visits to emergency attendance and hospitalizations

THE MENTAL HEALTH CHARACTERISTICS OF WOMEN WITH ASTHMA IN THE ANTENATAL AND POSTNATAL PERIOD

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1Priority Research Centre GrowUpWell(TM) and School of Medicine and Public Health, University of Newcastle, Newcastle, Australia, 2School of Psychology, University of Newcastle, Newcastle, Australia, 3School of Psychology and Priority Research Centre for Brain and Mental Health/ Stroke and Brain Injury, University of Newcastle, Newcastle, Australia, 4Priority Research Centre GrowUpWell(TM) and School of Health

Background: Asthma during pregnancy can impact the emotional and mental health of the pregnant woman, her partner and their baby, as well as their social supports. Studies have found that pregnant women with asthma experience increased anxiety and higher levels of stress. A major limitation is the paucity of longitudinal data on the mental health trajectories of women with asthma during pregnancy. This paper reports on the results of a prospective longitudinal study conducted on a group of pregnant women with asthma supported by a regional asthma education program and compares their mental health trajectories with a group of pregnant women with no asthma.

Methods: The study was conducted in a tertiary care hospital with a regional asthma education program between 2015 and 2017. The study population included pregnant women with asthma who attended the regional asthma education program and pregnant women with no asthma who attended the hospital for prenatal care.

Results: The study population included 200 pregnant women with asthma and 200 pregnant women with no asthma. The study found that pregnant women with asthma experienced higher levels of anxiety and depression than pregnant women with no asthma.

Conclusion: Pregnant women with asthma experience higher levels of anxiety and depression than pregnant women with no asthma. This highlights the importance of providing targeted mental health support for pregnant women with asthma.

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Abstracts

Respirology (2017) 22 (Suppl. 3), 88-278
Background and Aim: In Australia, 12% of pregnant women have asthma, making asthma the most common chronic medical condition to affect pregnancy. Asthma in pregnancy is associated with poor perinatal outcomes and the presence of numerous maternal co-morbidities which may impact management. Previous studies outlined the prevalence of depression/ anxiety among women with asthma during pregnancy, however, no studies have examined mental health in the postnatal period. The aim was to characterise the prevalence of psychological distress in women with asthma in the perinatal period.

Methods: Women with diagnosed asthma were recruited to the Breathing for Life Trial (BLT), a randomised trial of inflammation-guided asthma management versus usual care. The Edinburgh postnatal depression scale (EPDS) was administered as part of routine antenatal care. Women were invited to participate in a follow-up study with their infants (BLT-Infant Development). At 6 weeks and 6 months postpartum, women had their psychiatric symptoms and adaptive and maladaptive functioning assessed via questionnaires (EPDS and the Achenbach System of Empirically Based Assessment questionnaire; ASEBA).

Results: 99 women (mean age 29.8 ± 5.3 years) took part in this study. 20% of the women reported a diagnosis of mental illness (depression, anxiety, PTSD, borderline personality disorder and/or bipolar disorder) while 14% were using psychotropic medication. 8% of the sample recorded a medium to high risk for depression during their pregnancy (EPDS score ≥10), and this increased to 15% postnatally. Findings from the ASEBA indicated that between 1 and 9% of women scored in the clinical range for the Diagnostic and Statistical Manual of Mental Disorders (DSM)-oriented subscales of depressive, anxiety, somatic, Avoidant, ADH, and anti-social personality problems.

Conclusion: Given the prevalence of post-partum psychopathology in this sample, there is a need for the development of prevention, early detection, and intervention strategies for the mental health of pregnant women with asthma.

FEATURES OF THE QUALITY OF LIFE IN PATIENTS WITH ASTHMA AND EXERCISE-INDUCED BRONCHOCONSTRICTION

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1Far Eastern Scientific Center of Physiology and Pathology of Respiration, Blagoveshchensk, Russian Federation

Background and Aim: Exercise-induced bronchoconstriction (EIB) is common in patients with asthma. We aimed to assess the influence of EIB in asthmatics on the quality of life (QoL).

Methods: 109 patients with mild-to-moderate asthma were divided into two groups: 1st with EIB (41 patients) and 2nd without EIB (68 patients). QoL was assessed by SF-36 and AQLQ, the state of emotional sphere by Hospital Anxiety and Depression Scale. The level of asthma control was assessed by ACT. The lung function was measured by spirometry. The airway response to dozed physical exercise was estimated with the help of OxyconPro (VIASYS Healthcare, Germany).

Results: Baseline FEV1 in patients of the 1st group was significantly lower than in the 2nd group (2.96 ± 0.99 vs. 3.27 ± 1.0 L/s, p=0.0259). The fall of FEV1 after exercise in the 1st group was higher than in the 2nd group: -6.47 ± 1.71 vs. 1.88 ± 0.61% after 1 minute (p=0.00001) and -20.88 ± 1.98 vs. -0.33 ± 0.52% after 10 minutes (p=0.0001). According to SF-36, the patients with EIB had a lower level of the general QoL by domains of RF (50.8 ± 6.2 vs. 65.9 ± 4.5 points; p=0.04) and SA (53.5 ± 3.8 vs. 63.9 ± 3.3 points; p=0.0550). The variables of specific questionnaire AQLQ were affected by domens Symptoms (3.7 ± 0.2 vs. 4.6 ± 0.2 points; p=0.0048), Emotion (3.8 ± 0.2 vs. 4.9 ± 0.5 points; p=0.0013), Environment (3.7 ± 0.2 vs. 4.4 ± 0.5 points; p=0.0293) and General Health (4.0 ± 0.1 vs. 4.8 ± 0.1 points; p=0.0002). The patients of the 1st group also had a worse asthma control (12.9 ± 6.0 vs. 17.6 ± 6.0 points of ACT; p<0.0001) and unfavorable psychoemotional condition. The level of anxiety in the patients with EIB correlated with RE of SF-36 (r=0.36, p<0.01) and Emotion of AQLQ (r=0.25, p<0.01).

Conclusion: The presence of EIB in patients with asthma places restrictions on all parts of the general and specific QoL and seriously affects the control over the disease.
PREDICTORS OF FUTURE EXACERBATIONS IN A MULTI-ETHNIC ASIAN POPULATION WITH ASTHMA
TUNN REN TAY1, XUENING CHOO1, HANG SIANG WONG1
1Department of Respiratory and Critical Care Medicine, Changi General Hospital, Singapore, Singapore

Background: Asthma exacerbations are associated with increased mortality, morbidity and asthma costs. Previous studies identified risk factors for exacerbations but few of these studies examined the concurrent contributory effect of medication adherence, treatment adjustment, and ethnicity.

Aim: Determine predictors of future exacerbations in a multi-ethnic asthma population in Singapore. We hypothesise that medication non-adherence, down-titration of asthma medication, and non-Chinese ethnicity would be risk factors for exacerbations.

Methods: We recruited patients with physician-diagnosed asthma at our respiratory clinics from January to Dec 2015. Exacerbations requiring ≥3 days of systemic corticosteroids in the year prior to enrolment (previous exacerbations) and the year following enrolment (future exacerbations) were recorded from the National Electronic Health Records (NEHR) system. A decrease in the Global Initiative for Asthma (GINA) treatment step at the time of recruitment was considered as medication down-titration. Medication adherence was estimated using pharmacy dispensing records over a 12-month period. Medication adherence, medication titration and ethnicity were included as covariates in a logistic regression model, in addition to known risk factors (sinonasal disease, obesity, Asthma Control Test (ACT) score, frequency of previous exacerbations, lung function, blood eosinophil count, smoking) to determine predictors for future exacerbations.

Results: Three hundred and forty patients were included for analysis. Their baseline characteristics are shown in Table 1. Indian ethnicity (OR 3.75, 95% CI 1.077-13.051, p=0.038), ACT score (OR 0.913, 95% CI 0.839-0.995, p=0.037) and number of previous exacerbations (OR 1.84, 95% CI 1.416-2.391, p<0.001) were the only independent predictors of future exacerbations. 64.9% of patients with uncontrolled symptoms (ACT <20) and previous exacerbations had one or more future exacerbations, compared to 14.6% of patients with controlled asthma symptoms (ACT score ≥20) and no previous exacerbations (Figure 1).

Conclusion: In our multi-ethnic cohort, symptom control, exacerbation rates and Indian ethnicity are important predictors of future exacerbations.

Table 1. Baseline characteristics (n=340)

| Age, mean (SD) years | 53±18 |
| Female, n (%) | 178 (52.4%) |
| Race, n (%) | 181 (53.2%) |
| Chinese | 112 (32.9%) |
| Malay | 33 (9.7%) |
| Indian | 14 (4.1%) |
| Others | |
| Pre-bronchodilator FEV1, mean (SD) % | 77±22 |
| Smoking status, n (%) | 42 (12.4%) |
| Current | 50 (14.7%) |
| Ex-smoker | 244 (71.8%) |
| Never | 4 (1.2%) |
| Missing data | |
| History of chronic sinonasal disease, n (%) | 99 (29.1%) |
| Absolute blood eosinophils ≥0.3 x 10^9/L, n (%) | 133 (39.1%) |
| Any previous exacerbations in past one year, n (%) | 129 (37.9%) |
| GINA treatment step 4 or 5, n (%) | 76 (22.4%) |

Asthma Control Test score <20, n (%) 111 (32.6%)

FEV1 = forced expiratory volume in 1 second; GINA = Global Initiative for Asthma

Figure 1. Risk of any exacerbations in the year following enrolment stratified according to symptom control and previous exacerbations

ACT = Asthma Control Test

ASTHMA CONTROL AND SMALL AIRWAY DYSFUNCTION DETECTED BY SPIROMETRY AND IMPULSE OSCILLOMETRY (IOS) IN THAI ASTHMATIC PATIENTS
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1Division of Pulmonary and Critical Care Medicine, Department of Medicine Ramathibodi Hospital Bangkok Thailand, Bangkok, Thailand

Background and Aims: Small airway dysfunction is associated with severe asthma. We investigated it prevalence detected by spirometry and IOS in asthma and the association with asthma control.

Methods: Cross sectional study in asthma patients attended chest clinic was done. Asthma control was assessed using ACT. Pre-BD and post-BD spirometry and IOS were performed. (Jaeger, UK). Association between spirometric and IOS parameters with asthma control were tested. P value <0.05 indicates statistical significance.

Results: Total 106 consecutive asthma patients were recruited. They were classified controlled (ACT>20) and uncontrolled asthma (ACT ≤20). Two-third (62%) of patients have IOS detected small airway dysfunction. There was significant difference between pre-BD and post-BD FVC, FEV1 and FEV1/FVC between controlled and uncontrolled asthma. FEF25-75% and IOS parameters were not different between in patients with controlled and uncontrolled asthma.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Uncontrolled asthma (n =26)</th>
<th>Controlled asthma (n =80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-BD FEV1 (L)</td>
<td>1.57 (0.69)</td>
<td>1.94 (0.73)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Pre-BD FEV1 (% predicted)</td>
<td>73.2 (22.3)</td>
<td>78.2 (18.7)</td>
<td>0.26</td>
</tr>
<tr>
<td>Pre-BD FEF25-75% (L/s)</td>
<td>5.33 (1.90)</td>
<td>6.0 (2.1)</td>
<td>0.81</td>
</tr>
<tr>
<td>Pre-BD FEF25-75% (% predicted)</td>
<td>56.3 (36.9)</td>
<td>54.4 (25.4)</td>
<td>0.77</td>
</tr>
<tr>
<td>Pre-BD FEF25-75% (% predicted)</td>
<td>5.64 (2.52)</td>
<td>6.40 (2.43)</td>
<td>0.40</td>
</tr>
</tbody>
</table>
Background and Aim: Acute asthmatic attack is common problem in emergency room but many doctors do not know how to manage correctly. Furthermore, many asthmatic patients have frequent exacerbations due to inappropriate assessment after emergency visits. Simulation-based training and assessment may increase skills and confidence of the residents in managing acute asthmatic attack and difficult asthma.

Methods: Twenty two first or third-year residents in internal medicine or emergency medicine participated in one-day simulation-based training in management of acute asthmatic attack and difficult asthma. Prospective evaluation was conducted by self-assessment questionnaires for confidence level and by performance observation in simulated situation before and after simulation-based training. Three months later, they were re-evaluated with two simulated scenarios. The first scenario was identical to previous test and the second scenario was a new scenario of acute asthmatic attack.

Results: Significant improvements in self-reported confidence and performance scores in simulation-based assessment were demonstrated. The performance scores also maintained after three months. Pre-test, post-test and 3-month post-test scores were 26%, 54.7% and 60.76%, respectively (p < 0.05). The performance scores with new scenario also revealed no significant difference (56.99% vs 50.85%, p=0.1930).

Conclusion: Simulation-based training and assessment improve clinical skills and confidence of the residents in managing acute asthmatic attack and difficult asthma. Moreover, the effects of the training in residents’ performances maintain in long term and the trainees can apply their skills to different situation.

Results:

- **Post-BD FEF25-75% (L/s)**
  - Pre-BD: 60.76 (33.4)
  - Post-BD: 62.5 (31.9)
- **Post-BD FEF25-75% (% predicted)**
  - Pre-BD: 1.69 (1.2)
  - Post-BD: 1.39 (0.7)
- **Post-BD R5-R20 (cmH2O/L/s)**
  - Pre-BD: 1.62 (0.6)
  - Post-BD: 1.06 (0.5)
- **Post-BD AX (cmH2O/L)**
  - Pre-BD: 16.23 (12.2)
  - Post-BD: 12.76 (9.5)
- **Post-BD AX (cmH2O/L)**
  - Pre-BD: 11.27 (6.4)
  - Post-BD: 9.30 (6.08)

Performance scores in simulation-based assessment were demonstrated.

Conclusions: Small airway dysfunctions detected by either spirometry or ICS were not different between asthmatic patients with controlled and uncontrolled diseases in Thai tertiary care centre.
TIOTROPIUM RESPIMAT® ADDED ON TO INHALED CORTICOSTEROIDS REDUCES AIRFLOW OBSTRUCTION IN ASIAN PATIENTS WITH MODERATE ASTHMA, INDEPENDENT OF ALLERGIC STATUS

SHU HASHIMOTO, LIN JIANGTAO, MICHAEL ENGEL, RALF SIGMUND, HUIB AM KERSTJENS
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Background: The MezzoTinA-asthma® studies demonstrated that once-daily (QD) tiotropium added to medium-dose inhaled corticosteroids (ICS) improves lung function.

Aims: To assess whether QD tiotropium added on to ICS improves lung function independently of clinician-judged atopy and allergic status in a subgroup of Asian patients from the MezzoTinA-asthma® studies (NCT01172808, NCT01172821).

Methods: Patients with a 3-month history of asthma and aged 18–75 years were included. After screening and a 4-week run-in period, patients were randomized (1:1:1:1) to tiotropium (Respimat®) 2.5 or 5 µg in the evening, twice-daily (BID) salmeterol 50 µg, or placebo. All patients received maintenance treatment with stable medium-dose ICS throughout. Co-primary endpoints were peak and trough FEV₁ change from baseline in each of the trials and ACQ responder rate. Post-hoc analyses of peak and trough FEV₁ by allergic and inflammatory status were performed in Asian patients according to clinician judgement of atopy, total serum IgE ≤ or >430 µg/L, and blood eosinophils ≤ or >0.6 × 10⁹/L.

Results: Overall, 2100 patients were randomized, 670 (31.9%) of whom were Asian. Improvements in peak and trough FEV₁ were similar with tiotropium 2.5 and 5 µg and salmeterol, and consistently greater in Asian patients than the overall population. Peak and trough FEV₁ improvements were observed with both doses of tiotropium; importantly, these improvements were independent of clinician judgement of atopy (Table 1), IgE (Table 2) or eosinophil count (Table 3) (interaction p-value >0.05, all). The safety and tolerability profile of tiotropium was comparable to that of placebo.

Conclusions: QD tiotropium added on to ICS improves lung function regardless of allergic status as defined by clinician-judged atopy, IgE concentration, or eosinophil count, and thus may be a viable treatment option for Asian patients with moderate symptomatic asthma.

Acknowledgement: Funded by Boehringer Ingelheim

Table 1. Interaction analysis of peak and trough FEV₁ values by clinician judgement of atopy (24weeks)

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Peak FEV₁ Adjusted mean difference from placebo (95% CI), L</th>
<th>Trough FEV₁ Adjusted mean difference from placebo (95% CI), L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician judgement of atopy: No</td>
<td>Tiotropium Respimat® 2.5 µg</td>
<td>0.268 (0.170, 0.366)</td>
</tr>
<tr>
<td></td>
<td>Tiotropium Respimat® 5 µg</td>
<td>0.213 (0.113, 0.313)</td>
</tr>
<tr>
<td></td>
<td>Salmeterol</td>
<td>0.192 (0.287)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Clinician judgement of atopy: Yes</td>
<td>Tiotropium Respimat® 2.5 µg</td>
<td>0.236 (0.153, 0.319)</td>
</tr>
<tr>
<td></td>
<td>Tiotropium Respimat® 5 µg</td>
<td>0.254 (0.173, 0.335)</td>
</tr>
<tr>
<td></td>
<td>Salmeterol</td>
<td>0.164 (0.232)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Interaction p-value</td>
<td></td>
<td>0.768</td>
</tr>
</tbody>
</table>

n: number of patients with measurements at the respective time point

Table 2. Interaction analysis of peak and trough FEV₁ values by IgE concentration (24weeks)

<table>
<thead>
<tr>
<th>IgE ≤ 430 µg/L</th>
<th>Peak FEV₁ Adjusted mean difference from placebo (95% CI), L</th>
<th>Trough FEV₁ Adjusted mean difference from placebo (95% CI), L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiotropium Respimat® 2.5 µg</td>
<td>0.215 (0.113, 0.318)</td>
<td>65</td>
</tr>
<tr>
<td>Tiotropium Respimat® 5 µg</td>
<td>0.280 (0.172, 0.389)</td>
<td>51</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>0.215 (0.113, 0.318)</td>
<td>64</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td>58</td>
</tr>
<tr>
<td>IgE &gt; 430 µg/L</td>
<td>Tiotropium Respimat® 2.5 µg</td>
<td>0.271 (0.190, 0.353)</td>
</tr>
<tr>
<td>Tiotropium Respimat® 5 µg</td>
<td>0.223 (0.145, 0.301)</td>
<td>110</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>0.294 (0.213, 0.375)</td>
<td>97</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td>98</td>
</tr>
<tr>
<td>Interaction p-value</td>
<td></td>
<td>0.1128</td>
</tr>
</tbody>
</table>

n: number of patients with measurements at the respective time point

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Asthma, to maintain ICS is a critical problem in general clinical setting. Use of ICS for CVA is reported to be effective to prevent onset of typical asthma. Although early introduction of anti-inflammatory medication is necessary for the initial treatment for CVA. Smart therapy for CVA could lead to the recognition of continued therapy for CVA. Cough-variant asthma (CVA) is a type of asthma characterized only by chronic dry cough without wheezing and an attack of dyspnea. In Japan CVA is the most prevalent cause of chronic cough. The once-a-day use of inhaled steroid combined with a long acting beta-2 agonist (fluticasone furoate) combined with long-acting beta-2 agonist (vilanterol) was introduced for the patients. After 2 weeks of initial treatment, maintenance dose was stepped down to half dose for the patients who performed good control based upon clinical evaluation.

### Table 3. Interaction analysis of peak and trough FEV₁ values by eosinophil concentration (24weeks)

<table>
<thead>
<tr>
<th>Eosinophils ≤ 0.6×10⁹/L</th>
<th>Tiotropium Respimat® 2.5µg</th>
<th>Placebo</th>
<th>Eosinophils &gt; 0.6×10⁹/L</th>
<th>Tiotropium Respimat® 2.5µg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak FEV₁ Adjusted mean difference from placebo (95% CI), L</td>
<td>0.246 (0.172, 0.321)</td>
<td>0.201 (0.128, 0.274)</td>
<td>0.242 (0.168, 0.317)</td>
<td>0.270 (0.147, 0.393)</td>
<td>0.353 (0.228, 0.478)</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.175 (0.094, 0.255)</td>
<td>0.148 (0.069, 0.227)</td>
<td>0.144 (0.064, 0.225)</td>
<td>0.258 (0.117, 0.394)</td>
<td>0.310 (0.167, 0.453)</td>
</tr>
<tr>
<td>Interaction p-value</td>
<td>0.2215</td>
<td>0.6955</td>
<td>0.35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n: number of patients with measurements at the respective time point

### EFFECTS OF ONCE-A-DAY USE OF INHALED STEROID (FLUTICASONE FUROATE) COMBINED WITH LONG-ACTING BETA-2 AGONIST (VILANTEROL) ON VARIOUS FLOW DATA IN BRONCHIAL ASThma

Background and Aim: Japanese drug use system allowed “once-a-day use” of inhaled corticosteroid combined with a long acting beta 2 agonist against bronchial asthma for the first time in Dec, 2013. We investigated the efficacy and problems on this combined drug.

Methods: 54 bronchial asthma outpatients (100% Asians) were enrolled from 2014-2016 (IUWH ethical committee approval number: 13-B-66). Previous treatments of bronchial asthma (twice daily use of inhaled steroids combined with long-acting beta-2 agonists) were changed to the once-a-day use of inhaled steroid (fluticasone furoate) with long-acting beta-2 agonist (vilanterol). Subjects were evaluated by lung function tests prior to, and 2-3 months after the initiation of fluticasone furoate/vilanterol.

Results: 46 subjects (85%) completed the study. Peak Flow in fluticasone furoate/vilanterol-used subjects significantly increased (p < 0.01). V75 and V50 also significantly increased (p < 0.05). V25 did not show significant difference. 96% of subjects declared that they wanted to continue the new treatment in the future. Adverse effects of hoarseness and/or uncomfortable sensations in throats increased (30%).

### Table 4. Changes in various flow data by once-a-day use of fluticasone furoate/vilanterol

<table>
<thead>
<tr>
<th>Item</th>
<th>Before</th>
<th>After</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak flow (L/s)</td>
<td>5.50 ± 2.22</td>
<td>5.89 ± 2.22</td>
<td>0.003</td>
</tr>
<tr>
<td>V75 (L/s)</td>
<td>3.82 ± 2.17</td>
<td>4.25 ± 2.22</td>
<td>0.013</td>
</tr>
<tr>
<td>V50 (L/s)</td>
<td>1.93 ± 1.35</td>
<td>2.14 ± 1.46</td>
<td>0.023</td>
</tr>
<tr>
<td>V25 (L/s)</td>
<td>0.65 ± 0.61</td>
<td>0.69 ± 0.67</td>
<td>0.347</td>
</tr>
</tbody>
</table>

Conclusion: The once-a-day-use of fluticasone furoate/vilanterol is a potent and effective treatment. Its effect was clearer on larger airways and yielded high satisfactions to patients despite higher incidence of hoarseness and/or uncomfortable sensations in throats.
A FINE PARTICLE INHALED CORTICOSTEROID EXHALATION THROUGH THE NOSE IS A THERAPEUTIC OPTION FOR EOSINOPHILIC CHRONIC RHINOSINUSITIS WITH BRONCHIAL ASThma

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Background and Aims: Eosinophilic chronic rhinosinusitis (ECRS), a subgroup of chronic rhinosinusitis, is known as a refractory eosinophilic airway inflammation. ECRS is highly associated with bronchial asthma and requires ‘Airway Medicine’, comprehensive care of the upper to lower airway based on the concept of ‘one airway, one disease’. We recently reported on the efficacy of fine-particle inhaled corticosteroids (ICS) exhalation through the nose (ETN) for ECRS with asthma. Although this treatment provides beneficial effects for most patients, its effects can be transient or marginal. Here we examined the association between the effect of fine-particle ICS ETN treatment and the ideal flow conditions for this treatment.

Methods: One hundred ECRS patients with bronchial asthma under fine particle ETN treatment were recruited and evaluated for the efficacy of the treatment for their sinusitis and the optimal flow conditions under the ETN process retrospectively. The flow conditions were evaluated using a spirometer with a facemask. In addition, a particle counter system and the particle deposition model using a human nasal cavity cast was used for a visualization study.

Results: The efficacy of fine particle ICS ETN treatment was observed in 63 of study subjects. The ideal flow pattern (average 30.5 L/min of mid-expiratory flow rate and 1.6 L of flow volume) was observed in patients improved under ETN treatment. The visualization study suggested that exhalation through the nose at a rate under 10[30] L/min of expiratory flow allowed fine particles to deposit on middle meatus, including the sinus ostia.

Conclusions: We have found the ideal flow conditions for fine particle ICS ETN treatment in ECRS patients with asthma. An ETN treatment under the appropriate conditions could offer a new therapeutic strategy to deliver drug to a perilesional area.

Table 1. Spearman’s Rho Correlation Between Asthma-related Symptoms and Daily Diary Assessments at Baseline and End of Treatment

<table>
<thead>
<tr>
<th>Variables For Correlation</th>
<th>Baseline</th>
<th>Change From Baseline to End of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benralizumab</td>
<td>Placebo</td>
</tr>
<tr>
<td>Activity function: limitation of activities</td>
<td>0.77</td>
<td>0.76</td>
</tr>
<tr>
<td>Activity function: avoidance of activities</td>
<td>0.76</td>
<td>0.73</td>
</tr>
<tr>
<td>Activity function: need to pace self</td>
<td>0.76</td>
<td>0.72</td>
</tr>
<tr>
<td>Feeling tired</td>
<td>0.76</td>
<td>0.72</td>
</tr>
<tr>
<td>Feeling stressed</td>
<td>0.50</td>
<td>0.48</td>
</tr>
<tr>
<td>Percentage of night-time awakening</td>
<td>0.65</td>
<td>0.62</td>
</tr>
<tr>
<td>Total rescue medication use (puffs per day)</td>
<td>0.57</td>
<td>0.56</td>
</tr>
</tbody>
</table>

All p<0.05.

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REDUCTION IN EXACERBATIONS WITH RESLIZUMAB IN KOREAN PATIENTS WITH ASTHMA AND ELEVATED BLOOD EOSINOPHILS
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1Yonsei University College of Medicine, Seoul, South Korea, 2Seoul National University College of Medicine, Seoul, South Korea, 3Teva Branded Pharmaceutical Products R&D Inc., Malvern, USA

Background: Reslizumab (RES), anti-IL-5 monoclonal antibody, in duplicate multicenter phase 3 placebo (PBO)-controlled trials (PCTs), significantly reduced the risk of clinical asthma exacerbations (CAE) and improved asthma control, lung function, and quality of life (QOL) in patients with uncontrolled eosinophilic asthma (Castro et al Lancet Respir Med 2015:3:355-66).

Aims: To report the experience of Korean patients in a phase 3 PCT and open-label extension (OLE).

Methods: Patients who completed a PCT with IV RES 3 mg/kg Q4W (52 wks) could choose to enter an OLE for up to 2 yrs. Efficacy assessments included: rate of CAE, and change from baseline in FEV1, ACQ-6, and AQLQ(S)+12.

Results: 34 patients participated in the PCT; 21 continued into the OLE. Eosinophils decreased in the RES group from 669/μL at baseline to 47/μL by Week 4, with reduction sustained through 52 weeks. Decreases in overall CAE and CAE requiring ≥3 days of oral corticosteroids with RES were 87% (95% CI: 37%, 97%) and 89% (95% CI: 25%, 99%), respectively, versus PBO. These results were replicated in a cohort of all patients of Asian descent (N=120), with reductions of 70% (95% CI: 36%, 86%) and 74% (95% CI: 37%, 89%), respectively. Although not powered for this subgroup, trends toward improvements in FEV1, ACQ-7, and AQLQ for RES versus PBO existed at 52 weeks: 109 mL (95% CI: -156, 373mL), -0.06 (95% CI: 0.42, -0.53), and +0.3 (95% CI: -0.44, 1.04), respectively. RES-naive patients in the OLE experienced a decrease in eosinophils by 4 weeks; both RES-experienced and RES-naive patients experienced sustained decreases through the OLE period. The overall safety profile of this cohort was similar to the pivotal phase 3 trials (Castro 2015).

Conclusions: RES effectively reduced the CAE rate, and showed a trend in improved lung function, asthma control, and QOL in this Korean subcohort.

RESPONSE TOomalizumab treatment according to pre-treatment blood eosinophil count: results of a French real-world study (Stellair)
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1Université Paris-Sud, Service de Pneumologie, AP-HP, Hôpital Bicêtre, Le Kremlin-Bicêtre, France, 2Service de Pharmacologie, CHU Pellegrin, Bordeaux, France, 3Novartis Pharma S.A.S, Rueil-Malmaison, France, 4Novartis Pharma AG, Basel, Switzerland

Background and aims: Omalizumab (OMA) has been available for more than 10 years and has shown, in randomized and real-world studies, clinical benefits in severe allergic asthma (SAA). Novel biologics targeting interleukin-5 in the Th2 pathway are emerging for the treatment of severe eosinophilic asthma (SEA). The aim of this observational retrospective study was to describe, in real-world conditions, responders to OMA after 6 months. Response was assessed by using physician’s global evaluation and/or objective assessment based on a reduction of at least 40% in the annual exacerbation rate. Response rate (RR) was calculated according to blood eosinophil count per microliter (EOS) measured in the year prior to OMA initiation.

Methods: 872 SAA OMA-treated patients have been included in 78 French sites: 723 adults and 149 minors; 68 were 6-11 years, and 81 were 12-17 years of age.

Results: Median EOS count per μL was 308 in adults and 619 in minors. EOS was ≥300/μL in 52.1% of adults and 73.4% of minors. EOS was ≥150/μL in 77.5% of adults and 88.6% of minors. In adults, RR for the 2 combined criteria was 58.4% (95% CI, 53.2% to 63.4%) in EOS≥300 (n=377) and 58.1% (95% CI, 52.7% to 63.4%) in EOS<300 (n=346). The response rates were similar, irrespective of studied cut-off EOS and for all response definitions. Response was independent of the change in EOS counts observed during OMA treatment.

Conclusions: This large real-world study quantified the large overlap between SAA and SEA and showed that OMA efficacy was similar between high and low EOS SAA subgroups. These results confirm that OMA is an important treatment option in the management of SAA regardless of the pre-treatment EOS level.
THE DEVELOPMENT OF TH1-RELATED DISEASES DURING OMALIZUMAB TREATMENT: A CASE OF SARCOIDOSIS IN A PATIENT WITH SEVERE ASTHMA

HIROAKI HAYASHI1,2, YUMA FUKUTOMI1, CHIHIRO MITSUI1, YUTO NAKAMURA1, YUTO HAMADA1, YASUHITO TOMITA1,2, YOSUKE KAMIDE1, KIYOSHI SEKIYA1, TAKAHIRO TSUBURAI1, AYAKO HORITA1, IKUO SATO1, YOSHINORI HASEGAWA1, MASAMI TANIGUCHI1

1Clinical Research Center for Allergy and Rheumatology, Sagamihara National Hospital, Sagamihara, Japan, 2Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan, and 3Department of Pathology, Sagamihara National Hospital, Sagamihara, Japan

Background and Aims: Asthma is a Th2 helper 2 (Th2) induced chronic respiratory disorder. Omalizumab, a recombinant humanized monoclonal antibody that selectively binds to free IgE to suppress Th2 inflammatory responses, significantly improves disease control when used as an add-on to current asthma therapy. However, the side effects of omalizumab are unclear in asthma patients. This study describes a case of severe asthma who developed a Th1-related disease, pulmonary sarcoidosis.

Case presentation: The patient was a 56-year-old Japanese never-smoker woman with a history of aspirin-exacerbated respiratory disease. However, her symptoms remained uncontrolled despite being fully adherent to the treatment (budesonide/formoterol, montelukast and theophylline with salbutamol as needed). Within one month of omalizumab treatment initiation (May 2016), the asthma was controlled. However, she complained of worsening dyspnea without wheezing in August 2016. Chest computed tomography indicated ground-glass opacities, interlobular septal thickening, and centrilobular nodules. Furthermore, increased serum levels of soluble interleukin-2 receptor (1280 U/mL) were reported. Finally, omalizumab treatment was stopped in August 2016. In October 2016, video-assisted thoracic surgery of the right middle lobe indicated a non-caseating epithelioid cell granuloma with sarcoidosis by histopathology. In November 2016, daily oral prednisolone (20 mg/day) was administered and 3 months later, symptoms and lung infiltrate on chest radiography were improved.

Discussion: We experienced the development of pulmonary sarcoidosis in a patient with severe asthma treated with omalizumab. The development of sarcoidosis (induced by a predominant Th1 immune response) after omalizumab treatment might have been caused by the strong suppression of Th2-related inflammation. This case indicates that omalizumab might suppress Th2 related immune responses and promote Th1 related immune responses.

Conclusions: Physicians should pay attention to the potential development of Th1-related diseases in patients treated with omalizumab.

FEVIPIPRANT PHASE III EXACERBATION STUDIES: LUSTER-1 AND LUSTER-2 STUDY DESIGN

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1University of Leicester, Glenfield General Hospital, Leicester, United Kingdom, 2Novartis Pharmaceuticals Australia Pty Limited, Macquarie Park,, Australia, 3University of Pittsburgh, Pittsburg,, United States

Background and Aims: Clinical trials of fevipiprant, an orally administered, non-biologic prostaglandin D2 receptor 2 (DP2; also known as CRTh2), have shown promising effects on improving symptoms and exacerbation rates in patients with severe asthma. Methods: These 52-week, multicentre, double-blind, placebo-controlled parallel-group studies will randomise (1:1:1) patients (≥12 years age, n = 846 in each study) with uncontrolled severe asthma receiving GINA 2016 steps 4 and 5 SoC asthma therapy to 1 of 2 doses of fevipiprant or placebo once daily. The primary endpoint is the rate of moderate-to-severe exacerbations over the 52-week treatment period in severe asthma patients with high blood eosinophil counts (≥250 cells/μL), and in all patients with severe asthma receiving SoC. Secondary endpoints are change in asthma quality of life (measured via AQLQ +12), asthma control (measured via ACOG-5), and FEV1. Safety of fevipiprant in terms of adverse events, electrocardiograms, vital signs, and laboratory tests will also be assessed.

Conclusion: Results from LUSTER-1 and LUSTER-2 studies will clarify whether oral once-daily fevipiprant added to standard-of-care asthma therapy offers a well-tolerated, anti-inflammatory therapy that reduces exacerbations and improves symptoms in patients with uncontrolled severe asthma.
Cell Molecular Biology

by Yap and Taz, we performed gene expression microarray analysis in
erated by using a surfactant protein C-driven Cre recombinase, and ana-
adverse events associated with PATCH.

57.49
552
543
501
522
532
543
552
563
573
585
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1ERUUSHIYAMA1, HIROYUKI TAMIYA 1, SATOSHI NOGUCHI 1, AKIRA
1Department of Respiratory Medicine, Graduate School of Medicine,
University of Tokyo, Japan

Branching abnormalities. Microarray analysis revealed candidate down-

proper lung development. Furthermore, Taz cKO mice may serve as a

Conclusions:

Background and Aims:

reduced total immunoglobulin E (IgE) concentration (MD -42.10 IU/ml,
95% CI -44.09 to -40.12, I²=0%) and eosinophil (EOS) numbers (MD -
57.49±106.6L, 95% CI -118.98 to 4.01, I²=23%), and increased asthma
control test (ACT) score (MD 1.46 points, 95% CI 0.82 to 2.09, I²=0%).

Conclusions: Evidence suggests that PATCH may be a valid and
potential treatment for stable asthma. It contributes to improving lung
function and clinical symptoms, reducing total IgE concentration and EOS
numbers. However the benefits of PATCH still need further evaluation
due to study design and reporting weaknesses.

Background and Aims: Yes-associated protein (YAP) and Trans-
scriptional co-activator with PDZ-binding motif (TAZ) are key downstream
effectors of the Hippo pathway. These two transcriptional co-activators
share most of their structural and functional characteristics. We previously
reported that Taz knockout mice showed lung emphysema-like phenotype
in adult. Recently several studies reported that lung-specific Yap condi-
tional knockout (cKO) mice embryos showed abnormalities in bronchial
development. The aim of this study is to investigate the cause of these
differences between YAP and TAZ in lung development.

Methods: Lung epithelial specific Yap and Taz cKO mice were gen-
erated by using a surfactant protein C-driven Cre recombinase, and ana-
yzed pathologically and physiologically. To identify novel genes regulated
by Yap and Taz, we performed gene expression microarray analysis in
human lung epithelial cell lines, which YAP and TAZ were suppressed by
siRNA.

Results: In wild-type mice lungs, Yap was highly expressed in the
pseudoglandular stage of lung development, conversely Taz was highly
expressed in the early alveolar stage. Taz cKO adult mice showed
enlarged alveolar space in histological studies and decreased elastance
in physiological analysis. Yap cKO mice embryos showed bronchial
branching abnormalities. Microarray analysis revealed candidate down-
stream genes that were regulated by Yap and Taz in lung cells.

Conclusions: The results indicate that Yap and Taz function at dif-
f erent stages of lung development in lung epithelial cells and essential for
proper lung development. Furthermore, Taz cKO mice may serve as a
novel mouse model of human COPD.

Background and Aims: Primary ciliary dyskinesia (PCD) is a rare
heterogeneous genetic disorder. To identify the potential causative gene
in two affected siblings with PCD, who are from a consanguineous Chi-
nese family, we combined whole-exome sequencing (WES) and runs of
hozygosity (ROH) analysis.

Methods: (1) According to medical history, two affected siblings with
PCD were identified in a consanguineous family. (2) The peripheral blood
was collected to extract DNA (two patients and parents). Then genetic
analysis was performed. The filtering are as follows: (i) Variants within
intergenic, intronic, and UTR regions and synonymous mutations were
excluded; (ii) High-frequency (MAF>0.01) polymorphisms were excluded;
(iii) Extract the segregating variants in the two siblings using WES; (iv) ROH
was performed; (v) Sanger sequencing was used to validate the candidate
variants and segregation analyses were performed in the family mem-
bers; (vi) Bioinformatics software were used to predict the possible impacts
of variants; (vii) Domain and conservation analysis were performed; (vii)
The mutation identified was searched in pubmed, Google scholar and
HGM database.

Results: After WES and ROH analysis, a novel homozygous mutation,
c.384delC (p.Y128*) in DYX1C1, was identified, which leads to a truncation of the encoded pro-
teins. DYX1C1 (p.Y128*). This homozygous variant was not reported before.

Conclusions: (1) The novel variant c.384delC (p.Y128*) in DYX1C1 is the potential causal mutation for the consanguineous family. The identi-
fication helps the two siblings to make a genetics diagnoses. (2) It contri-
butes to the growing number of candidate mutational sites associated with
PCD and benefits the future genetic counseling for PCD. (3) WES in com-
bination with ROH analysis is a necessary choice in genetic research of
midget consanguineous family.

Background and Aims: In patients with asthma the inhalation of the
humid air can lead to spastic bronchial response, which becomes the rea-
son for the growth of exacerbation frequency. The aim was to study the
character and degree of changes in cilia motility of the bronchial epithe-
lium (BE) under the influence of hyposmolar stimulus on bronchial biopsy
sample in vitro.

Methods: Bronchoscopy with the biopsy of lobar bronchus mucosa
was performed in 39 patients with asthma (14 men and 25 women).
Biopsy sample was put into the chamber with Hank’s solution. Registra-
tion of the motion activity of BE cilia was done with the use of a micro-
scope, a camera in built highly sensitive digital full-frame matrix of high
definition and a computer. The recording of BE cilia beating was done immedi-
ately after the biopsy sample was put on the object-plate in
the Hank’s solution. Modelling of hyposmolar stress was carried out by
adding 0.01 ml of distilled water into 0.01 ml of Hank’s solution with the
help of the dispenser. Recording of cilia beating was repeated immedi-
ately after the addition of distilled water and after 1, 2, 3 and 4 minutes.

Results: The initial frequency of BE cilia beating fluctuated within the
range from 12.2 till 2.7 Hz (mean 8.73±1.27 Hz). When the distilled water
was added, the frequency was decreased till 6.51±1.71 Hz (p<0.001).
After the 1st minute of the experiment the frequency decreased till
5.94±1.57 Hz (by 9% in comparison with the initial value of the stress rea-
ction). During the 2nd, 3rd and 4th minutes of observation there was a

WHOLE-EXOME SEQUENCING AND RUNS OF
HOMOZYGOSITY IDENTIFIES A NOVEL MUTATION OF
DYX1C1 IN PRIMARY CILIARY DYSKINESIA FROM AN
INBRED CHINESE FAMILY

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Central South University, Changsha, China, and 2Research Unit of
Respiratory Disease, Central South University, Changsha, Hunan, China

Abstracts
steadiness of BE cilia beating frequency decrease (by 13, 15 17%, respectively). By the 4th minute the beating frequency was 5.33±1.29 Hz.

Conclusions: The motility activity of BE cilia is significantly decreased under the influence of hyposmolar stimulus.

AP217

EFFECTS OF DIESEL EXHAUST PARTICLE IN HUMAN BRONCHIAL EPITHELIAL CELL MIGRATION AND THE INTRACELLULAR SIGNALING PATHWAY

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Background and Aims: Diesel exhaust particle (DEP) is the major components of PM2.5. Many studies of molecular mechanisms have focused on the role of reactive oxygen species (ROS) generated directly and indirectly by exposure to DEP. We have confirmed that DEP was involved with induction of epithelial-mesenchymal transition (EMT) process in human bronchial epithelial cell (HBEC) by oxidative stress. The current study was designed to elucidate the effect of DEP and the intracellular signaling pathway of DEP in the cell migration on HBEC.

Methods: We used human bronchial epithelial cell line BET-1A. The cells were plated into 24-well plates in the culture medium (LHC-9). When 90% confluent, in the first experiment, DEP (Standard Reference Material 2975) was treated culture cells with various concentrations for 24hs; in the second experiment, DEP was treated with 25μg/ml and G1 Protein inhibitor (pertussis toxin solution, PT) or ROCK inhibitor (Y-27632) treated culture cells with various concentrations for 24hs. The cells were “wounded” using a pipette tip. Cultures were then incubated in basal medium (LHC-9) with 30% LHC-9 for 24hs, after which the cell layers were fixed and stained with May-Girnza. Photomicrographs were taken and then examined cells migration in each group.

Results: The cells migration was up-regulated by DEP exposure. The stimulation of cells migration by DEP exposure was blocked by PT treatment, however, no effect of Y27632 was observed.

Conclusions: Our results suggest that DEP might be involved with induction of EMT process in human bronchial epithelial cells, and the stimulation of EMT cells migration by DEP might be mediated by GTP-binding protein signaling pathway.

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DESTRUCTIVE-CYTOLYTIC ACTIVITY OF BRONCHIAL EPITHELIUM AND ITS INFLUENCE ON THE DEVELOPMENT OF COLD AIRWAY HYPERRESPONSIVENESS IN PATIENTS WITH ASTHMA

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Background and Aim: The destruction of airway epithelium under the influence of effectors of inflammation in asthmatics with cold airway hyperresponsiveness (CAHR) has not been studied yet. The aim was to study destructive and cytolytic activity of cells of bronchial epithelium in asthmatics in correlation with structural-functional profile of granulocytic segment of bronchial inflammation and to assess its influence on the development of CAHR.

Methods: FEV1, airway response (ΔFEV1) to 3-minute ultrasound inhalation with distilled water (IDW), the contents of myeloperoxidase (MPO, pixels) in the induced sputum (IS), the level of MPO (ng/ml), neutrophilic elastase (NE, ng/ml) and α1-antitrypsin (AAT, mg/dl) in the blood serum before and after IDW were studied in 36 patients with asthma (mean age 40.6±1.6 years old).

Results: According to the results of cytological study, 11 patients with low contents of neutrophils in IS (11.5±1.2%) were included in the 1st group. 25 patients with high contents of neutrophils (37.5±3.9%, p=0.0001) in the 2nd group. The level of asthma control was lower in the 2nd group than in the 1st group (17.1±0.98 vs. 20.0±1.0 points of ACT, p=0.05), FEV1 was lower (89.6±2.8 vs. 100.2±3.9%, p=0.04), and the response to IDW was more intensive (ΔFEV1 -6.5±1.5% vs. -1.8±1.9%, p=0.049). In response to IDW the patients of the 2nd group had a decrease of MPO from 267.5±48.4 till 159.9±32.8 (p=0.003), of NE from 411.1±71.8 till 223.1±41.5 (p=0.004), of AAT from 227.8±8.7 till 205.1±12.1 (p=0.042), whereas in the 1st group the values of MPO (170.4±50.3 vs. 164.0±59.6), NE (258.9±86.5 vs. 208.4±70.3) and AAT (213.8±11.4 vs. 211.5±14.5) did not change significantly.

Conclusions: Activation of neutrophilic component of bronchial inflammation in patients with asthma leads to worsening of the lung function and is concomitant with the decrease of the system level of peroxidase, protease and antiproteolytic activity in response to IDW.

THE ASSESSMENT OF DIFFERENCE LEVEL OF TISSUE INHIBITOR OF METALLOPROTEINASE (TIMP)-1 FROM PERIODONTAL FLUID AMONG SMOKERS

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Background and Aim: The periodontium is vulnerably exposed during smoking leading to the extracellular matrix (ECM) destruction due to active activity of proteases. Lowly balanced level of TIMP-1 from gingival crevicular fluid (GCF) in order to evaluate the presumed ECM destruction among smokers, especially ex smokers suffering from COPD.

Methods: The study included 30 male smokers, of whom 15 were ex smokers suffering from COPD. They underwent the physical examination and spirometry. The criteria of COPD based on post bronchodilator FEV1/FVC < 70% with FEV1% predicted <50%. Then, the gingival crevicular fluid (GCF) was absorbed by inserting a small piece of filter paper into the gingival sulci.

The measurement of TIMP-1 level from GCF used the ELISA method applying R&D system.

Abstracts

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Cadmium (Cd), a major component of cigarette smoke, disrupts the normal functions of airway cells and can lead to the development of various pulmonary diseases such as chronic obstructive pulmonary disease (COPD). However, the molecular mechanisms involved in Cd-induced pulmonary diseases are poorly understood.

Background and Aims: Acute lung injury (ALI) is an inflammatory response of the lung to various causes. Besides inflammation, apoptosis is related to tissue damage in ALI mechanism. PDRN is a compound extracted from spermatozoa of salmon. PDRN has showed both anti-inflammatory and anti-apoptotic effects. This study was conducted to confirm the possibility of PDRN as a therapeutic agent in acute lung injury.

Methods: 36 male SD rats were classified into control group, ALI group, and ALI+PDRN treatment group. ALI was induced by intra-tracheal Lipopolysaccharide administration. The PDRN was injected into the abdominal cavity once at a concentration of 8 mg/kg, 1 hour after LPS administration.

Results: Compared with the control group, in lung tissue, inflammatory makers in ALI group were significantly higher in lung tissue (TNF-a (1.00 ± 0.00 vs. 1.52 ± 0.08; P=0.001) and IL-6 (3h: 1.00 ± 0.00 vs. 1.60 ± 0.14; P=0.003)), and in the BALF (TNF-a (3h: 30.69 ± 3.07 vs. 3236.31 ± 162.06 pg/mL; P=0.0000) and IL-6 (3h: 35.37 ± 3.54 vs. 2495.50 ± 121.58 pg/mL; P=0.0000)). Between ALI group and ALI+PDRN treated group, ALI+PDRN treatment group showed significant inflammation lowering effect in lung tissue (TNF-a(1.52 ± 0.08 vs. 1.01 ± 0.03) and IL-6 (1.60 ± 0.12 vs. 0.55 ± 0.02), all P<0.05) and in BALF(TNF-a(3326.31 ± 162.06 pg/mL vs. 2112.16 ± 265.92 pg/mL), IL-6(3h: 2495.50 ± 121.58 pg/mL vs. 1545.23 ± 194.54 pg/mL) and improving pathologic change(Lung injury score ALI 1.62 ±0.18, ALI-PDRN 1.5±0.16 p<0.02).

Conclusion: The protective effect of PDRN on ALI may be associated with suppression of both apoptosis and inflammatory responses. Thus, it can be suggested that PDRN might be a potential therapeutic agent for ALI.
Background and Aims: Mucous cell hyperplasia and airway smooth muscle (ASM) hyperresponsiveness are hallmark features of inflammatory airway diseases, including asthma. Increasing evidence suggests that calcium-activated chloride channels (CaCCs) ANO1 play an important role in transepithelial transport and mucus overproduction in the airway epithelium. Recent data shows that ANO1 is increased in the airways of asthmatics, particularly in secretory cells and the treatment of inhibitor of ANO1 downregulates mucin secretion and methacholine-induced ASM contraction, two debilitating features of chronic asthma.

Spirodela polyrhiza (SP) has been used as a traditional remedy for the treatment of inflammation. In this study, we examined the effects of SP extract and its chemical constituents on the modulation of ANO1 channels to evaluate for use in therapeutic agents for treatment of asthma.

Methods: A 30% ethanolic extract of SP was prepared. Human ANO1 over-expressed HEK293T cells were treated with SP extract. Modulation of ANO1 activity was measured by using a conventional whole-cell patch-clamp technique. Continuous flow type Ussing chamber technique also applied to determine the changes of transepithelial voltage (Vte) and equivalent short-circuit current (Isc) induced in the epithelium of mouse trachea by the ACh analogue carbamylcholine (carbachol, CCh).

Results: SP extracts significantly inhibited ANO1 activity in ANO1 overexpressed HEK293T cells at −100 mV by 34.13 ± 2.14%, 57.10 ± 3.344% and 87.96 ± 1.02% at 30, 100 and 300 μg/mL, respectively. Furthermore, electrophysiological analysis revealed that luteolin, one of the chemical constituents in SP extract, inhibited ANO1 activity at a concentration of 30 μM (62.14 ± 4.3% inhibition at -100 mV). Isc measurement in the epithelium of mouse trachea showed that luteolin significantly blocked ANO1 chloride current activated by application of CCh.

Conclusions: SP extract and its chemical constituent, luteolin, may have a therapeutic potential for respiratory inflammatory disease through modulating the activities of ANO1.

ASSSESSMENT OF INTENSIVE CARE UNIT MRSA PATIENT OUTCOMES USING IN SILICO GENOMIC VIRULENCE SIGNATURES SCREENING

Background and Aim: Next generation sequencing (NGS) technology allowed in silico detection of genomic virulence signatures of clinical methicillin-resistant Staphylococcus aureus (MRSA) isolates. A correlation study between these signatures and clinical data would serve as an NGS application for intensive care unit (ICU) patient outcome assessment.

Methods: Genomic DNA of 71 MRSA isolates obtained from the specimens of intensive care unit (ICU) patients treated at a university hospital from year 2009 (15/71) and year 2013 (56/71) was extracted and sequenced using Illumina® MiSeq. VirulenceFinder sequence mapping tool was used to identify the genomic virulence signatures. Correlation analysis was performed between the signatures and the patient outcomes as categorized into fatal and non-fatal cases.

Results: Eighty four MRSA genomic virulence signatures were detected from the genomic sequence data. Singular in silico detections of eap (q value=0.283, P=0.043) and lukS (q value=0.287, P=0.030) and combined detection of eap-lukS (q value=0.399, P=0.027) were correlated with the outcome. The positive signature detections were found primarily in the non-fatal cases.

Conclusion: The MRSA genomic virulence signatures obtained from sequence data were correlated with the outcome of ICU patients, wherein positive signature detections were found in non-fatal cases. The conspicuous finding was attributed by the disproportional sample size, the limited clinical course data, and the lack of accompanying method for genomic confirmation; nevertheless, this study served as an insight for the future NGS study applications for clinical infection surveillance.

Keywords: genomic MRSA signature, virulence study, next-generation analysis study, intensive care infection surveillance

EFFECT OF HYPOXÆMIA AND HYPERCAPNIA ON COGNITION IN INDIAN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background: Cognitive deterioration is emerging as an important comorbidity in patients with COPD.

Aims: We attempted to assess the effect of hypoxæmia and hypercapnia on cognitive dysfunction in Indian patients with stable COPD.

Methods: Eighty five out of 55 (82%) patients in group A, and all patients in groups B, C and D had some degree of cognitive impairment (MMSE <24). When the MMSE score of the different groups were compared, there was no statistical significance between groups A & B only. However, a significant difference (p<0.05) was found in the MMSE scores between groups A & C, A & D, B & C, B & D, and C & D. Analyses of the TMT-A times also revealed a statistically significant difference (p<0.05) between groups A & C, A & D, B & C, B & D, and C & D.

Conclusions: Patients with COPD have some degree of cognitive decline, which worsens with disease severity. Oxygen therapy helps in preserving cognition, but this protection is lost in the presence of hypercapnia.
Background and Aims: Depression has been well identified as co-morbidity of COPD. Where studies have suggested COPD patients to be at risk of anxiety and depression other studies have identified depression to increase the risk of exacerbation and hospitalization in COPD patients. Aim of this study is to find the prevalence, correlation and risk of Depression in patients with Chronic Respiratory Diseases (CRD).

Methods: A case control study was designed with 234 patients with stable CRD as cases including 106 COPD, 82 Bronchiectasis, 46 ILD (21 IPF, 8 Hypersensitivity Pneumonitis, 17 NSIP) and 214 individuals above 45years of age without any respiratory symptoms as control. Depression was assessed using Hamilton Depression Rating Scale (HAM-D). Cases assessed for Severity of disease using FEV1, 6-minute walk distance (6MWD), dyspnoea, SGRQ score, C Reactive Protein level and socio-economic factors.

Results: Case group with CRD had significantly higher prevalence of Depression (48.7% v/s 9.2%) with mean HAM-D score 15.2±2.1 v/s 7.9±2.4 in control group. Subset Analysis revealed highest prevalence in ILD patients (76%). No significant co-relation was found between degree of depression CRP levels. Subjects with depression had higher SGRQ score, persistent symptoms and lower 6MWD. Subjects with CRD had significantly higher risk of Depression (OR= 2.9, 95% CI 1.9 to 4.9) than age and co-morbidity adjusted controls. Depression on HAM-D scale was significantly associated with lower socio-economic status, dependence on family member, non-working subjects and history of smoking.

Conclusions: Our study on Indian population shows that debilitating CRD are significantly associated with increased risk of mental depression.

**PSYCHOSOMATIC SYMPTOMS IN STABLE COPD: IDENTIFYING THE LEADS IN PRIMARY CARE SETTING**

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Background and Aims: Stable COPD patients on pharmacological treatment often present with symptoms having no clear etiology. It is often difficult to reach a definitive diagnosis more so in primary care setting. We attempted to identify common symptoms in stable COPD patients and evaluate them using a structured diagnostic algorithm

Methods: Total 164 Group-B COPD patients without co-morbidities were evaluated over 10 month period. Diagnosis of COPD was established clinically and confirmed by spirometry. Patients were followed monthly on Pharmacotherapy and pulmonary rehab as needed. Most common Symptoms identified were Chest Pain, Dry Cough, Lower limb Pain (LLP), Headache, Palpitation.

ECG, Chest X-ray, Blood pressure monitoring, psychological evaluation, Spirometry lower Limb colour doppler, and other tests were run as needed after thorough examination. Necessary change in treatment was advised

Results: Loss of follow-up- 14, loss to exacerbation: 6, N=144 (Male=84, Female=60). Most common identified cause was Depression and Anxiety [cough (66.2%), Chest Pain (48%) headache (72%), LLP (42%), palpitation (28%)]. Among others were GERD for cough and chest pain, arrhythmia for chest pain and palpitation and drug induced symptoms attributing variable to each symptom.

Conclusions: Depression and anxiety often remain unreported by patients themselves in chronic debilitating diseases like COPD and may present with psychosomatic symptoms. General physicians should pick up the clue for further evaluation
Background and Aim: Roflumilast is a potent and selective inhibitor of phosphodiesterase-4 (PDE4) and is indicated for maintenance treatment to reduce the risk of exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Several clinical trials have been conducted on the efficacy and safety of roflumilast and the data from these trials has been widely published. This study aims to capture real life data and performance of roflumilast in standard clinical practice.

Methods: Patients were prescribed roflumilast, available as 500 μg tablets, by treating physician according to their clinical practice and local standards, and observed for up to twelve months. The following data were documented during roflumilast treatment: frequency and severity of exacerbations, changes in lung function, changes in the dyspnoea levels using modified Medical Research Council (mMRC) scale, changes in COPD Assessment Test (CAT) score, changes in blood oxygen saturation assessed with pulse oximetry, and changes in weight.

Results: 132 patients were included in the study. Prior to roflumilast treatment there were 93 (71%) patients with any exacerbation; 28 (30%) with one and 65 (70%) with more than one exacerbation. From treatment start to last visit, 75 (56.8%) had any exacerbation; 30 (40%) had one and 45 (60%) had more than one exacerbation. The number of exacerbation for COPD phenotypes during the one year follow-up was as follows: 1 (5% - 95% percentile: (0 - 4)) exacerbation for emphysema and 0 (5% - 95% percentile: 0 - 2) exacerbation for chronic bronchitis. When comparing number of exacerbation during treatment and prior, decrease of exacerbations was the most apparent for chronic bronchitis subgroup (from 1 (0, 10) to 0 (0, 2) exacerbation). Finally, the median time to first exacerbation was 236 days (95% CI: 144; 318 days).

Conclusion: Exacerbations were less frequent in patients with chronic bronchitis after one year of treatment with roflumilast.

Background and Aim: Claudin-5 is critical to the control of endothelial cellular polarity and paracellular permeability. The role of CLDN5 in chronic obstructive pulmonary disease (COPD) remains unclear.

Methods: In total, 30 patients with COPD and 30 healthy controls were enrolled in the study. Plasma CLDN5 level was heacked in patients with stable and exacerbated COPD, and in healthy controls.

Results: The mean plasma CLDN5 level of patients with COPD was 0.63 ± 0.05 ng/mL and that of healthy controls was 6.9 ± 0.78 ng/mL (p<0.001). The mean plasma CLDN5 level was 0.71 ± 0.05 ng/mL in exacerbated COPD patients and 0.63 ± 0.04 ng/mL in stable patients with COPD (p<0.05). The plasma CLDN5 level among all subjects was correlated with the smoking amount (r = -0.530, p = 0.001), initial white blood cell count (r = -0.447, p = 0.002), and body mass index (r = 0.496, p = 0.001). The plasma CLDN5 level in stable COPD patients was correlated with forced expiratory volume in one second (FEV1, % pred.) (r = -0.481, p = 0.037). The plasma CLDN5 level was not correlated with age.

Conclusions: CLDN5 may be a marker of COPD exacerbation and is implicated in its pathogenesis.

Acknowledgement: This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: H15C2032) and Soonchunhyang University Research Fund.

Background and Aims: The St. George’s Respiratory Questionnaire for COPD (SGRQ-C) is a well-recognised multi-dimensional tool for the assessment of quality of life (QoL) in patients with COPD. It consists of three components: symptoms, activity and impacts, providing information on changes in the physical and psychological states of patients with COPD. The FLAME study demonstrated superior efficacy of indacaterol/glycopyrornium (IND/GLY) in reducing the rate of exacerbations and improving QoL versus salmeterol/fluticasone (SFC) in patients with moderate-to-very severe COPD and ≥1 exacerbation within the previous year.1 Here, we present data demonstrating improvement in the SGRQ-C component scores with IND/GLY compared with SFC, from the FLAME study.

Methods: FLAME was a 52-week, multicentre, randomised (1:1), double-blind, double-dummy parallel-group, active-controlled study that compared IND/GLY 110/50 μg o.d. and SFC 50/500 μg b.i.d. SGRQ-C component scores were analysed at different time intervals during 52 weeks.

AN OBSERVATIONAL, NON-COMPARATIVE, PROSPECTIVE COHORT STUDY TO CAPTURE REAL LIFE DATA IN COPD PATIENTS TREATED WITH ROFLUMILAST IN ASIA

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Background and Aim: The impact of claudin-5 on the clinical factors of patients with chronic obstructive pulmonary disease (COPD) remains unclear.

Methods: In total, 30 patients with COPD and 30 healthy controls were enrolled in the study. Plasma CLDN5 level was heacked in patients with stable and exacerbated COPD, and in healthy controls.

Results: The mean plasma CLDN5 level of patients with COPD was 0.63 ± 0.05 ng/mL and that of healthy controls was 6.9 ± 0.78 ng/mL (p<0.001). The mean plasma CLDN5 level was 0.71 ± 0.05 ng/mL in exacerbated COPD patients and 0.63 ± 0.04 ng/mL in stable patients with COPD (p<0.05). The plasma CLDN5 level among all subjects was correlated with the smoking amount (r = -0.530, p = 0.001), initial white blood cell count (r = -0.447, p = 0.002), and body mass index (r = 0.496, p = 0.001). The plasma CLDN5 level in stable COPD patients was correlated with forced expiratory volume in one second (FEV1, % pred.) (r = -0.481, p = 0.037). The plasma CLDN5 level was not correlated with age.

Conclusions: CLDN5 may be a marker of COPD exacerbation and is implicated in its pathogenesis.

Acknowledgement: This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: H15C2032) and Soonchunhyang University Research Fund.

Improvement in SGRQ component score with indacaterol/glycopyrornium versus salmeterol/fluticasone: Results from the FLAME study.

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Background and Aims: The St. George’s Respiratory Questionnaire for COPD (SGRQ-C) is a well-recognised multi-dimensional tool for the assessment of quality of life (QoL) in patients with COPD. It consists of three components: symptoms, activity and impacts, providing information on changes in the physical and psychological states of patients with COPD. The FLAME study demonstrated superior efficacy of indacaterol/glycopyrornium (IND/GLY) in reducing the rate of exacerbations and improving QoL versus salmeterol/fluticasone (SFC) in patients with moderate-to-very severe COPD and ≥1 exacerbation within the previous year.1 Here, we present data demonstrating improvement in the SGRQ-C component scores with IND/GLY compared with SFC, from the FLAME study.

Methods: FLAME was a 52-week, multicentre, randomised (1:1), double-blind, double-dummy parallel-group, active-controlled study that compared IND/GLY 110/50 μg o.d. and SFC 50/500 μg b.i.d. SGRQ-C component scores were analysed at different time intervals during 52 weeks.
**INDACATEROL/GLYCOPPYRRONIUM IMPROVES LUNG FUNCTION AND HEALTH STATUS VERSUS SALMETEROL/FLUTICASONE IN MODERATE-TO-VERY SEVERE COPD PATIENTS IRRESPECTIVE OF PRIOR ICS/LABA/LAMA THERAPY: THE FLAME STUDY**

Nicolas Roche1, Jadwiga A. Wedzicha2, James F Donohue3, Sebastien Fucile4, Anthony Yadoo5, Tim Ayres6, Samopriyo Maitra7, Angel Fowler Taylor8, Robert Fogel9, Francesco Patalano9, Donald Banerji9

**Background and Aims:** Current guidelines recommend LABA/ICS/LAMA as the first-line treatment option for GOLD group D patients and ICS/LABA/LAMA (triple therapy) for patients who are at a higher risk of exacerbations.1 The FLAME study demonstrated the superiority of indacaterol/glycopyrronium (IND/GLY) in reducing exacerbations and improving lung function and health status versus salmeterol/fluticasone (SFC) in moderate-to-very severe COPD patients with a history of exacerbations.2 We compared the effect of IND/GLY versus SFC on lung function and health status in COPD patients based on their baseline triple therapy use.

**Methods:** FLAME was a 52-week, multicentre, double-blind, parallel-group, double-dummy active-controlled study. Eligible patients were randomised (1:1) to IND/GLY 110/50 μg o.d. and SFC 50/500 μg b.i.d. Change from baseline in pre-dose trough FEV1 and St. George’s Respiratory Questionnaire for COPD (SGRQ-C) total score was assessed using a mixed model of repeated measures at post-baseline visits (Weeks 4, 12, 26, 38, and 52) in patients with/without prior triple therapy use.

**Results:** Of 3362 patients randomised, 1149 (34.2%) received triple therapy use N = 1074 therapy use and 2121 therapy use. Pre-dose trough FEV1 was significantly improved in patients receiving IND/GLY versus SFC, irrespective of prior triple therapy use, and this improvement was maintained throughout the treatment period (all P values < 0.001). Improvement in SGRQ-C score was greater with IND/GLY versus SFC at Week 12 and was maintained over the entire 52-week treatment period in patients without prior triple therapy use. In patients taking prior triple therapy, SGRQ-C improvement was numerically greater with IND/GLY and this difference was statistically significant at Week 38 (Table).}

**Conclusion:** Indacaterol/glycopyrronium was more effective in improving lung function and health status in symptomatic patients with moderate-to-very severe COPD, irrespective of prior triple therapy use.

**REFERENCE**


**Table.** Change from baseline in SGRQ-C component scores by visit with indacaterol/glycopyrronium versus salmeterol/fluticasone (full analysis set)

<table>
<thead>
<tr>
<th>Time points</th>
<th>SGRQ-C component scores</th>
<th>SGRQ-C total score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Symptom</td>
<td>Activity</td>
</tr>
<tr>
<td>Week 12</td>
<td>-13 [-2.4]</td>
<td>-1.7 [-2.6]</td>
</tr>
<tr>
<td></td>
<td>to -0.3**</td>
<td>to -0.8**</td>
</tr>
<tr>
<td>Week 26</td>
<td>-0.9 [-2.1]</td>
<td>-1.5 [-2.4]</td>
</tr>
<tr>
<td></td>
<td>to 0.2</td>
<td>to -0.6**</td>
</tr>
<tr>
<td>Week 38</td>
<td>-1.9 [-3.1]</td>
<td>-1.7 [-2.7]</td>
</tr>
<tr>
<td></td>
<td>to -0.7**</td>
<td>to -0.7**</td>
</tr>
<tr>
<td>Week 52</td>
<td>-2.0 [-3.2]</td>
<td>-1.4 [-2.4]</td>
</tr>
<tr>
<td></td>
<td>to -0.8**</td>
<td>to -0.3**</td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.01; ***P < 0.001; Data are presented as least squares mean treatment difference (95% CI) between indacaterol/glycopyrronium (110/50 μg once daily) and salmeterol/fluticasone (50/500 μg twice daily); CI, confidence interval; SGRQ-C, St. George’s Respiratory Questionnaire for COPD.

**Table.** Treatment differences between indacaterol/glycopyrronium 110/50 μg once daily and salmeterol/fluticasone 50/500 μg twice daily in subgroup of patients receiving triple therapy and not receiving triple therapy at baseline.

<table>
<thead>
<tr>
<th>Pre-dose trough FEV1, L</th>
<th>SGRQ-C total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>With prior triple therapy use N = 1073</td>
<td>Without prior triple therapy use N = 2119</td>
</tr>
<tr>
<td>Week 4</td>
<td>0.071 (0.051 to 0.092); P &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-0.2 [-1.3 to 0.9]; P = 0.666</td>
</tr>
<tr>
<td>Week 12</td>
<td>0.009 (0.047 to 0.091); P &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-0.9 [-2.1 to 0.4]; P = 0.163</td>
</tr>
<tr>
<td>Week 26</td>
<td>0.036 (0.062 to 0.110); P &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-1.3 [-2.6 to 0.0]; P = 0.057</td>
</tr>
<tr>
<td>Week 38</td>
<td>0.060 (0.036 to 0.035); P &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-2.7 [-4.1 to 1.2]; P = 0.012</td>
</tr>
<tr>
<td>Week 52</td>
<td>0.055 (0.030 to 0.080); P &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>-1.3 [-2.8 to 0.1]; P = 0.083</td>
</tr>
</tbody>
</table>

Data presented as LSM (95% CI); CI, confidence interval; FEV1, forced expiratory volume 1 second; LSM, least squares mean; SGRQ-C, St. George’s Respiratory Questionnaire for COPD.
These results confirm the place of indacaterol/glycopyrronium as a first-line treatment option for COPD patients at risk of exacerbations.

REFERENCES

**AP233**

INDACATEROL/GLYCOPYRRONIUM (IND/GLY) REDUCES THE RISK OF CLINICALLY IMPORTANT DETERIORATION (CID) VERSUS SALMETEROL/FLUTICASONE (SFC): THE FLAME STUDY

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**Background and Aims:** COPD is a progressive disease and a composite endpoint could be an indicator of treatment effect on disease worsening. This post-hoc analysis assessed whether IND/GLY 110/50 μg o.d. reduced the risk of first CID and sustained CID versus SFC 50/500 μg b.i.d. in moderate-to-severe COPD patients from the FLAME study.

**Methods:** First CID was defined as ≥100 mL decrease in FEV1, or ≥4 unit increase in St. George’s Respiratory Questionnaire (SGRQ) total score, or a moderate-to-severe COPD exacerbation. Sustained CID was defined as ≥100 mL decrease in FEV1, or ≥4 unit increase in SGRQ total score on two consecutive visits (≥4 weeks apart) or >50% of all subsequent visits, or a moderate-to-severe COPD exacerbation. Changes from baseline in rate of moderate-to-severe exacerbations, time to first CID and sustained CID versus SFC 50/500 μg b.i.d. in moderate-to-severe COPD patients from the FLAME study, Any parameters in pulmonary function tests did not show significant difference from baseline until 52 weeks:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CID+ versus CID-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate-to-severe exacerbations</td>
<td>RR: 1.8 [1.60 to 2.02]; P &lt; 0.0001</td>
</tr>
<tr>
<td>(N1 = 1615; N2 = 1334)</td>
<td></td>
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<tr>
<td>Time to first moderate-to-severe</td>
<td>HR: 2.24 [2.02 to 2.50]; P &lt; 0.0001</td>
</tr>
<tr>
<td>exacerbations</td>
<td></td>
</tr>
<tr>
<td>(N1 = 1615; N2 = 1334)</td>
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</table>

**Conclusions:** Indacaterol/glycopyrronium reduces the risk of clinically important deterioration versus salmeterol/fluticasone. Clinically important deterioration had a significant impact on long-term exacerbations outcomes in patients with history of exacerbation and with moderate-to-severe COPD.

**Table. Exacerbations and quality-of-life outcomes after 12 weeks until 52 weeks according to occurrence of CID**

<table>
<thead>
<tr>
<th>Outcome</th>
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</tr>
</thead>
<tbody>
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<td></td>
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<tr>
<td>(N1 = 1615; N2 = 1334)</td>
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**AP234**

ADDITIONAL EFFECT OF INHALED CORTICO STEROID (ICS) ON PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE RECEIVING LONG-ACTING MUSCARINIC ANTAGONIST(LAMA)/ LONG-ACTING β2-AGONIST(LABA) - SINGLE-CENTRE, PROSPECTIVE, REAL-WORLD STUDY

**YOSUKE TANAKA1, CHIKA YAJIMA1, MITSUNORI HINO1, YOZO SAITO1, SHUNICHI NISHIMA1, SEIJI KOSAHIRA1, NORIHISA MOTOHASHI2, AKIHIKO GEMMA2**

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**Background and Aims:** To evaluate ICS add-on LAMA/LABA in its efficacy and effects in COPD patients.

**Methods:** After 4 weeks ICS add-on LAMA/LABA combination therapy in patients with COPD, pulmonary function tests, SF-36, St. George’s Respiratory Questionnaire(SGRQ), COPD Assessment Test (CAT) scores, modified Medical Research Council scores, and airway resistance were investigated with impedance-oscillation system (IOS).

**Results:** In 20 men [74.38 ± 4.60 y.o. (mean ± SD)] who participated in the study, Any parameters in pulmonary function tests did not show significant effect (FEV1.0 showed mean difference from baseline: +0.048, p < 0.0001; FEV1.0%: +1.96, p = 0.059; FVC: -0.012, p = 0.84); but IOS showed significant change from baseline in Frc (mean difference from baseline: -1.0012, p = 0.0082) as well as BP score in SGRQ (mean difference from baseline: -6.33, p = 0.037).

**Conclusions:** ICS add-on LAMA/LABA shows the effect of reducing airway inertial resistance that lead to improve airway condition in COPD patients. We will publish details of the study results at the 21st congress of the APSR.

**AP235**

EXACERBATION RISK DOES NOT INCREASE FOLLOWING SWITCH FROM LABA/ICS TO INDACATEROL/ GLYCOPHYRRONIUM (IND/GLY) IN PATIENTS WITH COPD: THE DACCORD REAL LIFE STUDY

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**Background and Aims:** The non-interventional DACCORD study is collecting data from COPD patients recruited in primary and secondary
care across Germany. Here, we report 1-year data from a subset of patients switching from LABA/ICS (fixed or free combination) to indacaterol/glycopyrronium (IND/GLY) on entry.

**Methods:** Patients were recruited following change or initiation of COPD maintenance medication. Data collected at baseline and every 3 months include exacerbations and COPD medication use; COPD assessment test (CAT) data were collected annually.

**Results:** In a total of 467 patients (mean 67.1 years of age), the treating physician decided to switch the therapy regimen from LABA/ICS to IND/GLY on entry to DACCORD, which are included in this 1-year analysis (56.7% men, 43.3% women). At baseline, 95.1% of patients had ≥1 symptom; 68.5% had not exacerbated during the previous 6 months. By 1 year, 87.8% of patients were still receiving only LABA/LAMA; 9.5% of patients were receiving ICS as part of their regimen. The annualised exacerbation rate over the 1-year follow-up was 0.242 (95% CI, 0.188 to 0.313), with 77.9% of patients not exacerbating. The mean CAT total score improved (decreased) by 3.4 units from baseline to 1 year, with 0.313, with 77.9% of patients not exacerbating. The mean CAT total score improved (decreased) by 3.4 units from baseline to 1 year, with 67.5% patients having a clinically relevant improvement.

**Conclusion:** In this group of patients with COPD switched from LABA/ICS to indacaterol/glycopyrronium in ‘real life’ clinical practice, there was no increased risk of exacerbations over the 1-year follow-up, with the majority of patients experiencing a clinically relevant improvement in health status.

**ICS WITHDRAWAL AND TREATMENT WITH A FIXED-DOSE LABA/LAMA COMBINATION: THE GERMAN REAL-LIFE DACCORD COPD COHORT**

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1Facharztforum Fürth, Fürth, Germany, 2Novartis Pharma AG, Basel, Switzerland, 3Pulmonary Department, University Hospital Mainz, Mainz, Germany, 4Department of Sleep and Respiratory Medicine, Evangelical Hospital Göttingen-Weende, Bovenden, Germany, 5Group Practice and Centre for Allergy, Respiratory and Sleep Medicine, Red Cross Maingau Hospital, Frankfurt am Main, Germany, 6Novartis Pharma GmbH, Nürnberg, Germany, and 7Department of Respiratory Diseases, University of Marburg, Marburg, Germany

**Background and Aims:** The prospective, non-interventional DACCORD study is collecting data over 2 years from a cohort of COPD patients recruited in primary and secondary care across Germany who either initiated or changed COPD maintenance medication prior to study entry. After approval of LABA/LAMA fixed-dose combination (FDC), the study was broadened to follow a patient cohort receiving this regimen. Here, we report 1-year follow-up data of 2nd cohort subgroup who discontinued ICS-containing therapy at entry and initiated LABA/LAMA FDC therapy.

**Methods:** Baseline demographics were collected and COPD severity was determined in patients from 2nd cohort. Exacerbations were recorded ≥6 months prior to study and every 3 months during study. Current COPD medication was recorded at each visit. Health status was assessed at baseline and after one year using CAT.

**Results:** Of 4227 patients in 2nd cohort with 1-year data, 766 discontinued ICS and initiated LABA/LAMA FDC at study entry (58% men, 42% women, mean age 67.2 years, baseline mean FEV1 63.4% predicted). Proportion of patients receiving maintenance medication prior to entry is shown in Figure 1. 27.9% of patients reported ≥1 exacerbation, 6 months prior to study. Despite ICS discontinuation, only 19.5% patients exacerbated during 1-year follow-up (annualized exacerbation rate 0.28 events/patient versus 0.30 of the total population). Exacerbations were comparable across 1-year observational period (Figure 2). Change in proportion of patients in GOLD A and D groups at baseline and year 1 are shown in Table. Mean CAT total score improved from 20.0 at baseline to 17.2 after 1 year.

**Conclusion:** Recent interventional studies have analysed the effect of ICS withdrawal in COPD. We extend these findings into a real-life cohort, to show that ICS withdrawal followed by initiation of LABA/LAMA FDC did not lead to increased exacerbations in the following year and was associated with improved health status.

**REFERENCES**


**Table 1. COPD severity classification based on GOLD 2011**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Year 1</th>
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<tbody>
<tr>
<td>GOLD Category B</td>
<td>43.9%</td>
<td>60.8%</td>
</tr>
<tr>
<td>GOLD Category D</td>
<td>46.3%</td>
<td>24.7%</td>
</tr>
</tbody>
</table>

**INDACATERO/GLYCOPYRRONIUM REDUCES THE RISK OF CLINICALLY IMPORTANT DETERIORATION IN PATIENTS WITH MODERATE COPD: RESULTS FROM THE CRYSTAL STUDY**

TIMM GREULICH1, KONSTANTINOS KOSTIKAS2, MINA GAGA3, MARYAM AALAMIAN-MATTHEIS2, FRANCESCO PATALANO2, XAVIER NUNEZ4, VERONICA ANNA PAGANO 4, ANDREAS CLEMENS2, ROBERT FOGEL5, CLAUS F VOGELMEIER1

**Background and Aims**

Decreases in health status, lung function, and the occurrence of exacerbations are important markers of disease progression in patients with...
COPD. As a marker of preventing disease progression, clinically important
deterioration (CID) has been proposed as a composite endpoint to
evaluate COPD treatment effects. Here, we report the efficacy of indaca-
terol/glycopyrronium (IND/GLY) on CID in patients with moderate
cOPD, after direct switch from LABA+ICS, or on a LABA or a LAMA,
monotherapy compared with those remaining on their baseline medication.

Methods: CRYSTAL, a 12-week, prospective, multicentre, ran-
omised, open-label, pragmatic trial, evaluated the effect of IND/GLY or
GLY after a direct 3:1 switch from previous treatments in moderate COPD
patients. CID was defined as a ≥100 mL decrease in trough FEV₁ or a ≥1
point decrease in transition dyspnoea index or a ≥0.4 point increase in
cOPD questionnaire score or a moderate/severe exacerbation. A
subgroup analyses were done based on age, sex, smoking status, history of
exacerbations in the previous year, baseline trough FEV₁, bronchodilata-
tor reversibility, mMRC or baseline treatments.

Results: Of 2159 patients analysed in the IND/GLY treatment arms,
1622 switched to IND/GLY and 537 continued their baseline treatment.
The percentage of patients experiencing a CID was signifi-
cantly reduced in patients who switched to IND/GLY versus patients who
continued on LABA+ICS, or on a LABA or a LAMA, using different CID
definitions (Table). Subgroup analyses were consistent with the overall results.

Conclusion: Indacaterol/glycopyrronium significantly reduced the
risk of clinically important deterioration in patients with moderate COPD,
after direct switch from LABA+ICS, or a LABA or a LAMA.

The effect of dietary antioxidant vitamins on lung
function according to gender and smoking
status: KNHANES 2007-2014

Myung Goo Lee¹, Chang Youl Lee¹, Ji Young Hong¹
¹Hallym University Chuncheon Sacred Heart Hospital, Chuncheon, South Korea

Background and Aim: Cigarette smoke-triggered oxidative stress
plays an important role in the pathogenesis of COPD. Dietary antioxidants
have been suggested to prevent smoke-induced oxidative damage.

The aim of present study was to investigate the association between
antioxidant vitamin intake and lung function in relation to gender and
smoking status in a representative sample of Korean adults.

Methods: 21,148 participants from the Korea National Health and
Nutrition Examination Survey (2007-2014) were divided into 4 groups
based on smoking history and gender. Multivariate regression models
were used to evaluate the association of lung function measurement with
dietary antioxidants intake after adjustment.

Results: Subjects in the highest quintile intake (Q5) of vitamin A, Car-
otene and vitamin C had mean forced expiratory volume in 1 second (FEV₁)
measurement that were 25 mL, 27 mL and 36 mL higher than those of Q1
of vitamin A, Carotenoids and vitamin C increased by 5.42-fold (95% CI=4.09-
7.18), 5.27-fold (95% CI=3.96-6.48) and 5.61-fold (4.26-7.39) greater than
those of female nonsmokers with Q5 of vitamin A, Carotenoids and vitamin 
C. Among COPD patients, male smokers, those smoked more than
20 pack-year had mean FEV₁ measurement that were 124 mL, 94 mL
and 113 mL higher than those of Q1 (P for trend, P=0.032, P=0.038 and
P=0.004, respectively). The risk of COPD for male smokers with Q1 of
vitamin A, Carotenoids and vitamin C increased by 5.42-fold (95% CI=4.09-
7.18), 5.27-fold (95% CI=3.96-6.48) and 5.61-fold (4.26-7.39) greater than
those of female nonsmokers with Q5 of vitamin A, Carotenoids and vitamin 
C. Among COPD patients, male smokers, those smoked more than
20 pack-year had mean FEV₁ measurement that were 124 mL, 94 mL
and 113 mL higher than those of Q1 (P for trend, P=0.032, P=0.038 and
P=0.004, respectively).

Conclusion: These results indicate that lung function in Korean gen-
eral population is related to antioxidant vitamin intake and the effect of
antioxidant vitamin intake on lung function may depend on gender and
smoking status in Korean population.
Background and Aims: Cough is a common symptom in the community. The prevalence of cough by 15% in children and 20% in adults. Cough can cause change in respiratory system such as ventilation reduction resulted from sputum. The study the impact of asam jawa (Tamarindus indica L) in improving FEV1 score of patients suffering from cough.

Methods: To study was a quasi experiment with non random sampling and pretest-post-test control group design as well as cohort approach. Subjects consisted of 40 mothers that did not suffer from cough measured using FEV1 once as a control and 40 mothers suffering from cough measured using FEV1 twice (before drinking asam jawa steeping and there days after drinking). FEV1 measurement device used was spyrometer Vitalograph with COPD-G, result was indicated in percentage.

Results: Avarage FEV1 score of mothers that did not cough was 78.33% at deviation standard 6.29%. Avarage FEV1 score og mothers suffering from cough before drinking asam jawa steeping was 56.45% at deviation standart 7.97% and after drinking for three days subsequently the score was 73.6% at deviation standard 12.44%. The average FEV1 score mothers that did not have cough was much lower than those suffering from cough. The results of statistical test of FEV1 score in mothers suffering from cough p <0.05. There was signifi cant difference between before and after drinking asam jawa steeping.

Conclusions: Use of asam jawa as traditional cough medicine could improve FEV1 score of cough patients.

Whole Evidence Synthesis of Chinese Herbal Medicine for COPD
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Background and Aims: There is an overall lack of high quality clinical evidence for Chinese herbal medicine (CHM) for chronic obstructive pulmonary disease (COPD). However, there is extensive historical literature dating over 2,500 years and expert experience that is still important
for Chinese medicine practice. Therefore, synthesizing different sources of evidence (clinical and historical) of CHM may help to improve clinical practice. The aim of this paper is to provide a synthesis of the different sources and of evidence of CHM for COPD.

Methods: Textbooks, monographs, clinical guidelines were summarized. The ‘Encyclopedia of Traditional Chinese Medicine’ was also used to analyze historical evidence, based on the characteristic symptoms and diagnosis of COPD. Clinical trial evidence was found by searching five English and four Chinese databases. The Cochrane Collaboration Risk of Bias Tool and the GRADE Summary of Findings were used to evaluate quality of trials. The historical literature was then compared and contrasted with the modern evidence. CHM treatments that were recommended in the historical literature and in clinical trials were considered to be higher level evidence.

Results: During stable COPD the herbal formula ‘Bu fei tang’ has been consistently used over time and is recommended in CHM guidelines. Clinical trials also showed it can improve lung function (FEV1%) (Quality of evidence: low). The herbs that constitute Bu fei tang have pharmacological actions that may improve COPD including anti-inflammatory and anti-oxidation. During COPD exacerbations ‘Xiao qing long tang’ has been used to treat COPD from ancient times and is still recommended in CHM guidelines. Clinical trials showed that it can improve FEV1%, PaO2 and quality of life (Quality of evidence: low).

Conclusions: Synthesis of historical and modern literature showed consistency over time in terms of the CHM used to treat COPD. This method of literature analysis is a useful way to give depth to clinical practice recommendations and help to guide research.

REAL WORLD COMPLIANCE OF GOLD GUIDELINE AND INFLUENCE THE RISK OF COPD EXACERBATION
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Background and Aims: The Global Initiative for Obstructive Lung Disease (GOLD) guidelines are the standard international guidelines for treatment of chronic obstructive pulmonary disease (COPD). Patients with persistent symptoms should be started on a bronchodilator and assessed risk for future exacerbations. This study is aim to evaluate the real world compliance of GOLD guidelines and the usage of bronchodilators influence risk of COPD exacerbation.

Methods: From 2015 to 2016, patients who had symptoms with the spirometry presence of a post-bronchodilator FEV1/FVC < 0.70 diagnosed as COPD were enrolled. The medical records were reviewed and clinical data including age, gender, smoking status, co-morbidities, inhaled medications including long-acting muscarinic antagonist (LAMA), long-acting beta agonists (LABA), and inhaled corticosteroid (ICS), frequency and severity of exacerbation were analyzed.

Results: A total of 597 COPD patients were included. 197 patients (33.0%) were group A, 243 patients (40.7%) were group B, 119 patients (19.9%) were group C, and 38 patients (6.4%) were group D. The overall compliance rate according to GOLD guidelines was 72.0%. The COPD patients treated under GOLD guidelines had lower exacerbation rates. In group A, patients treated with short-acting beta agonists (SABA) had longer time to exacerbation (SABA v.s. others, 18.3 ± 11.5 vs. 13.7 ± 7.8 months, p < 0.02). In group B, patients treated with LAMA had longer time to exacerbation (LAMA v.s. others, 12.4 ± 7.7 vs. 6.2 ± 5.8 months, p < 0.001). In group C, patients treated with bronchodilator combinations had longer time to exacerbation (ICS/LABA v.s. LABA/LAMA vs. others, 12.3 ± 8.3 vs. 9.6 ± 8.3 vs. 5.9 ± 5.4 months, p < 0.001). However, the difference of time to exacerbation between distinct therapeutic strategies was not significantly in group D.

Conclusions: COPD patients treated based on GOLD guidelines recommendations had lower exacerbation rate and longer time to exacerbation.

EVALUATION OF MEDICATION NON-ADHERENCE IN ELDERLY PATIENTS WITH COPD AT SRINAGARIND HOSPITAL
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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a common disease in elderly patients. Medication non-adherence in elderly COPD patients leads to poor clinical outcome, increases healthcare expenditure and remains a major problem even in setting with multidisciplinary care team approach towards adherence. This study aims to evaluate non-adherence problems in the elderly COPD patients and find potential areas for interventions to help improve this problem.

Methods: Data for 262 elderly COPD patients from pharmaceutical care database were retrieved and analyzed. This database was developed between 2011 and 2016 at COPD clinic Srinagarind hospital. Medication adherence was measured by using patient self-reported.

Results: A total of 262 elderly COPD patients and 670 non-adherence problems were evaluated. 72.6 ± 7.8 years of age, predominantly male 85.9%. Three types of non-adherence can be identified; underuse 63.7%, incorrect inhaler technic 27.9% and overuse 8.4%. For-getfulness (41.6%) is the most frequently mentioned reason for unintentional non-adherence followed by disruption to daily routine (13.6%) and running out of medication (11.2%). Being asymptomatic (13.6%) was the most commonly report for intentional non-adherence. Patients performed at least one step incorrectly from the pressurised metered-dose inhaler (pMDI) 76.5% and dry powder inhaler ( DPI) 23.5%. The most common critical step of errors was observed in the inhalation 72.7%. We then focused on potential areas for interventions to create strategies that can improve adherence.

Conclusions: Despite the challenges, the findings from this study can guide potential intervention for multidisciplinary team to create strategies for improving adherence in elderly COPD patients.

DESKTOP HELPER: A GUIDANCE TOOL ON APPROPRIATENESS OF INHALED CORTICOSTEROID (ICS)
THERAPY AND ICS WITHDRAWAL IN PATIENTS WITH COPD
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Background: ICS are over-prescribed in GOLD groups A and B patients1, contrary to current recommendations2. Additionally, ICS-containing combinations are often started at early stages of COPD, when benefits may be negligible. Moreover, ICS have significant side effects,
and similar/better exacerbation prevention has been demonstrated withLABA/LAMA combination, thus providing an ICS-free pharmacotherapy option. In partnership with IPCRG, a desktop helper was created to educate and guide clinicians on appropriateness of using ICS therapy andICS withdrawal in COPD patients, when appropriate.

Methods: Literature reviews were conducted in order to create algorithms to: determine appropriateness of ICS therapy; provide a stepwise process for ICS withdrawal to maximise outcomes and minimize harm. An existing algorithm was modified to improve clinical utility, while ensuring appropriate safety. The algorithm utilized the data from the FLAME and WISDOM studies that support switching from LABA/ICS or triple therapy to LABA/LAMA. The algorithm also describes required follow-up to minimize risk during ICS withdrawal.

Results: The algorithm would identify patients with COPD and who might benefit from ICS treatment and patients in whom this treatment may not be appropriate; and an approach to withdrawing ICS in those patients who do not need ICS is provided. This clear, practical, and efficient process of guidance, in addition to new guidelines and evidence, would encourage clinicians to make changes in current therapy. Implementation will require a significant change in thinking and behaviour of clinicians, and clear communication on: why change (evidence); who says (guidelines); and who supports (IPCRG).

Conclusion: The desktop helper would help clinicians in reducing inappropriate exposure to ICS in COPD patients, while effectively managing symptoms and exacerbation risk.

Figure. Desktop helper A. Algorithm on appropriateness of ICS therapy; B. Stepwise process of ICS withdrawal in suitable patients; C. Guidance on switching doses upon changing treatments

REFERENCES

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REAL-LIFE EXPERIENCE OF COPD PATIENTS ON EASE AND ACCURACY OF INHALER USE: THE REAL SURVEY

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Background and Aims: Many patients with COPD achieve incomplete benefit from their treatment, due to inadequate device training or incorrect inhaler technique. Inhaler overuse/underuse are the most common forms of nonadherence, leading to inhaler use errors and may negatively impact treatment adherence. This computer-assisted telephonic survey evaluated patient-reported insights on inhaler/medication use, device attributes and overall adherence.

Methods: Patients with mild-to-very severe COPD using maintenance inhaled treatment were included. Patient-reported data on correct inhaler use (training and check), inhalation pattern, and device attributes (ease of use and confidence of inhaling full dose), adherence and potential underuse/overuse were collected.

Results: A total of 764 patients (Breezhaler©, 186; Ellipta®©, 191; Genuair®©, 194; Respimat®©, 201) with a mean ± SD age 56 ± 9.8 years, completed the survey. Approximately, 30% of patients reported not receiving any inhaler use training. Majority of the patients found different training materials "very helpful" (Figure). About 29% of patients reported never being checked for correct inhaler technique. Most patients (76%–93%) were confident/very confident of inhaling the full dose. Approximately, 4%–33% of patients were uncomfortable inhaling the full dose, and took another inhaled dose at the same time. Most patients (91%–97%) inhaled correct dose (1 puff/dose/day) with Breezhaler©, Ellipta® and Genuair®; however, 50% inhaled correct dose (2 puffs/dose/day) with Respimat®.

*Total number of patients lower than sum of patients as some patients were using multiple devices

Figure. Patients (%) who found different training materials as "very helpful".

Conclusion: This survey shows low incidence of training/monitoring (by HCPs) for correct inhaler use. Devices that provide low confidence of having inhaled the full dose may result in underuse/overuse of medication, which may also impact patients' efficacy and/or safety outcomes. Thus, there is a need for enhancing the HCP-patient interaction through effective training programs. Considering that patients with COPD self-
THE EFFICACY OF THORACIC CONDITIONING USING BIPHASIC CUIRASS VENTILATOR IN THE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE
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Background and Aims: The conditioning of respiratory rehabilitation, such as thoracic stretch and relaxation, is one of important factors in chronic obstructive pulmonary disease (COPD). And Biphasic Cuirass Ventilator (BCV) is positive and negative pressured non-invasive extra-thoracic ventilator. It is used to cover thorax with cuirass, and to ventilate by adding negative and positive pressure into inside of cuirass alternately. The actions of inflating and deflating thorax by BCV are similar to conditioning of respiratory rehabilitation performed by physiotherapists. Therefore BCV might work as respiratory rehabilitation besides ventilator.

The aim of this study is to show the conditioning effect of BCV in the patients with COPD.

Methods: Six acute exacerbated and eight stable COPD patients were evaluated.

Before and after treatment with BCV (using RTX, United Hayec Medical, London, UK) we investigated spirogram, thoracic circumference and changes of dyspnea sensation assessed by visual analogue scale. RTX was performed for thirty minutes under the condition of control and clearance mode in each patients.

Moreover, we compared the effects between treatment with RTX and performance by physiotherapists.

Results: In COPD acute exacerbated cases, thoracic circumference were increased, and also improved dyspnea sensation in two of six patients. And forced vital capacity were increased after treatment with RTX in four of five patients who could investigate spirogram. On the other hands, in stable patients, there were no improvement by RTX. There were also no differences between treatment with RTX and performance by physiotherapists.

Conclusions: We concluded that there might be conditioning effect in BCV using RTX in respiratory rehabilitation of COPD. However, the effect was limited in some cases with acute exacerbation of COPD.

AP245

USE OF NON-INVASIVE VENTILATION (NIV) IN ACUTE TYPE 2 RESPIRATORY FAILURE (T2RF) IN PATIENTS WITH COPD AT A TERTIARY HOSPITAL IN NEW ZEALAND
MATIF MOHD SLIM1, KHAN1
1Waikato Hospital, Hamilton, New Zealand

Background: Appropriate use of NIV in COPD patients with T2RF improves patient outcomes. Inappropriate use can increase morbidity, detract from other appropriate treatments, and stretch limited resources.

Aims: We wished to demonstrate whether our practice was in line with the 2008 British Thoracic Society (BTS) Guideline on NIV.

Method: Episodes of inpatient NIV between January 2014 and January 2015 were identified by ICD-10 coding followed by retrospective notes review. Management was audited against the standards in the BTS Guideline. Results were compared to the 2013 BTS NIV audit.

Results: 22 patients received NIV during the study period, across 25 admissions (3 patients had multiple presentations). 4 patients received NIV twice during the same admission, for a total of 29 episodes of NIV. NIV was commenced by respiratory medicine in 17 cases, emergency medicine in 10, and critical care in 2. NIV was delivered in ED in 7 cases, HDU in 18, ICU in 1, and the ward in 3. Mortality rate across all admissions was 16%. In a subgroup of 14 episodes of NIV use with first arterial blood gas (ABG) diagnostic for acute T2RF, mortality was 28.6%. Other results are detailed in the tables.

Conclusion: In our institution, NIV is frequently commenced without a confirmed diagnosis of respiratory acidosis. Median ABG pH and PaCO2 at NIV commencement were similar to the BTS audit. Our NIV success rate was lower by ABG criteria (57.1% vs. 66%). Delays were noted in time to recommended first follow-up ABG of one hour. Initial and subsequent NIV pressures were frequently not specified. Deficiencies were noted in controlled oxygen use and documentation of resuscitation status. Mortality rate (28.5%) was less than the BTS audit (34%). A multidisciplinary NIV guideline has been developed for hospital-wide use. A re-audit will occur one year after implementation.

Table 1. Patient characteristics (25 admissions)

<table>
<thead>
<tr>
<th>Mean age, years</th>
<th>66.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>Maori ethnicity</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>European ethnicity</td>
<td>17 (68%)</td>
</tr>
<tr>
<td>Ethnicity other/not specified</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Primary diagnosis of COPD on admission*</td>
<td>20 (80%)</td>
</tr>
<tr>
<td>Mean percent predicted FEV1 (documented in 18 cases)</td>
<td>32.5%</td>
</tr>
<tr>
<td>Mean Medical Research Council dyspnoea scale (documented in 8 cases)</td>
<td>4.65</td>
</tr>
<tr>
<td>Radiographic consolidation on admission</td>
<td>6 (24%)</td>
</tr>
</tbody>
</table>

*Other primary diagnoses were: one each of asthma, asthma/COPD overlap syndrome (ACOS), airways disease not otherwise specified, interstitial lung disease, and urinary tract infection.

Table 2. Medical management (29 episodes of NIV)

| Controlled oxygen* | 11 (37.9%) |
| NIV commencement settings specified | 14 (48.3%) |
| NIV titration plan documented | 15 (51.7%) |
| Steroids (IV or oral) | 25 (86.2%) |
| Inhaled beta-agonist | 27 (93.1%) |
| Inhaled anti-muscarinic | 25 (86.2%) |
| Antibiotics | 23 (79.3%) |
| Resuscitation status documented | 21 (72.4%) |

*Defined as oxygen delivered by Venturi mask and/or titrated to a target saturation range of 88-92% (or lower specified target)

Table 3. Blood gases

| ABG performed prior to commencement of NIV | 65.5% |
| Median pH of first ABG | 7.27 |
| Median PaCO2 of first ABG | 10.7 kPa |
| First ABG diagnostic for acute T2RF* | 14 (73.7%) |
| Time to follow-up blood gas following NIV commencement** | 2.2 |

*Defined as oxygen delivered by Venturi mask and/or titrated to a target saturation range of 88-92% (or lower specified target)
CLINICAL EFFICACY OF HIGH-FLOW NASAL CANNULA IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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1Department of Pulmonary and Critical Care Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

Background and Aims: High-flow nasal cannula (HFNC) oxygen therapy has been used in patients with hypoxic respiratory failure, but the clinical benefit in acute exacerbation patients of chronic obstructive pulmonary disease (COPD) remains unclear. The aim of this study was to evaluate the clinical efficacy of HFNC, especially at hypercapnic respiratory failure.

Methods: A historic retrospective cohort analysis was performed at a single medical center in South Korea. In total, 52 patients with acute exacerbation of COPD were enrolled: 37 patients with arterial carbon dioxide of < 45 mmHg (non-hypercapnic group) and 15 patients with arterial carbon dioxide of ≥ 45 mmHg (hypercapnic group) from April 2011 to December 2015.

Results: Mean of baseline arterial carbon dioxide level was 38.3 ± 11.76 in total patients, 32.4 ± 6.96 mmHg in non-hypercapnic group and 52.8 ± 7.80 mmHg in hypercapnic group. There was a significant decrease of arterial carbon dioxide level at the time of 12 (-4.3 mmHg, p=0.01), 24 (-5.8 mmHg, p=0.003) and 72 (-2.0 mmHg, p=0.026) hours after application of HFNC in hypercapnic group. The rate of intubation was not different between the non-hypercapnic group (48.6%) and hypercapnic group (53.3%, p = 0.761).

Conclusions: HFNC is likely to be effective at COPD acute exacerbation patients, not only non-hypercapnic respiratory failure but also hypercapnic respiratory failure.
bronchoscopy. The secondary aims were to find the risk factors for lung cancer, type of lung cancer and treatment.

**Methods:** Observational cross sectional study was carried out from November 2013 to June 2016 at chest clinic, Phrae Hospital. Patients both sexes and more than 18 years old who had lung nodules or lung masses from CXR or chest CT scan and underwent bronchoscopy with transbronchial pulmonary biopsy were enrolled.

**Results:** A total of 100 patients who presented with lung nodules or lung masses from CXR or chest CT scan were enrolled. 17 patients were excluded and 83 patients met inclusion criteria. There were 57 male patients (68.7%) and 26 female patients (31.3%). There were 67 smoker patients (80.7%) and 16 non smoker patients (19.3%). The prevalence of lung cancer was 51.8% (95%CI=41.8-61.8). Smoking was significant risk factor for lung cancer (p-value=0.031, RR=3.698, 95%CI=1.069-12.795). 88.37% of them were non-small cell lung cancer (NSCLC) while 11.63% were small cell lung cancer (SCLC). Most NSCLC patients were stage IV (39.47%) and most of them were treated with chemotherapy (65.1%).

**Conclusions:** Prevalence of lung cancer of patients who presented with lung nodules or lung masses in this study was 51.8%. Smoking was significant risk factor for lung cancer.

### Table 3. Treatment and Management of all lung cancer patients

<table>
<thead>
<tr>
<th>Treatment and Management</th>
<th>Number (n=43)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>28</td>
<td>65.12</td>
</tr>
<tr>
<td>Surgical + Chemotherapy</td>
<td>5</td>
<td>11.63</td>
</tr>
<tr>
<td>Chemotherapy + Radiation</td>
<td>3</td>
<td>6.98</td>
</tr>
<tr>
<td>Radiation</td>
<td>1</td>
<td>2.33</td>
</tr>
<tr>
<td>Palliative care</td>
<td>6</td>
<td>13.95</td>
</tr>
<tr>
<td>Dead</td>
<td>4</td>
<td>9.30</td>
</tr>
</tbody>
</table>

**Figure 1. Smoking status of the patients with lung cancer and patients with no lung cancer.**

**Figure 2. Histological types of patients with lung cancer, n=43**

**Figure 3. Histological types of patients with no lung cancer, n=40**

### AP248

**TYPICAL PULMONARY CARCINOID WITH UNUSUAL LEFT CARDIAC VALVULAR INVOLVEMENT**

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**Background and Aim:** 50% of patients with carcinoid tumor have cardiac involvement which typically causes abnormalities of the right side of the heart. We report unusual presentation of cardiac involvement of left side in a typical pulmonary carcinoid patient.

**Methods/Case Presentation:** Patient is 43 years old female non-smoker, resident of Iraq presented with complaints of cough and breathlessness and on and off flushing since 6 months. X-ray showed a well defined rounded opacity at left hilum. 2D Echo showed moderate Mitral stenosis with mild Mitral regurgitation, dilated left atrium, Trivial Aortic Regurgitation, Trivial Tricuspid Regurgitation left ventricular ejection fraction 55 %. Chest CT revealed soft tissue density mass with foci of calcification located in the left upper lobe with extrinsic compression of anterior, apical segmental bronchi, abutting the left pulmonary artery and pulmonary veins. Bronchoscopy showed endobronchial mass occluding the left upper lobe bronchus which bled profusely on taking biopsy. Endobronchial biopsy confirmed typical pulmonary carcinoid (cytokeratin, synaptobravin, chromogranin positive). 24 hours SHIAA was 15.64 mg(normal range <8mg). PET Scan confirmed localised disease with involvement of pulmonary veins. Patient underwent left lung upper lobe resection with ligation of pulmonary veins. Intra-operative finding showed well defined mass lesion with pulmonary vein thickened and enlarged with adhesions to tumour. Our patient had typical pulmonary carcinoid with pulmonary veins involvement. These hyperactive substances
bypassed the lung enzymatic degradation and reached the left atrium and thus caused the cardiac valvular lesion on left and right cardiac valves.

**Conclusion:** The direct drainage of hyperactive substances in pulmonary veins affected the valves on left as well as right side as the lung enzymatic degradation was bypassed. Carcinoid with left cardiac valve involvement is unusual and surgery is best possible treatment.

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**SUPERIOR VENA CAVA OBSTRUCTION EVALUATION WITH MDCT**

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**Background and Aims:** Superior vena cava syndrome (SVC) a common presentation of bronchogenic carcinoma. Superior vena cava syndrome is a condition resulting from the obstruction of venous blood flow from the superior vena cava into the right atrium of the heart. Mechanism of obstruction is by compression of the superior vena cava by the tumour itself or by the enlarged mediastinal lymph nodes.

**Methods:** We report a case of SVC obstruction secondary to bronchogenic carcinoma of the lung. A 69 year old male presented with progressive swelling of his face and right upper limb for one month duration. He also had dry cough and breathlessness for two months duration. General examination revealed facial puffiness, conjunctival injection, engorged neck veins and tortuous dilated superficial veins over the chest with venous flow directing towards umbilicus indicating superior vena cava obstruction. A chest X-ray showed mediastinal widening with flattened right dome of dia-phragm. Contrast enhanced computed tomography (CT) of thorax revealed right hilar mass causing complete occlusion of superior vena cava with extensive collaterals. Bronchoscopy showed a polypoid growth in the right upper lobe bronchus, which was biopsied and the report was consistent with bronchogenic squamous cell carcinoma. The patient received chemotherapy and radiotherapy after which his symptoms subsided.

**Results:** Over 85% of SVC syndromes are caused by malignant diseases; among them lung cancer is responsible for 60% of cases, of which most are seen in patients with small cell carcinoma followed by squamous cell carcinoma, adenocarcinoma and large cell carcinoma. Radiation therapy combined with chemotherapy is the mainstay of treatment for most patients.

**Conclusions:** Multi-detector computed tomography (MDCT) plays a major role in finding the level and extent of obstruction, delineation of collaterals apart from detecting the cause of SVC obstruction.

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**PATIENT WITH GERM CELL TUMOR AND ENDOBRONCHIAL METASTASIS**

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**Introduction:** Endobronchial metastasis (EBM) of extrapulmonary tumors is a rare condition. The frequencies are ranging from 2 to 50%. The most frequent tumors with EBM are breast, kidney and colorectal cancer. Testis cancer is even more rare. We report a case with mixed germ tumor and bilateral endobronchial metastasis.

**Case report:** Thirty nine years old male patient admitted to hospital with dyspnea, cough, hemoptysis, weight loss and right scrotal swelling. There was non-tender, painless right scrotal swelling on physical examination. Chest x-ray showed left nodular lesion. Computed tomography of thorax revealed left upper lobe and right middle lobe mass with left hilar and mediastinal lymph node enlargement. (Figure 1) Scrotal ultrasonography revealed right testicular mass.

Fiberoptic bronchoscopy performed and endobronchial lesion was noted in the left upper lobe and right main bronchus. (Figure 2). Histopathological examination of bronchoscopic biopsy reported as embryonal cell carcinoma.

Patient underwent orchietomy and histopathology reported as mixed germ tumor with areas of teratoma and choriocarcinoma.

There wasn’t any other distant metastasis. Patient referred to the medical oncology department for treatment.
In conclusion, although it’s rare, GCTs should be kept in mind in patients with pulmonary mass and endobrochial metastasis, especially in young male patients. And testicular examination should be done.

AP251

PRIMARY PULMONARY LEIOMYOSARCOMA WITH BRAIN METASTASIS IN A 38-YEAR OLD FILIPINO FEMALE

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2Department of Cardiothoracic Surgery, Faculty of Medicine, University of Sumatera Utara, University Hospital of Sumatera Utara, Medan, Indonesia.

Background and Aim: Accounting for only less than 0.5 per cent of all malignant pulmonary tumors, primary pulmonary sarcoma (PPS) appears to originate from the smooth muscle of the pulmonary parenchyma, pulmonary arteries and bronchi. In the Philippines and its neighboring South East Asian countries, PPS is an extremely rare disease worth documenting.

This case report primarily demonstrates the clinical course of a Filipino female who developed primary pulmonary sarcoma, leiomyosarcoma in particular, with brain metastasis. Secondly, this paper reviews the epidemiology, previously reported cases, diagnostic approach and therapeutic strategies of PPS.

Case Report: A 38-year old non-smoking Filipino female was admitted due to non-productive cough for two months, accompanied by left-sided hemiparesis. The patient has no known co-morbidities, is nulliparous, and has no gynecologic symptoms. Her chest computed tomographic (CT) scan revealed a right upper lobe anterior segment mass measuring 9.1 x 18 x 9.5 cm with multiple nodules on the whole right lung. Brain CT bared a right frontal lobe mass measuring 26.3 x 22.4 x 22.8 cm. Whole abdominal ultrasound was essentially unremarkable. Ultrasound-guided needle thoracic aspiration biopsy of the right pulmonary mass was carried out.

Histopathologic findings and immunohistochemical studies disclosed leiomyosarcoma. The patient underwent cranial irradiation that improved the hemiparesis. Subsequently, the patient opted to be discharged; a week after, succumbed to the disease.

Conclusion: In conclusion, previous cases underscore PPS as an extremely rare, hematogenously spreading and a rapidly progressive malignant neoplasm. A similar case in 1965 reported a 70-year old man presenting with left hemiplegia and right lung consolidation, which on necropsy revealed pulmonary sarcoma with cerebral metastasis. Most of the case reports suggest that chest radiography and post-surgical histopathologic studies are keys to disease detection, and that complete resection may improve survival.

AP252

CASE REPORT: PRIMARY GIANT MEDIASTINAL DEDIFFERENTIATED LIPOSARCOMA

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Background and Aims: Liposarcoma is malignancy of fat cells which comprises about 1% of all malignancies, particularly found in lower extremity. Primary liposarcoma of the mediastinum is extremely rare, usually occurs in 6th decades, commonly in the anterior mediastinum. Dedifferentiated liposarcoma was defined as an atypical liposarcoma that progresses over time with variable histologic grade. This is essentially a low grade liposarcoma admixed with a high grade spindle cell sarcoma. Approximately 40% of mediastinal liposarcomas recur after surgery. The aim of this study is to report one case of primary mediastinal dedifferentiated liposarcoma.

Methods: This is a case report study of one extremely rare patient diagnosed with primary giant mediastinal dedifferentiated liposarcoma.

Results: A 54-year-old male, admitted to emergency room with main complain shortness of breath, worsening since 3 months before admission. Chest x-ray showed homogenous consolidation in the whole left lung. Thorax CT scan with contrast revealed giant fat-containing mass with heterogeneous density compressing great vessels, enhanced with contrast, with multiple calcifications. Patient underwent sternotomy for tumour removal and open biopsy. The tumour was 50 x 30 cm in size, capsulated, and histopathology report along with CD-30, Vimentin and Pancytokeratin immunohistochemistry confirmed the diagnosis of dedifferentiated liposarcoma. After surgery, patient was scheduled for adjuvant chemo-radiotherapy.

Conclusions: Primary mediastinal liposarcoma is an extremely rare case which is quite challenging to diagnose. Treatments include surgical excision followed by radiotherapy and/or chemotherapy.

Keywords: Mediastinal liposarcoma, Giant, Rare, Surgery

AP253

QUALITY AND COMPLETENESS OF SMOKING HISTORY DATA IN A DEDICATED LUNG CANCER MDT DATABASE

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1St Vincent’s Hospital, Darlinghurst, Sydney, Australia, and 2The Kingshorn Cancer Centre, Darlinghurst, Sydney, Australia

Background and Aims: Accuracy of smoking history data is crucial for lung cancer patient risk analysis and is frequently collected at Multi-Disciplinary Team (MDT) meetings, but may rely on physician recall. We aimed to establish if use of an integrated FileMaker™ platform improved smoking data capture compared with the previous stand-alone Microsoft Access™ platform.

Methods: Single centre retrospective audit of our lung cancer MDT database for: (1) Were patients smokers? (2) Were patients current smokers? (3) What age did patients quit? (4) How many ‘pack-years’? (5) Years since ceasing? Ethics approval was sought and granted (HREC File no. LNR/14/SVH/221). Microsoft Access was used June 2006 - January 2011, FileMaker was used January 2011 - 21 March 2017. Complete data transfer between platforms occurred in January 2011. The Bensoul distribution was used to compare the two periods. A small prospective series of 25 MDT patients was performed comparing smoking data capture from the Electronic Health Record (EHR) versus physician recall.

Results: 1000 cases were entered into the database between June 2006 and 21 March 2017 (vide infra).

Table 1. Patients for whom data points were captured.

<table>
<thead>
<tr>
<th>Data points</th>
<th>Microsoft Access (n=356)</th>
<th>FileMaker (n=644)</th>
<th>Total (n=1000)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were patients smokers?</td>
<td>229 (64.3%)</td>
<td>531 (82%)</td>
<td>760 (76.0%)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

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Abstracts

<table>
<thead>
<tr>
<th>Were patients</th>
<th>Current smokers?</th>
<th>What age did patients quit?</th>
<th>How many 'pack-years'?</th>
<th>Year since ceasing?</th>
</tr>
</thead>
<tbody>
<tr>
<td>138</td>
<td>(38.8%)</td>
<td>31 (8.7%) (27.6%)</td>
<td>97 (27.2%) (51.1%)</td>
<td>32 (8.0%) (27.3%)</td>
</tr>
<tr>
<td>428</td>
<td>(66.5%)</td>
<td>178 (20.9%)</td>
<td>329 (42.6%)</td>
<td>176 (20.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

All points were incompletely captured. Best captured was ‘Were patients smokers?’. Most incomplete points were: ‘What age did patients quit?’ and ‘Years since ceasing?’.

Conclusions: Smoking data capture remained incomplete across the 5 selected domains, but showed significant improvement with FileMaker. Further information will arise from finalization of the prospective series. As tobacco smoking remains the predominant lung cancer risk factor, better data capture may lead to an improved understanding of individual risks as well as identifying opportunities to implement targeted smoking cessation therapies.

LUNG CANCER IN A VERY YOUNG MALES
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Hospital National Guido Valadares, Dili, Timor Leste, Dili, East Timor

Cancer of the lungs is rare in adolescent patients, particularly in those under 20 years of age. A cancer that begins in the lungs is most often found in older patients with a history of tobacco use. The first case here is a report of lung cancer diagnosed in a 17-year-old male with a history of tobacco use. The patient reported smoking an average of one pack of cigarettes a day since he was 10 years old. The second case is of a 15-year-old boy with no history of tobacco use who complained of several months of cough, dyspnea and 10.5kg weight loss. Both patients were smokers.

Conclusions: Smoking data capture remained incomplete across the 5 selected domains, but showed significant improvement with FileMaker. Further information will arise from finalization of the prospective series. As tobacco smoking remains the predominant lung cancer risk factor, better data capture may lead to an improved understanding of individual risks as well as identifying opportunities to implement targeted smoking cessation therapies.

FUNCTIONAL ASSESSMENT OF CANCER THERAPY–LUNG (FACT-L) CAN ENHANCE PATIENT CARE PROVIDED BY LUNG CANCER CASE MANAGER
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Respiratory Division, Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR, China

Background: An integrated lung cancer case management program has been established in Queen Elizabeth Hospital since February 2013. By using Functional Assessment of Cancer Therapy–Lung (FACT-L), Lung cancer case manager (LCCM) identified individual’s condition, need and problems.

Aims: To examine the impact of FACT-L in LCCM programme.

Methods: This is a retrospective study from February 2013 to December 2015.

Patients self-administrated the FACT-L at baseline (pre-treatment) and 4 months after treatments, including lung surgery, chemotherapy, radiotherapy and target therapy.

The four general subscales include Physical-Well-Being (PWB), Social-Well-Being (SWB), Emotional-Well-Being (EWB), and Functional-Well-Being (FWB). It also includes a lung cancer symptom-specific scores.
subscale (LCS) assessing patients' symptoms. The higher the score, the better the quality of life. According to the score and patient journey, LCCM reacted and referred to relevant departments for further investigation and support.

**Results:** 376 newly diagnosed lung cancer cases were recruited and total 126 attendees of the clinic. Patient's mean age was 68.5, male dominant (61.2%). The mean pre-treatment FACT-L score was 93.7 over 136. 78 (21%) patients had nutritional problems and nutritional educations were provided to all of these cases. 44% of them further referred to dieticians.

46% of the patients were ex-smokers, current and non-smokers were 28%, 26% respectively. One-third of the current and ex-smokers regretted their histories of tobacco smoking after diagnosed of lung cancer. Total 98 proactive phone enquiries from patients received for their treatment opinions, daily care and expressed worries. 78% of the patients and their families received LCCM counselling.

Most significant improvements on SWB (13%) & EWB (14%) after 4-months of LCCM programme. A written patient satisfaction survey about LCCM service was conducted, with 90% return rate and the satisfaction mean was 91/100.

**Conclusion:** FACT-L facilitates the fast assess of lung cancer patients' physical, social and emotional conditions in LCCM programme.

**POSTOPERATIVE TRANSITION OF RESPIRATORY MUSCLE STRENGTH IN DIFFERENT SURGICAL APPROACHES FOR LUNG CANCER**

**KYOKO MAKITA1, HIRODAI HARA2, RIO TAKAMATSU1, AYAKO MIZOGUCHI1, JUNICHI NAKAO1, TAKESHI MIMURA1, YOSHINORI YAMASHITA1, KIYOMI TANIYAMA1**

1Institution for Clinical Research, NHO Kure Medical Center/Chugoku Cancer Center, Kure, Japan, 2Department of Respiratory Surgery, NHO Higashihiroshima Medical Center, Higashihiroshima, Japan, and 3Department of Rehabilitation, NHO Yamaguchi-Ube Medical Center, Ube, Japan

**Background and Aims:** Video-assisted thoracic surgery (VATS) has been widely performed in the field of thoracic surgery. There are different approaches in VATS procedure, such as complete VATS and hybrid VATS; however, the clinical distinction between these different approaches is still controversial. Since the main difference between complete VATS and hybrid VATS involves the length of intercostal muscle dissection, we explored the postoperative transition of respiratory muscle strength in the two approaches.

**Methods:** From 2011 to 2016, 474 patients underwent surgery for non-small cell lung cancer. In 338 of 474 patients, the data on respiratory muscle strength and spirometric values, was measured before and one month after surgery. The transition rates of collected data were assessed according to the different surgical approaches. Complete VATS was performed via a 2 to 4cm access thoracotomy with same length intercostal muscle dissection. Hybrid VATS was performed via a 6 to 8cm skin incision with an approximately 20cm intercostal muscle dissection. A rib spreader was not used in either approach. Twenty patients who underwent a standard open thoracotomy were excluded from this analysis.

**Results:** The average transition rates of maximal expiratory pressure (PEmax) and maximal inspiratory pressure (Pinmax) in the complete VATS procedure (n = 230) were 95.2% and 101.1%, respectively. Those for the hybrid VATS procedure (n = 88) were 92.2% and 98.4%, respectively. Statistically significant differences between the two approaches were not detected in the transition rates of PEmax and Pinmax (p = 0.3371) or Pinmax (p = 0.4177). In addition, the average transition rates of VC and FEV1.0 limited in patients who underwent lobectomy did not show statistically significant difference between the two approaches.

**CONCLUSIONS:** The transition rate of respiratory muscle strength one month post-surgery was equivalent between complete VATS and hybrid VATS, although the length of the intercostal muscle dissection distinctly varied.

<table>
<thead>
<tr>
<th>Table 1. Main characteristics of complete VATS and hybrid VATS procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length of skin incision</strong></td>
</tr>
<tr>
<td>Complete VATS</td>
</tr>
<tr>
<td>Hybrid VATS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postoperative transition rates of respiratory muscle strength and spirometric values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete VATS</strong></td>
</tr>
<tr>
<td>(post/pre) PEmax</td>
</tr>
<tr>
<td>(post/pre) Pinmax</td>
</tr>
<tr>
<td>(post/pre) VC</td>
</tr>
<tr>
<td>(post/pre) FEV1.0</td>
</tr>
</tbody>
</table>

**SEMI-RIGID THORACOSCOPY FOR DIAGNOSING MALIGNANT PLEURAL MESOTHELIOMA**

**AKANE ISHIDA1, MASAHIDE OKI1, HIDEO SAKA2, ATSUSHI TORII3, ARISA YAMADA1, FUMIE SHIGEMATSU1, HIDEYUKI NIWA1, SAORI OKA1, MASASHI NAKAHATA1, YOSHINORI KOGURE1, CHIYOE KITAGAWA1**

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**Background and Aims:** Malignant pleural mesothelioma is an asbestosis-related cancer that is difficult to diagnose. Thoracoscopy has become popular for making a histological diagnosis of mesothelioma. This study evaluated the diagnostic efficacy and thoracoscopic findings of medical thoracoscopy in patients with malignant mesothelioma.

**Methods:** Patients with malignant mesothelioma who underwent thoracoscopy using a semi-rigid thoracoscope under local anesthesia and conscious sedation in a single center were retrospectively reviewed.

**Results:** Fourteen patients (median age 65 [range 56-85] years, 12 males) with final diagnoses of malignant mesothelioma were analyzed. The pathological subtypes comprised six epithelioid, three sarcomatoid, two bipsasic and two desmoplastic types, and one other. Five patients (36%) underwent a thoracoscopic biopsy and talc poudrage simultaneously. The diagnostic yield of thoracoscopy was 71% (10 of 14 patients). Four patients were diagnosed using other procedures, including cervical lymph node biopsy, bone biopsy, cell block pleural effusion, and autopsy. The thoracoscopic findings included thickening of the pleura in five, malignant-looking pachypleuritis in three, nodules or masses in three, and a grape-like appearance in two. The parietal pleura of the remaining patient could not be examined because of thick fibrous adhesions. One pneumothorax occurred.

**Conclusions:** Thoracoscopy is safe and effective for diagnosing malignant mesothelioma. A wide variety of pleural appearances can be seen, and thickening of the pleura, malignant-looking pachypleuritis, and nodules or masses are the frequent thoracoscopic findings.
Background and Aim: Malignant pleural effusion(s) (MPEs) are common in patients with neoplastic disease. Few data exist that guide clinicians in making important therapeutic decisions in its management. The LENT prognostic score is the first validated risk stratification system in MPEs that is meant to assist physicians in (1) predicting the survival of patients and (2) determining the extent of treatment options. Our study aims to determine the prognostic value of the LENT score in patients with MPEs admitted at the Chinese General Hospital and Medical Center (CGHMC).

Table 1. Distribution of Patients Based on their Profile

<table>
<thead>
<tr>
<th>Profile</th>
<th>f</th>
<th>%</th>
<th>Mean</th>
<th>SE</th>
<th>95% CI</th>
<th>Median</th>
<th>SE</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Overall</td>
<td>43</td>
<td>48.9</td>
<td>4.60</td>
<td>0.47</td>
<td>(3.68, 5.52)</td>
<td>2.00</td>
<td>0.76</td>
<td>(0.50, 3.50)</td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&gt; 61.66</td>
<td>45</td>
<td>51.1</td>
<td>5.56</td>
<td>0.80</td>
<td>(3.99, 7.13)</td>
<td>4.00</td>
<td>1.19</td>
<td>(1.66, 6.34)</td>
</tr>
<tr>
<td>≤ 61.66</td>
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<td></td>
<td></td>
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<tr>
<td>Sex</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>56</td>
<td>63.6</td>
<td>4.57</td>
<td>0.64</td>
<td>(3.31, 5.83)</td>
<td>2.00</td>
<td>0.36</td>
<td>(1.29, 2.71)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tumor type</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematologic malignancy</td>
<td>6</td>
<td>6.8</td>
<td>14.00</td>
<td>2.12</td>
<td>(9.84, 18.16)</td>
<td>12.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gynecologic malignancy</td>
<td>6</td>
<td>6.8</td>
<td>8.92</td>
<td>2.32</td>
<td>(4.37, 13.46)</td>
<td>10.00</td>
<td>1.77</td>
<td>(6.53,13.47)</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>22</td>
<td>25.0</td>
<td>3.59</td>
<td>0.80</td>
<td>(2.02, 5.16)</td>
<td>2.00</td>
<td>0.45</td>
<td>(1.12, 2.88)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>9</td>
<td>10.2</td>
<td>2.33</td>
<td>0.80</td>
<td>(0.77,3.9)</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Gastrointestinal cancer</td>
<td>3</td>
<td>3.4</td>
<td>6.33</td>
<td>2.73</td>
<td>(0.99,11.68)</td>
<td>8.00</td>
<td>5.72</td>
<td>(0.00,19.20)</td>
</tr>
<tr>
<td>Urologic cancer</td>
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<td>3.4</td>
<td>1.00</td>
<td>0.00</td>
<td>(1.00,1.00)</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neck cancer (Thyroid, Laryngeal)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Location of pleural effusion</td>
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</tr>
<tr>
<td>Bilateral</td>
<td>36</td>
<td>40.9</td>
<td>5.58</td>
<td>0.82</td>
<td>(3.99, 7.18)</td>
<td>6.00</td>
<td>1.55</td>
<td>(2.95, 9.05)</td>
</tr>
<tr>
<td>Right</td>
<td>20</td>
<td>22.7</td>
<td>3.60</td>
<td>0.74</td>
<td>(2.15, 5.05)</td>
<td>2.00</td>
<td>0.55</td>
<td>(0.93, 3.07)</td>
</tr>
<tr>
<td>Pleural fluid LDH</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>&gt; 1500 IU/L</td>
<td>14</td>
<td>15.9</td>
<td>2.71</td>
<td>1.10</td>
<td>(0.57, 4.86)</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>≤ 1500 IU/L</td>
<td>74</td>
<td>84.1</td>
<td>4.92</td>
<td>0.49</td>
<td>(3.95, 5.88)</td>
<td>4.00</td>
<td>0.86</td>
<td>(2.31, 5.69)</td>
</tr>
<tr>
<td>ECOG-PS Score</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>14</td>
<td>14.8</td>
<td>8.46</td>
<td>1.48</td>
<td>(5.57, 11.36)</td>
<td>7.00</td>
<td>0.84</td>
<td>(5.35, 8.65)</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>37.5</td>
<td>5.69</td>
<td>0.73</td>
<td>(4.27, 7.11)</td>
<td>6.00</td>
<td>1.22</td>
<td>(3.61, 8.39)</td>
</tr>
<tr>
<td>3</td>
<td>41</td>
<td>46.6</td>
<td>2.49</td>
<td>0.45</td>
<td>(1.60, 3.38)</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Serum NLR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 9</td>
<td>24</td>
<td>27.3</td>
<td>2.21</td>
<td>0.48</td>
<td>(1.27, 3.15)</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>≤ 9</td>
<td>64</td>
<td>72.7</td>
<td>5.51</td>
<td>0.58</td>
<td>(4.37, 6.65)</td>
<td>6.00</td>
<td>1.35</td>
<td>(3.36, 8.64)</td>
</tr>
<tr>
<td>Tumor category</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>6</td>
<td>6.8</td>
<td>14.00</td>
<td>2.12</td>
<td>(9.84, 18.16)</td>
<td>-</td>
<td>0.43</td>
<td>-</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>53</td>
<td>60.2</td>
<td>3.75</td>
<td>0.44</td>
<td>(2.88, 4.61)</td>
<td>2.00</td>
<td>0.45</td>
<td>(1.12, 2.88)</td>
</tr>
<tr>
<td>High risk</td>
<td>3</td>
<td>3.4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Methods: This is a retrospective cohort study reviewing medical records of patients with MPEs diagnosed at CGHMC. LENT risk stratification was determined based on patient variables and characteristics. (1) Survival time was calculated from the date of MPE diagnosis to death. (2) Median survival was computed per LENT risk categories. Diagnostic values were computed to determine the predicting ability of LENT, area under the curve (AUROC). All test of significance is at 5%. Cox-hazard regression was used to determine other factors affecting overall survival. Statistical comparisons were performed using Kaplan-Meier method with log-rank test.

Results: Eighty-eight patients were included; 63.6% female, 36.4% male. The most frequently diagnosed tumors were lung cancer (44.3%), breast cancer (25.0%), and gastrointestinal cancer (10.2%). Average survival time is 4.60 months. The age group (X^2=3.864, p=0.049), tumor type (X^2=29.996, p=0.001), tumor risk category (X^2=14.624, p=0.001), ECOG-PS score (X^2=19.166, p=0.001), and serum NLR (X^2=13.281, p=0.001) significantly affect the survival distributions of patients with MPE. Patients with a higher LENT score have lower survival times compared with lower LENT scores who have higher survival rates (r= -0.597, p<0.001).
Conclusions: The age group, tumor type, tumor category, ECOG-PS score, and serum NLR significantly affect the survival of patients with MPE. A high LENT score has lower survival rates (1.58 months) while a low LENT score has higher survival rates (6.09 months). The LENT score is a superior indicator of survival than the ECOG-PS score. It is easy to calculate and has a clinically relevant prognostic scoring.

Figure 10. Survival Plot of Patients by LENT Category

Table 2. Testing Differences in the Survival Functions By Profile

<table>
<thead>
<tr>
<th>Profile</th>
<th>Log Rank Test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>3.864*</td>
<td>0.049</td>
</tr>
<tr>
<td>Sex</td>
<td>0.005</td>
<td>0.945</td>
</tr>
<tr>
<td>Tumor type</td>
<td>29.996**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Location of pleural effusion</td>
<td>3.041</td>
<td>0.219</td>
</tr>
<tr>
<td>Pleural fluid LDH</td>
<td>2.131</td>
<td>0.144</td>
</tr>
<tr>
<td>ECOG-PS Score</td>
<td>19.166**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum NLR</td>
<td>13.281**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tumor category</td>
<td>14.624**</td>
<td>0.001</td>
</tr>
<tr>
<td>LENT score category</td>
<td>36.640**</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Significant at 5%. ** Significant at 1%

Table 3. Summary Result of Cox Regression Model

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Wald/Score</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>2.252</td>
<td>1</td>
<td>0.133</td>
</tr>
<tr>
<td>Tumor type</td>
<td>9.848</td>
<td>6</td>
<td>0.127</td>
</tr>
<tr>
<td>ECOG-PS Score</td>
<td>2.929</td>
<td>1</td>
<td>0.087</td>
</tr>
<tr>
<td>Serum NLR</td>
<td>0.706</td>
<td>1</td>
<td>0.401</td>
</tr>
<tr>
<td>Tumor category</td>
<td>4.496</td>
<td>2</td>
<td>0.106</td>
</tr>
<tr>
<td>LENT score category</td>
<td>22.186**</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

** Significant at 1%

Background and Aim: Prognosis of patients with malignant pleural mesothelioma (MPM) is generally poor, and leukocytosis is reported as one of the worst prognostic factor in patients with MPM. Patients with granulocyte-colony stimulating factor (G-CSF)-producing MPM have been reported, and leukocytosis is generally seen among these patients. However, whether leukocytosis in patients with G-CSF-producing MPM is a poor prognostic factor or not seems to be controversial. We evaluated the prognostic factors including leukocyte count at diagnosis in patients with Japanese G-CSF-producing MPM.

Methods: Reviewing English and Japanese literatures and two cases of our own, we retrospectively evaluated factors including leukocyte count at diagnosis and overall survival as a prognosis in Japanese patients with G-CSF-producing MPM. Spearman’s rank correlation coefficient was applied to evaluate the correlation between leukocyte count at diagnosis and overall survival.

Results: There were 19 cases (17 reported G-CSF-producing MPM case reports and two patients of our own) of G-CSF-producing MPM. All of the patients were male, and average age was 59.4 years old. Pathological types of MPM were biphasic(6 cases), sarcomatoid(5), epithelial(3), mixed(4), desmoplastic(1) and unknown(1). Serum G-CSF was measured in 14 cases, and G-CSF production by MPM were confirmed by immuno-histochemical measurement in 6 cases. Among these 19 cases, 14 cases had the data of leukocyte count at diagnosis and overall survival, and statistically significant inverse correlation between leukocyte count at diagnosis and overall survival was observed (r=0.569, p<0.05) by Spearman’s rank correlation coefficient.

Conclusion: Leukocytosis at diagnosis is a significant poor prognostic factor in patients with G-CSF-producing MPM.

THE EFFICACY AND SAFETY OF ULTRASOUND (US) GUIDED PERCUTANEOUS CORE-NEEDLE BIOPSY FOR PERIPHERAL LUNG OR PLEURAL LESIONS; COMPARISON WITH COMPUTED TOMOGRAPHY (CT) GUIDED NEEDLE BIOPSY

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Background and Aims: US-guided percutaneous core-needle biopsy is a useful diagnostic technique with short examination time, and real-time monitoring of both needle movement and lesion visualization at the patient’s bedside without radiation exposure. However, few studies have reported, whereas CT-guided biopsy has well established and accepted. There are also limited data comparing US- and CT-guided biopsy of thoracic lesions. To clarify the efficacy and safety of US-guided biopsies for peripheral lung or pleural lesions adjacent to the chest wall.

Methods: We retrospectively enrolled US- or CT-guided percutaneous core-needle biopsies for peripheral lung or pleural lesions adjacent to the chest wall performed in consecutive patients from April 2012 to April 2017. These lesions were sampled by using an 18-gauge needle, Bird®Magnum® (US-guided) or a 18-gauge needle Bird®Magnum® (CT-guided). Age, sex, body mass index (BMI), lesion size, lesion-pleura contact arc lung (LPCAL), diagnostic rate, and complications were compared between US- and CT-guided groups.
**Abstracts**

**AP262**

**THE DIAGNOSTIC VALUE OF PARALLEL DETECTION OF CYTOKERATIN 19 FRAGMENT-BASED TUMOR MARKERS IN MALIGNANT PLEURAL EFFUSION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background and Aims:** Cytokeratin 19 Fragment (CYFRA 21-1) is one of the commonly used tumor markers in clinical practice. The examination of CYFRA 21-1 in pleural effusions may help establish the diagnosis of malignant pleural effusion (MPE). However, given the relatively low sensitivity, it is often used in combination with other tumor markers. We performed this systematic review and meta-analysis, aiming to explore the diagnostic performance of parallel diagnostic algorithms based on CYFRA 21-1 in MPE.

**Methods:** The databases of Pubmed, Embase, and the Cochrane Library were searched from their inception to February 2017 for eligible studies. We included studies that reported the performance of CYFRA 21-1 plus another tumor marker for diagnosing MPE. The STATA software was employed for data analysis, using the bivariate random-effects model.

**Results:** Eleven studies assessed the diagnostic performance of pleural CYFRA 21-1 plus CEA for MPE. The pooled data showed that the sensitivity was 88% (76%-94%) and the specificity was 87% (83%-90%). The positive likelihood ratio (PLR) was 6.6 (4.8-8.9), and the negative LR (NLR) was 0.14 (0.07-0.29). Four studies reported the diagnostic accuracy of pleural CYFRA 21-1 plus serum CYFRA 21-1 in MPE. The aggregated results revealed that the sensitivity was 76% (66%-84%), with a specificity of 87% (75%-93%). The PLR was 5.7 (2.8-11.5), with a NLR of 0.28 (0.19-0.41).

**Conclusions:** The parallel diagnostic algorithms, including pleural CYFRA 21-1 plus CEA, and pleural CYFRA 21-1 plus serum CYFRA 21-1, showed satisfactory and reliable diagnostic values in MPE. When compared with single tumor marker, the parallel test substantially increased the sensitivity and the diagnostic accuracy.

**AP263**

**DIAGNOSTIC SIGNIFICANCE OF MICRORN A FEATURES IN PATIENTS WITH MALIGNANT PLEURAL EFFUSION**

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1Department of Respiratory Medicine, Nagoya Medical Center, Nagoya, Japan

**Background and Aim:** The diagnosis of malignant effusions (MPE) mainly relies on cytological analysis. However, the sensitivity is still limited even with repeated analyses, and alternative methods are in need to assist in the diagnosis. MicroRNAs (miRNAs) isolated from exosome in serum reflects the miRNA signature of the parental tumor. Therefore, exosomal miRNA in pleural effusion (PE) also could be a useful and noninvasive biomarker to distinguish MPE and benign (non-neoplastic) pleural effusion (BPE). The aim of this study is to compare miRNA profiles in MPE, including lung adenocarcinoma pleural effusion (Ad-MPE), and BPE.

**Methods:** Exosomes in PE and serum were isolated, and exosomal miRNA expressions were evaluated using real-time reverse transcription quantitative polymerase chain reaction. The area under the receiver operating characteristic curve (AUC) was used to evaluate the diagnostic performance of each miRNA.

**Results:** A total of 41 PE samples from patients with lung cancer (Ad-MPE, n = 24; other malignancies, n = 7) and non-neoplastic diseases (BPE, n = 10) were collected by thoracocentesis, performed during the diagnostic workup of patients with PE or prior to tube thoracostomy. We observed that the expression level of miR-182 (MPE vs BPE, p < 0.001; Ad-MPE vs BPE, p < 0.001 and miR-210 (Ad-MPE vs BPE, p < 0.05) was significantly higher in neoplastic effusion samples than BPE. The Receiver Operating Curve analysis of miR-210 for diagnosis of MPE and Ad-MPE yielded an AUC of 0.76 (95% confidence interval, 0.568 to 0.951) and 0.78 (95% confidence interval, 0.596 to 0.960), respectively. In the subject with lung adenocarcinoma, no correlation was detected between serum and PE miRNA expression level.

**Conclusion:** The expression level of miR-182 and miR-210 in PE may have diagnostic potential for differentiating MPE or Ad-MPE from BPE.

**AP264**

**TALC SLURRY PLEURODESI S FOR MALIGNANT PLEURAL EFFUSION IN LUNG CANCER PATIENTS: A RETROSPECTIVE STUDY**

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1Department of Respiratory Medicine, Nagoya Medical Center, Nagoya, Japan

**Background and Aim:** Talc is considered the most effective agent for pleurodesis of malignant pleural effusion. Compared with talc poudrage pleurodesis, talc slurry pleurodesis is an effective, less invasive, and more durable procedure. We investigated the effectiveness and safety of talc slurry pleurodesis for malignant pleural effusion due to lung cancer.

**Methods:** This retrospective study included patients with lung cancer accompanied by pleural effusion who underwent talc slurry pleurodesis at our institution between April 2012 and November 2016. Successful pleurodesis was defined by the nonrequirement of thoracic drainage and no development of progressive dyspnea at 28 days after the procedure.

**Results:** Following the exclusion of patients who died or were lost to follow-up, 49 patients with a median age of 73 (range, 54–91) years, including 33 men (67.3%), were investigated. The Eastern Cooperative Oncology Group PS of 3 or 4 was observed in 7 (14.3%) patients. The mean duration from pleurodesis to chest tube removal was 5 (2–17) days.
The pleurodesis success rate was 87.8% (43/49). Fever more than 100 °F, liver dysfunction, and elevated C-reactive protein (CRP) levels occurred in 10 (20.4%), 8 (16.3%), and 20 (40.8%) patients, respectively. The adverse event rate was higher in the success group than in the failure group. There was no case of acute respiratory distress syndrome. The median drainage volume on the day before pleurodesis was lesser [170 (10–1410) mL vs. 245 (20–700) mL] and the median duration from pleurodesis to chest tube removal was shorter [5 (2–17) days vs. 6.5 (3–12) days] in the success group than in the failure group.

Conclusions: Talc slurry pleurodesis is effective and safe for malignant pleural effusion. Fever, liver dysfunction, and elevated CRP levels may be predictors of successful pleurodesis.

AP265

AN EXPERIENCE WITH GRADED TALC PLEURODESIS IN TREATMENT OF MALIGNANT PLEURAL EFFUSION

CARMEN TAN1, JOHN ABISHEGANADEN1

1Department of Respiratory & Critical Care Medicine, Tan Tock Seng Hospital, Singapore, Singapore

Background and Aims: Malignant pleural effusion (MPE) contributes to a rapidly rising healthcare burden. It represents advanced disease and aim of treatment includes effective prevention of recurrence and shorter length of hospital stay (LOS). Indwelling pleural catheter (IPC) is reportedly gaining popularity in selected MPE patients. However, in many countries, including Singapore, talc pleurodesis remains the preferred option of treatment.

In Nov 2015, our center switched to graded talc (Stentalc). Our retrospective study aims to track our center’s continued efficacy of talc pleurodesis and more importantly, perform audit on talc-related complications and LOS-effusion related.

Methods: Patients were identified using inpatient pharmacy’s records of talc (slurry) prescribed between 1 Jan 2016 to 31 Dec 2016. Previously collected data between 1 Jan 2012- 31 Dec 2013 were used as comparison. We included all patients who underwent talc pleurodesis for MPE (diagnosed cytologically and/or radiologically).

Results: 40 patients were studied. 34 (64%) had primary lung cancer, 7 (15%) had breast cancer and the rest had gastrointestinal, genitourinary and ovarian cancer (Table 1). Success rate of pleurodesis with Stentalc was maintained at 70%. We observed a reduction in all talc-related complications (Figure 1) including pain 38% (2013); 8% (2016), fever 62% (2013); 50% (2016), dysarhythmias 25% (2013); 20% (2016), talc-related hypoxaemia 15% (2013); 10% (2016) and pleural infection 2% (2013); 0% (2016). However, LOS-effusion related was 7 hospital bed days which was longer than existing literature.

Conclusions: Graded talc has been shown to be superior in our centre’s experience in terms of safety profile with similar efficacy from previous talc used. Nonetheless, more could be done to improve the management of MPE to enable earlier discharge.
pleural effusion. Because combination therapy may make complication increase.

AP267
EFFICACY OF POVIDONE IODINE VERSUS OXYTETRACYCLINE IN PLEURODESIS OF PATIENTS WITH RECURRENT MALIGNANT PLEURAL EFFUSION
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Background and Aims: Fifty percent of patients with recurrent pleural effusion have dyspnea which limits their ADL and quality of life. Pleurodesis is done to prevent recurrence of effusion and alleviate dyspnea through sclerosing agents like Oxytetracycline. Povidone iodine, however, has recently gained attention. This study aimed to determine the sclerosing agent with higher efficacy rate and least side effects.

Methods: A double-blind, randomized, controlled trial of patients with histologic diagnosis of malignant pleural effusion who underwent chest tube thoracostomy (CTT) insertion. After Pleurodesis, vital signs, Borg Dyspnea Scale, Visual Analogue Pain Scale and drainage days were measured. Once the pleural fluid reached <100 ml/day, CTT was pulled out. A chest radiograph was repeated after 30 days. The response was categorized as total success (no recurrence of effusion), partial success (with recurrence but does not warrant CTT reinsertion) or failed pleurodesis (output >100ml or CTT maintained).

Results: The population (n=21) was divided into the Oxytetracycline/ control (11 patients) and Povidone Iodine/intervention (10 patients). Drainage days in Povidone Iodine was significantly shorter (4.4 ± 1.1 days) compared to Oxytetracycline (6.9 ± 1.9 days) (p-value 0.002). Most common adverse event was dyspnea (80%). Oxytetracycline has slightly higher incidence of dyspnea, fever, and hypotension. Povidone Iodine has slightly increased level of pain but were not statistically significant. Significantly higher complete success rate was seen in Povidone Iodine (6/10, 60%) versus Oxytetracycline (1/11, 9.10%) (p-value 0.013). No significant difference in partial success (p-value 0.131). One failed pleurodesis in Oxytetracycline while none in Povidone.

Conclusions: Povidone Iodine is safe and effective with higher complete success rates and shorter drainage duration.

AP268
HOME CARE MANAGEMENT ON INDWELLING PLEURAL CATHETER (IPC) FOR PATIENTS WITH MALIGNANT PLEURAL EFFUSIONS
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Background: Patients with malignant pleural effusions (MPE) can suffer from recurrent dyspneic episodes due to fluid re-accumulations. “Indwelling Pleural catheter” (IPC) is a recently introduced self-financed option. The pleural fluid can be intermittently drained at home or day-care without repeated hospitalizations.

Aims: To evaluate the initial results of the IPC in QEH

Methods: A prospective analysis was conducted (September 2013 to September 2015). A nursing assessment on the IPC eligibility includes: 1. General conditions: daily activities dependency, psychological status, motor functional status and visual acuity. 2. Social support: living environment and availability of carers; 3. Financial status; 4. carer’s ability for IPC management. Eligible patients and caregivers were educated on home care of IPC with re-evaluations at two to four-weeks intervals. Dyspnea and pain scores, body mass index, exercise tolerance, anxiety level and wound complications were measured before insertion and three-months afterwards. Psychological counseling, dyspnea management and problem-solving skills were provided. Help-line or phone follow-up was offered.

Results: Six patients (mean age 70.6) were put on IPC. Five had been admitted twice and one admitted thrice due to dyspnea in the year before drainage, with an average 76 days’ length-of-stay. None were readmitted again via emergency room and only one had mild wound inflammation. There were no significant improvement in mean anxiety (9.3 vs. 7.5) and pain scores (3.3 vs. 4). However, the mean dyspnea score by Visual Analogue Scale (range 1-10) was obviously improved (7.3 vs. 3 p<0.001). There was a mean of 16 nurse clinic consultations per patient after IPC insertions. Mean phone enquiries and follow-up calls was 2.8 per patient. All regarded IPC as useful with reduced dyspnea and improved well-being. Four patients died during the study period.

Conclusion: IPC improves dyspnea and well-being with minimal complications in MPE patients with limited life expectancy.
Background: The coexistence of TB and cancer has attracted many attention for several years and remains a debate. Correlation between them is interesting and diverse, in which the simultaneous occurrence of both TB and cancer in the same organ causes a diagnostic dilemma.

Case presentation: A 62 years old man came with chief complaint shortness of breath since 7 days before admitted. He was diagnosed with pulmonary TB with AFB smear positive 10 months prior and already received 6 month ATD therapy without any previously history of lung cancer. Recent CXR showed homogenous opacity on left hemithorax, which was the same predilection with the TB lesion seen from the previous CXR 10 months before. Chest CT showed solid heterogeneity mass, irregular edge with calcification and central necrotic, with invasion to thoracic wall and caused destruction of costa 2,3,4,5. Histopathological examination results from the FNAB of chest wall mass showed a cytromorphological appearance of an invasive carcinoma, suggesting a squamous cell carcinoma. Patient then continue to receive chemotherapy afterwards.

Conclusion: The diagnosis of lung cancer was delayed mainly due to masking from the tuberculous lesion. The presence of lung cancer and pulmonary TB coexist in the same lobe is possible because cancer cause decreased immunity that facilitates the occurrence of an infection. Patients with pulmonary tuberculosis in whom a predominant or growing nodule is present and showed little improvement of symptoms despite antituberculous therapy, should be suspected as coexisting cancer.

Keywords: Pulmonary Tuberculosis, Squamous cell carcinoma, diagnostic problems

AP271
PRIMARY LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE LUNG: A DESCRIPTIVE CASE SERIES OF AN UNCOMMON MALIGNANCY
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Background and Aim: Primary lymphoepithelioma-like carcinoma (LELC) of the lung is one of the rare histological types of lung cancer, with relatively better prognosis. In Singapore, the National Cancer Registry reported only 39 cases from 2003 to 2012. We noticed a spike of pulmonary LELC diagnosed at our centre from 2010 to 2016.

Methods: We retrospectively analysed medical records of consecutive patients with biopsy proven LELC, at our centre from November 2010 to January 2016. We described baseline characteristics, staging, therapeutic interventions and median survival.

Results: Ten patients were diagnosed with pulmonary LELC during the study period. The average age at diagnosis was 61 years with a female preponderance ratio of 8:2. Seven patients were non-smokers. Five patients were diagnosed by endobronchial ultrasound transbronchial needle aspiration and three by transthoracic needle aspiration of lung mass. Six (60%) patients were staged as advanced metastatic cancer, while three were stage IIIA and one was stage IIA. All had Epstein-Barr virus encoded small non-polyadenylated ribonucleic acid positive status. The median survival was 21 months (95% CI 16.0 to 26.0) and 2-year survival rate was 50%. Seven patients with primary pulmonary LELC received chemotherapy and five of them had gemcitabine/carboplatin as first line. All patients had progression of disease requiring second line chemotherapy and three patients required third line chemotherapy. The average duration of disease progression after first line chemotherapy was 8.4 months.

Conclusion: As the survival rates in pulmonary LELC are shown to be better than other types of lung cancers, it is important to achieve an early diagnosis. Current therapeutic experience with pulmonary LELC seems to be limited, hence the choice of first line chemotherapy is usually empirical. Further studies are needed to determine the choice of first line chemotherapy in advanced pulmonary LELC.

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AP272
A CASE OF PRIMARY THYMUS MALT LYMPHOMA NOT ASSOCIATED WITH AUTOIMMUNE DISEASE
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Background and Aims: MALT lymphoma is a low grade B-lymphoid tumor, which appears more commonly in gastrointestinal tract. MALT lymphoma is highly associated with autoimmune disease, approximately 70%. Especially, Sjogren’s syndrome is frequently associated. We experienced a case of anterior mediastinal tumor, diagnosed as MALT lymphoma by histopathologic examination but not associated with autoimmune disease.

Results: A 50-year-old woman underwent operation for sigmoid colon cancer in 21 month ago. During follow up, the 15mm anterior mediastinal tumor was detected on chest CT. Chest MRI reveals the low intensity mass on T1 imaging, high intensity on T2 imaging at the anterior mediastinum. She had no neurologic manifestation and antiacetylcholine receptor antibody was within normal limit. So we suspected she had thymoma and we performed 2-port video-assisted thoracoscopic thymus partial resection. There was no invasion in surrounding tissues. The histopathological findings from the surgically resected specimens revealed lymphoepithelial lesion, CD20(+) and CD3(-) by immunostaining. Thus we diagnosed as MALT lymphoma. She had no clinical manifestation and autoantibody was within normal limit. Therefore, we judged her MALT lymphoma is not associated with autoimmune disease. 6 month have passed since she underwent the operation, she has no recurrence and no autoimmune disease.

Conclusions: We report a case of MALT lymphoma which was considered to be thymoma. It is reported that primary thymus MALT lymphoma is rare case. But we should consider that MALT lymphoma is one of the differential diagnosis when anterior mediastinal tumor was pointed out. We will report with some literature consideration.
Background and Aims: Neuromyotonia (NMT) and autoimmune autonomic ganglionopathy (AAG) are both rare paraneoplastic syndrome associated with thymoma. Although the exact mechanisms remain unclear, autoantibodies have been implicated in disease pathogenesis.

Results: A 50-year-old female suffering from invasive thymoma achieved complete remission by multidisciplinary modalities of treatment. During medical follow-up, slowly growing recurrent tumor was detected but conservatively monitored without symptomatic worsening. She complained of walking difficulties due to lower limb pain after 3 years of recurrence. Physical examinations showed tachycardia, painful muscle stiffness, muscle cramp, fasciculation, and myokymia accompanied by hyperhidrosis. We diagnosed as NMT based on the findings of electromyography revealing fibrillation potential and myokymic discharge. These muscle symptoms were completely improved by treatment with dantrolene, carbamazepine and corticosteroid. However the pain in the lower extremity remained unresolved. Although symptoms of autonomic neuropathy were not obvious except for hyperhidrosis and tachycardia, the edrophonium test, which was tried as a pain treatment, turned out positive. Neurophysiological (NMT) and AAG diagnoses were further confirmed by the existence of antibodies to voltage-gated potassium channel (VGKC) and to Ganglionic Nicotinic Acetylcholine Receptor (gAChR).

Conclusions: To our knowledge, this is the first case report of invasive thymoma showing simultaneous onset of NMT and AAG, which is efficiently treated with combination of sodium-channel blocker and cholinesterase inhibitor.

A CASE OF CAVITATING LUNG METASTASIS OF GRANULOCYTE COLONY-STIMULATING FACTOR PRODUCING UROTHELIAL CARCINOMA

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Introduction: Carcinomas producing ectopic G-CSF are most frequently of lung origin; and those originating from urothelial tissues are rare. Here we describe a case, in which a G-CSF producing urothelial carcinoma of the renal pelvis had metastasized to the lung and formed multiple nodular and cavitary lesions.

Case: A 78-year-old Japanese male who had multiple episodes of urtiilitis walked in our hospital, complaining of a dry cough and running fever. Blood test showed a marked leukocytosis (19,000/μl), and CT scan revealed multiple cavitary lung lesions, pleural effusion and a mass (7 x 5 cm). The patient was treated with chemotherapy, but chemotherapy was not effective and the lesions progressed. The patient died 6 months after diagnosis.

AP274

PRIMARY PULMONARY CHORIOCARCINOMA, A RARE MALIGNANCY OF LUNGS

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Background and Aims: Choriocarcinoma commonly metastasizes to lungs. However, primary pulmonary choriocarcinoma is rare. We reported here the first reported case of primary pulmonary chorocarcinoma in Thailand.

Method: A 24-year-old woman presented to an antenatal care clinic because her urine pregnancy test was positive. After regular follow-ups, obstetric ultrasound was due to poor weight gain. The ultrasonography revealed no fetus despite high level of β-hCG, more than 60,000 mIU/ml. As a result, she was investigated for extra-gonadal germ cell tumor. Neither pelvic mass nor abdominal mass was identified. However, her chest radiograph showed patchy opacity at left lower lung zone. Computed tomography (CT) detected a mass-liked consolidation, which was consistent with the lesion found in chest (figure 1). Bronchoscopy with transbronchial biopsy was done. The pathological findings were compatible with choriocarcinoma. The patient was treated with cisplatin and etoposide. After completion of chemotherapy session, CT scan showed the resolution of the lung mass, and only some fibrotic scar left. The level of β-hCG significantly fell to <5 μIU/ml.

Conclusion: Primary pulmonary chorocarcinoma is a rare pulmonary cancer. Most of patients, who were previous reported, were asymptomatic and were accidentally found by routine chest radiography or false positive of pregnancy test, similar to our case. There are lack of evidence-based treatments for this condition. Complete resection with or without chemotherapy seems to be effective, but overall 5-year survival is less than 5%. Our patient received only chemotherapy. After one year of following up, she has been doing well without recurrence.
8 cm) in the left renal pelvis. PET-CT scan exhibited remarkable uptakes of 18F-FDG with the SUV value of 4 to 6 at the sternum, vertebra and ilium (in addition to the lung and kidney. There was no evidence of osteolysis.) Cytological analysis of sputum, pleural effusion, and urine indicated the diagnosis of urothelial carcinoma with lung metastasis. The serum G-CSF concentration was 220 pg/ml, and the white blood cell count increased to 71,400/μl by the 22nd day of admission when he died. Necropsy confirmed the diagnosis of primary urothelial carcinoma of the left renal pelvis and its lung metastasis. The specimen was immunohistochemically positive for G-CSF production. Bone marrow examination did not reveal any malignancy.

Discussion: The leukocytosis seems to have been caused by ectopic production of G-CSF from the urothelial carcinoma. In general, G-CSF producing urothelial carcinoma is diagnosed at late stages. In the present case, in particular, the remarkable presentation as multiple lung lesions with cavitation mimicking pulmonary tuberculosis caused a delay in the diagnosis.

Discussion: The leukocytosis seems to have been caused by ectopic production of G-CSF from the urothelial carcinoma. In general, G-CSF producing urothelial carcinoma is diagnosed at late stages. In the present case, in particular, the remarkable presentation as multiple lung lesions with cavitation mimicking pulmonary tuberculosis caused a delay in the diagnosis.

Figure 1. CT scan revealed multiple cavitary lung lesions and pleural effusion.

Figure 2. PET-CT scan exhibited uptakes of 18F-FDG at the sternum, vertebra and ilium.

Figure 1. CT scan revealed multiple cavitary lung lesions and pleural effusion.

Figure 2. PET-CT scan exhibited uptakes of 18F-FDG at the sternum, vertebra and ilium.

Interstitial Lung Disease 1

AP276

A CASE OF PULMONARY RENAL SYNDROME, INITIALLY DIAGNOSED AS PNEUMONIA

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Introduction: Pulmonary-renal syndromes are a group of disorders characterised by necrotising glomerulonephritis and pulmonary haemorrhage.

Case Report: 56 years old female patient presented to with dyspnea, cough, mild hemoptysis, mild hypoxemia and opacities at chest X-ray. She was diagnosed as pneumonia and hospitalized. A few days later her condition has worsened and referred to our intensive care unit. She denied any diseases, drug use, occupational or environmental exposure. Thorax computed tomography revealed bilateral patchy alveolar opacities. She had low hemoglobin levels with high creatinine levels. She admitted to intensive care unit. Bedside bronchoscopy was done. Bronchoalveolar lavage (BAL) was diagnostic of diffuse alveolar hemorrhage. Antineutrophil cytoplasmic antibodies (ANCA) was positive. Renal biopsy showed pauci-immune vasculitic, glomerulonephritis. Final diagnosis was pulmonary renal syndrome ANCA-MPO associated necrotizing vasculopathy. She was commenced on high dose steroid and cyclophosphamide. Two weeks later infiltrations were disappeared and partial oxygen pressure increased to normal limits.

Conclusions: Clinical presentation is variable, symptoms don’t have to occur simultaneously and similarities exist with pneumonia. As result patients may initially be diagnosed as pneumonia. Fall in Hb levels, presence of renal failure, proteinuria and haematuria can help to differentiate from pneumonia.

Patients may deteriorate rapidly and life threatening respiratory and/or renal failure may occur. Therefore rapid diagnosis and proper treatment is mandatory.

AP277

DESIGN AND BASELINE CHARACTERISTICS OF THE JAPANESE IDIOPATHIC INTERSTITIAL PNEUMONIAS REGISTRY: JIPS REGISTRY

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Background and Aims: Nonspecific interstitial pneumonia (NSIP) have heterogeneous characteristics of background, disease behaviour, and prognosis. The aims of this study on fibrotic NSIP (f-NSIP) were to elucidate the prognosis and disease behaviour from the viewpoint of clinical background, and whether long-term change of pulmonary function could be provide useful prognostic information.

Methods: We retrospectively analysed medical records of 157 patients diagnosed with f-NSIP by surgical lung biopsy. Disease behaviour was categorized into two groups of “progressive type” (relative ≥5% per year decline in either slope of forced vital capacity or %diffusing capacity of lung carbon monoxide) or “stable type” depending on long-term change of pulmonary function. Predictors of disease behaviour and prognosis were determined using logistic and Cox regression models.

Results: Our f-NSIP cohort included interstitial pneumonia with autoimmune features (IPAF) (36.9%), idiopathic (non-IPAF) (22.3%), and connective tissue disease-associated interstitial lung disease (40.8%). Although the overall survival rate was poorer in idiopathic (non-IPAF) f-NSIP than the other two groups, some IPAF f-NSIP also showed progressive course despite therapy as idiopathic (non-IPAF) f-NSIP. Idiopathic (non-IPAF) f-NSIP and progressive type disease were negative prognostic factors of all-cause mortality.

Conclusions: A designation of IPAF is useful in identification of the subgroup with good prognosis in idiopathic f-NSIP. On the other hand, some patients with idiopathic f-NSIP with or without IPAF tended to show poor disease behaviour despite therapy as previously reports. Additionally, the definition as progressive type disease may be useful in clinical decision-making therapy of f-NSIP.
The 30-day/180-day mortality rates were 25%/50%, 25%/50%, 47%/67%, respectively.

Conclusions: This study indicated that the prognosis of the first AE of IP in HP group and RA-MPO group was better than in IPF group. We should note heterogeneity in treatment response to AE in patients with definite UIP pattern on HRCT.

AP281

CLINICAL INVESTIGATION OF INTERSTITIAL PNEUMONIA ACCOMPANIED BY DEEP VEIN THROMBOSIS.

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Background and Aims: In the active phase of interstitial pneumonia (IP), hypercoagulability caused by hypoxemia and thrombosis due to suppression of the fibrinolytic system has been recognized. Because DVT could proceed to PE, the search for risk factors is important. However, reports on background factors responsible for DVT merged with IP are limited. We examined the clinical background of DVT associated with IP in our facility.

Methods: Among IP cases hospitalized from August 2009 to May 2016, 11 patients were involved in DVT. We studied there clinical features retrospectively.

Results: Eleven IP patients comprised 7 males and 4 females with median age of 69 years. Five cases exhibited collagen disease, 3 cases had idiopathic pulmonary fibrosis, 2 cases had drug induced IP, 1 case presented hypersensitivity pneumonia. Eight cases exhibited acute phase/acute exacerbation phase with average D-dimer score 29.3 μg/ml (3.2-114.8) and KL-6 1383 U/ml (413-2257). Six cases developed PE, 4 cases had cancer diseases. 7 cases had been treated with steroid therapy. 2 cases had taken home oxygen therapy. 3 cases were receiving anticoagulant therapy.

Conclusions: In the acute phase/acute exacerbation phase of IP, the risk of developing DVT increases. Reduction of blood oxygen and ADL via progression of IP and collagen disease are seemed to affect the development of DVT. So the precaution for Hypoxemia and poor ADL of IP with collagen diseases is necessary to avoid DVT merger.

AP282

SERUM HYALURONAN IN PATIENTS WITH ACUTE EXACERBATION OF IDIOPATHIC INTERSTITIAL PNEUMONIA

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Background and Aims: Hyaluronan is an important constituent of the extracellular matrix in lungs, and growing evidence shows its important biological properties in the lung. We have previously demonstrated that serum hyaluronan was significantly higher in patients with clinically stable idiopathic interstitial pneumonia (IIP) than healthy controls, and was positively correlated with CRP and SP-D. In addition, in BAL fluid, hyaluronan was positively correlated with the percentage of inflammatory cells and CXCL8. These results suggest that hyaluronan is involved in the pathogenesis of IIP and serum hyaluronan is a possible biomarker in IIP, however, the clinical significance of serum hyaluronan in acute exacerbation of IIP (AE-IIP) remains to be elucidated. The goal of this study was to determine if serum hyaluronan is a clinically useful biomarker in AE-IIP.

Methods: Review patients with AE-IIP admitted to our hospital, and retrospective analysis was performed. At first, serum hyaluronan on admission was measured, and analyzed the relationship with clinical parameters. Next, serum hyaluronan in AE-IIP was compared with clinically stable IIP (SD-IIP). Furthermore, the relationship between serum hyaluronan and prognosis was evaluated.

Results: Serum hyaluronan in AE-IIP was significantly higher than SD-IIP, and had a significant positive correlation with procalcitonin, SIRS score and APACHE II score and a significant negative correlation with fibrinogen and PF ratio. In addition, when the hyaluronan ratio (acute exacerbation/stable phase) was analysed in identical patients in whom serum hyaluronan was measured in both clinically stable and acute exacerbation phases, the low hyaluronan ratio had a tendency to better survival in IIP patients. Furthermore, in IPF, the survival was significantly better for patients with low hyaluronan ration than with high hyaluronan ratio.

Conclusions: Serum hyaluronan might be a possible prognostic biomarker in patients with AE-IIP, especially IPF, when analyzed in both clinically stable and acute exacerbation phases.

AP283

CLINICAL SIGNIFICANCE OF SSA ANTIBODY IN PATIENTS WITH ARS ANTIBODY POSITIVE INTERSTITIAL PNEUMONIA

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Background and Aims: Anti-synthetase syndrome (ASS) is characterized by the presence of aminoclyl-transfer RNA synthetase (ARS) antibodies accompanied by some clinical features such as myositis, arthritis, and interstitial lung diseases. Interstitial pneumonia is one of the main clinical features of ASS, and ARS antibody is frequently positive in patients with interstitial pneumonia, even idiopathic interstitial pneumonia (IIP). SSA antibody is one of the myositis-associated antibodies and often positive in patients with ASS. It has been reported that patients with SSA antibody positive ASS had severe interstitial pneumonia and were resistant to immunosuppressive therapy compared to those with SSA antibody negative ASS. However, the clinical characteristics of patients with SSA antibody positive ASS has not been clarified in detail. The goal of this study was to determine if analysis of SSA antibody is clinically useful in interstitial pneumonia patients with ARS antibodies.

Methods: Review interstitial pneumonia patients with ARS antibodies, and clinical characteristics were compared between SSA antibody positive and negative patients. ARS antibody was analyzed by MESACUP™ anti-ARS test (MBL, Nagoya, Japan), which can detected Jo-1, PL-7, PL-12, EJ and KS antibodies.

Results: In interstitial pneumonia patients with ARS antibodies, SSA antibody was positive in more than half of patients (15/29, 52%). However, there was no difference in clinical characteristics between SSA antibody positive and negative patients. In contrast, higher KL-6 and SP-D as well as lower %VC, %FEV1 and %TLC were found in SSA antibody positive patients compared with SSA antibody negative patients, when polymyositis/dermatomyositis (PM/DM) patients in whom SSA antibody was positive in 69% of patients (9/13) were analyzed.

Conclusions: Positive SSA antibody is frequently found in interstitial pneumonia patients with ARS antibodies, and may be related to severe interstitial pneumonia in PM/DM patients.
CAUSATIVE DRUGS AND CLINICAL CHARACTERISTICS OF DRUG-INDUCED INTERSTITIAL LUNG DISEASES BY SPONTANEOUS REPORTS IN KOREA
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Background and Aims: Many drugs can cause interstitial lung diseases by various mechanisms. However, the epidemiology and causes of drug-induced interstitial lung diseases (DILD) have not been well described yet. This study aimed to assess the characteristics of the subjects with DILD and the causative drugs of DILD cases, which has been reported spontaneously in Korea.

Methods: Cases of DILD were recruited from the spontaneously reported pharmacovigilance data which has been recorded in the Korea Institute of Drug Safety & Risk Management-Korea Adverse Event Reporting System database (KIDS-KAERS database) over recent 10 years (from July 2005 to June 2015). DILD was defined as adverse drug events with WHO-Adverse Reaction Terminology indicative of interstitial lung diseases.

Results: From 767,960 cases of spontaneously reported adverse drug event cases, 445 cases (0.06%) were identified as DILD. Of the subjects with DILD, males were more common than females (65.1% vs. 34.9%). Regarding severity, 315 cases (70.8%) were classified as serious based on WHO criteria. The most common causative drugs were antineoplastic and immunomodulating agents (70.7%), followed by antiinfectives and cardiovascular drugs.

Conclusions: The prevalence of DILD among the spontaneously reported adverse drug event cases in Korea was low. Males were more frequently affected and the majority of cases were induced by antineoplastic immunomodulating agents.

BUBBLE ARTEFACTS ON LUNG_ULTRASOUND ARE ASSOCIATED WITH RADIOLOGICAL HONEYCOMBING
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Background and Aim: Honeycombing is characteristic for the usual interstitial pneumonia pattern on high resolution computed tomography (HRCT). The presence of sub-pleural hyper-echogenicities on lung ultrasound (LUS), which we term “bubble” artefacts, has previously been described in patients with interstitial lung disease (ILD). We hypothesised that these sub-pleural changes on LUS are associated with honeycomb changes on HRCT.

Methods: Lung ultrasound assessment was performed at four predefined regions for each hemithorax in 22 patients with ILD. Two investigators analysed the blinded dynamic clips of LUS to determine the presence of sub-pleural hyper-echogenicities. The corresponding sequential HRCT slices at each region were assessed by two independent investigators for the presence of honeycombing.

Results: Mean time spent for LUS assessment was 16 (standard deviation = 6.4) minutes. Of the 176 areas, 62 (35%) had honeycomb changes on HRCT. There was a significant difference in the total number of sub-pleural hyper-echogenicities in patients with and without honeycomb changes on HRCT (median [interquartile range]: 29 [17-48] vs 19 [8-37], p = 0.01). Using a receiver operating characteristics curve, five sub-pleural hyper-echogenicities was chosen as the cut-off, considered positive for the “bubbles” artefact. For intra-examiner concordant cases, the presence of at least one positive region on LUS had a sensitivity of 86% and specificity of 44% in recognition of a patient with honeycomb changes on HRCT.

Conclusion: “Bubble” artefacts are detected on LUS in patients with ILD and honeycomb changes on HRCT. This method may be used as an adjunct for bedside assessment in patients with ILD.
UNILATERAL UPPER LUNGFIELD PULMONARY FIBROSIS RADIOLOGICALLY CONSISTENT WITH PLEUROPARENCHYMAL FIBROELASTOSIS AFTER THORACOTOMY: A NEW DISEASE ENTITY RELATED TO THORACOTOMY
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Background and Aims: Pleuroparenchymal fibroelastosis (PPFE) is a rare bilateral idiopathic interstitial pneumonia defined by pleural-parenchymal involvement. In clinical practice, we encountered patients of upper-lung field pulmonary fibrosis (Upper-PF), which was radiologically consistent with PPFE, but apparently limited in unilateral lung. The aim of the study was to clarify the clinical characteristics in those patients.

Methods: We examined the medical records of all the consecutive patients from 2012 to 2016, to see whether there were patients having unilateral Upper-PF.

Results: We found 6 patients with unilateral Upper-PF. Most common symptom was dyspnea, and all patients had a low body mass index and a severe restrictive pulmonary impairment. Notably, all patients had a history of thoracotomy for resecting lung or esophageal cancer, and the lesions were limited in the operated side. Dynamic breathing chest MRI showed an impaired thoracic movement in the operated side. Serial chest CT from pre-thoracotomy to first visit was obtained in 5 patients: Before thoracotomy, only an apical cap, defined as wedge- and triangle-shaped opacity with broad pleural contact, was observed in the operated side, but progressed into the lesion in a median of 8.4 years after thoracotomy. After first visit, the unilateral lesion rapidly deteriorated in all patients.

Conclusions: Unilateral Upper-PF had some characteristics in common with PPFE. Because the lesion was limited in the operated side, unilateral upper-PF would be a new disease entity related to thoracotomy. Our results indicate that thoracotomy impairs thoracic movement in the operated side and subsequently triggers unilateral Upper-PF development, especially in patients with apical cap.

GASTROESOPHAGEAL REFLUX IN IDIOPATHIC PULMONARY FIBROSIS: ANALYSIS FROM THE AUSTRALIAN IPF REGISTRY
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1Royal Prince Alfred Hospital, Sydney, Australia, 2University of Sydney, Sydney, Australia, 3The Alfred Hospital, Melbourne, Australia, 4Monash University, Melbourne, Australia, 5The Prince Charles Hospital, Brisbane, Australia, 6Fiona Stanley Hospital, Perth, Australia, 7Royal Adelaide Hospital, Adelaide, Australia, 8University of Tasmania, Hobart, Australia, 9Royal Brisbane and Women’s Hospital, Brisbane, Australia, 10Lung Foundation Australia, Brisbane, Australia, 11John Hunter Hospital, Newcastle, Australia, 12Princess Alexandra Hospital, Brisbane, Australia, and 13University of Technology, Sydney, Australia

Background: Gastroesophageal reflux disease (GORD) is common in patients with Idiopathic Pulmonary Fibrosis (IPF) and chronic micro-aspiration may contribute to its pathogenesis. We sought to investigate the impact of GORD on the Australian IPF Registry (AIPFR) cohort.

Methods: Data collected for the AIPFR include a questionnaire recording comorbidities, medication use, and symptoms scores (cough severity, and a detailed questionnaire for GORD symptoms). The prevalence of patient-reported GORD, GORD medication use and GORD symptoms was assessed, and the relationship of these parameters evaluated against survival.

Results: Of 569 patients enrolled in the AIPFR with complete questionnaires, 230 (40.4%) reported a history of GORD diagnosis. 176/230 (76.5%) of these patients and 117/339 (34.5%) without GORD were receiving GORD treatment. 530/569 (93.1%) patients reported at least one GORD symptom. Patients with GORD had higher GORD symptom scores than those without GORD (median 9.5, p < 0.001). GORD symptom scores were higher in patients on GORD treatment than those not receiving treatment (median 9.5, p < 0.001). Higher GORD symptom scores were independently associated with improved survival (HR 0.96, 95%CI 0.92-0.99; p=0.019) after adjustments for age, gender, smoking and disease severity. Specifically, symptoms of heartburn, bloated stomach and acid taste were associated with improved survival. The presence of cough was also highly predictive of increased mortality (HR 4.42, 95%CI 1.07-18.2; p=0.039). GORD treatment had no relationship with survival.

Conclusion: GORD and GORD medication use is common in IPF. Increased GORD symptoms were associated with better survival. This suggests that symptomatic GORD is important in the pathobiology of IPF.
patients (42%) had a change in diagnosis after ILD MDM. The referring diagnoses were CTD-ILD (24; 73%), idiopathic pulmonary fibrosis (2; 6%), ILD-uncertain (4; 12%) and others (3; 9%). ILD MDM resulted in a consensus diagnosis of 25 (76%) patients with CTD-ILD, 3 (9%) patients with IPAF and 5 (15%) patients with other diagnoses. The commonest CTD was rheumatoid arthritis (9; 30%) with the other diagnoses shown in Table 1.

Eighteen (55%) patients had a change in management after ILD MDM, majority (12; 67%) were a direct result of a change in diagnosis. Five patients (28%) required additional immunomodulation due to ILD progression and in one patient, immunosuppression was reduced as the ILD was deemed to be mild.

Conclusion: ILD MDM allows a more accurate diagnosis of CTD-ILDs with a significant impact on subsequent management.

Table 1. CTD subtypes

<table>
<thead>
<tr>
<th>CTD diagnosis</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Rheumatoid arthritis (RA)</td>
<td>9 (30.0%)</td>
</tr>
<tr>
<td>Systemic sclerosis (SSc)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>Idiopathic inflammatory myositis (IIM)</td>
<td>5 (16.7%)</td>
</tr>
<tr>
<td>Overlap CTDs</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>Sjögren’s syndrome</td>
<td>3 (10.0%)</td>
</tr>
<tr>
<td>Others</td>
<td>2 (6.7%)</td>
</tr>
</tbody>
</table>

The other diagnoses included mixed connective tissue disease (n=1), systemic lupus erythematosus (SLE) (n=1), SSC/SLE (n=1), IIM/RA (n=1), IIM/SLE (n=1).

Results: Patient’s mean (±SD) age was 66 (±11) years with 34 females (52.3%). Forty-three (66%) were non-smokers. Mean (±SD) forced vital capacity (FVC) was 1.75 (±0.64) litres, 64 (±19) percent predicted. The referral diagnoses were ILD-uncertain (22; 33.8%), connective tissue disease (CTD) ILD (16; 24.6%) and idiopathic pulmonary fibrosis (IPF) (13; 20%). ILD MDM resulted in a change of diagnosis in 43 (66%) patients (Table 1). There were 5/13 (38%) patients referred for IPF who had an alternative diagnosis. We also diagnosed an additional 11 patients with IPF.

MDM resulted in a change of management in 46 (71%) patients. This included initiating anti-fibrotics for IPF (n=19, 29%) and initiating immuno-modulation (n=19, 29%) in patients who had chronic hypersensitivity pneumonitis (HP), unclassifiable disease or interstitial pneumonia with autoimmune features (IPAF).

Table 1: Distribution of referral diagnoses and diagnoses after ILD clinic and multi-disciplinary evaluation. Other MDM diagnoses included pleuroparenchymal fibroelastosis (n=2), Lymphangioleiomyomatosis (n=1), radiation fibrosis (n=1), connective tissue disease (CTD-ILD) related obliterative bronchiolitis (n=1), cryptogenic organizing pneumonia (n=1), drug induced ILD (n=1), nodular amyloidosis with CTD-ILD (n=1), pulmonary alveolar proteinosis (n=1), not ILD (n=5).

<table>
<thead>
<tr>
<th>Referral diagnosis, n (%)</th>
<th>Multi-disciplinary diagnosis, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILD-uncertain</td>
<td>22 (33.8%) 0 (0%)</td>
</tr>
<tr>
<td>CTD-ILD</td>
<td>16 (24.6%) 19 (29.2%)</td>
</tr>
<tr>
<td>IPF</td>
<td>13 (20.0%) 19 (29.2%)</td>
</tr>
<tr>
<td>Idiopathic non-specific interstitial pneumonia (NSIP)</td>
<td>7 (10.8%) 0 (0%)</td>
</tr>
<tr>
<td>Others</td>
<td>7 (10.8%) 12 (18.5%)</td>
</tr>
<tr>
<td>Chronic HP</td>
<td>0 (0%) 5 (7.7%)</td>
</tr>
<tr>
<td>Unclassifiable</td>
<td>0 (0%) 7 (10.8%)</td>
</tr>
<tr>
<td>Interstitial pneumonia with autoimmune features (IPAF)</td>
<td>0 (0%) 3 (4.6%)</td>
</tr>
</tbody>
</table>

Conclusion: The ILD service has significant impact in diagnosis and management of ILDs in this newly established unit. It allows more precise subtyping of various ILDs, particularly IPF, where they can benefit from anti-fibrotics.

Respiratory Infections (non-tuberculosis) 1

DO WE NEED RESPIRATORY INTENSIVE CARE UNIT?

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Background and Aims: Respiratory failure is one complication of pneumonia that needs intensive care. We tried to identify the amount of pneumonia with respiratory failure who admit the intensive care unit in Dr. Moewardi General Hospital Surakarta at 2014-2016 with the comorbid factors that affect it.

Methods: A retrospective cohort study during the period of January 2014 to December 2016 in Dr. Moewardi General Hospital Surakarta. Subjects were patients diagnosed pneumonia with respiratory failure.
Statistical descriptive analysis using frequency and percentage, chi-square test to determine the comorbid factors for the outcome.

Results: The amount of pneumonia patient with respiratory failure in non intensive care unit at Dr. Moewardi General Hospital is larger than in the intensive care unit. There are a significant result (p < 0.05) between the two outcome and the comorbid factor include sepsis and sputum culture.

There are significant result (p < 0.05) between type of microorganism, heart disease and sepsis affect patient’s length of stay. Patient with length of stay more than 10 days, has an increasing mortality rate.

Conclusions: Comorbid factors in pneumonia patient with respiratory failure has important role for the patient outcome, a respiratory intensive care unit is needed.

Background and Aims: Syndecan-4 is a transmembrane heparan sulfate proteoglycan which is expressed in a variety of cells such as epithelial cells and macrophages, and its heparan sulfate glycosaminoglycan side chains have been reported to bind to several proteins exhibiting various biological roles. In our previous study, we found that syndecan-4 limits the extent of pulmonary inflammation and lung injury in murine LPS-induced lung inflammation model, suggesting the critical role of syndecan-4 on bacterial lung inflammation. However, the role of syndecan-4 in viral lung infection has not been clarified. The goal of this study was to determine if syndecan-4 plays critical roles in viral lung inflammation.

Methods: To evaluate the role of syndecan-4 in viral lung inflammation, we used polyinosine-polycytidylic acid (poly[I:C]), a viral double-stranded RNA surrogate in this study.

At first, BEAS-2B, human bronchial epithelial cells were stimulated with poly[I:C], and the effect of syndecan-4 knock-down by siRNA on mRNA expression of inflammatory mediators was evaluated. Next, wild-type and syndecan-4 deficient mice were injected with poly[I:C] intratracheally, and BAL fluid findings and mRNA expression of inflammatory mediators in lung tissues were compared between two groups.

Results: In BEAS-2B bronchial epithelial cells, mRNA expression of IFN-β and ICAM-1 after poly[I:C] stimulation was significantly enhanced by syndecan-4 knock-down. In syndecan-4 deficient mice, more neutrophils and lymphocytes in BAL fluid and higher mRNA expression of IFN-β, IL-6, MCP-1 and ICAM-1 were found compared to wild type mice after poly[I:C] injection.

Conclusions: Syndecan-4 deficiency exaggerates viral lung inflammation.

Background and Aims: Inflammatory lung disease is a cluster of entities including various post inflammatory sequelae like, Aspergilloma/bronchectasis/hydatid predominantly affecting the younger population and are the most commonly referred cases for thoracic surgery in our institution. These patients have obliterated pleural space and dense adhesions making surgery an uphill task. Most of these patients have failed medical, interventional and endoscopic treatment and surgery is usually the last but the best available remedy. Aim-To share the disease spectrum and surgical outcome in inflammatory lung disease.

Methods: This is retrospective analysis of prospectively collected data. 87 patients undergoing thoracic surgeries for inflammatory lung disease were included in the study. Routine haematological investigations, Chest X-ray, CT Chest, PFT were performed on all patients. These were supplemented by bronchoscopy, 6 minute walk test, CPET and V/Q scan whenever indicated. Open approach was used in 72(82%) and VATS 15(18%). The operating time and blood loss were noted in all patients, the post operative morbidity operative rates and readmissions were noted

Results: 60 of the 87 patients were male. Age:16-61 years median (29years). Pulmonary Aspergilloma was the commonest pathology (36%). The commonest symptom was haemoptysis(60%) followed by cough(19.5%),54(62%) patients received antitubercular treatment for proven or suspected pulmonary tuberculosis. 42(48%) patients had an additional pulmonary pathology of which, pulmonary parenchymal fibrosis and volume loss were predominant. Surgical procedures performed were lobectomy(39), wedge resection(14), decortication(13) pneumonectomy (8). Median operative time-195minutes(range 95-480minutes). Median intra operative blood loss-600ml(range 100-4900ml) and the median post operative hospital stay-6days. Post operative complications were encountered in 37 patients(42%), of which 11(29.7%) had prolonged air leak. Pneumothorax 8(21.6%), empyema-2(5.4%), bpf-4(10.8%). There were 10(11.3%) reoperations and 7(8%) readmissions. Mortality-0%

Surgical management in inflammatory lung diseases poses a distinct surgical challenge. Our experience suggests, that surgery remains an integral part of the armamentarium for management of inflammatory lung disease it can be carried out with low morbidity

Background and Aims: Rhinosporidiosis is a chronic granulomatous infectious disease caused by mesomycetozoea Rhinosporidium seeberi. This highly recurrent polypoid lesion commonly affects nose and nasopharynx. Though it may involve different body parts, involvement of tracheobronchial tree is very rare, and poses challenge for diagnosis and management. We are presenting a case of tracheobronchial rhinosporidiosis, who developed acute respiratory distress and prompt intervention salvaged life.

Methods: A 30-year-old male of rural background presented to primary care physician with dry cough for 6 months and was treated as a case of asthma. Four months later, he developed hemoptysis and breathlessness. He was seen by a pulmonologist and fiberoptic bronchoscopy (FOB) was done. Histopathology revealed rhinosporidiosis. He was referred to our institute. He is a farmer and had habit of dipping in pond water to catch fish. He gave history of surgery of nasal mass two times eight and five years back. On admission, he was dyspnoeic with absence of breath sound in right lung and poor air entry in left lung. Next day he developed sudden respiratory distress with fall of SpO2 below 35%.
Emergency rigid bronchoscopy was done under GA. A mulberry like mass was seen completely occluding the lower trachea with bleeding. Mass was removed as much as possible by forceps and gentle suction. Bleeding was secured. Post-operative period was uneventful.

Results: Follow-up FOB one week later revealed complete removal of tracheal mass and some residual lesion in proximal right principal bronchus and left supraglottic region. Dapsone was started. Electrocautery/ APC was planned to remove residual disease.

Conclusions: Rhinosporidiosis in tracheobronchial tree may be secondary to implantation of spores from previous surgery for nasal/hospharyngeal rhinosporidiosis. Delay in the diagnosis may lead to life threatening airway obstruction as occurred in our case. Prompt bronchoscopic intervention can save life.

AP295
UNUSUAL PRESENTATION OF TRICHIOMONIASIS
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2Department of Microbiology, Al-Amiri Hospital, Kuwait, Kuwait

Introduction: We describe a case of pulmonary infection with marked eosinophilia due to Trichomonas species. Its rare pulmonary presentation associated with persistent eosinophilia is the first described case in Kuwait.

Case Presentation: A 72 years old Indian male presented with 10-day history of persistent dry cough, with anorexia and chills/rigors.

Initial investigations showed leukocytosis with predominant eosinophils. Chest imaging showed bilateral upper lobar consolidations. After failing empirical antibiotic regimen a bronchoscopic evaluation lavage from the upper lobes revealed eosinophilic predominance. The examination of fresh wet smear from the lavage showed multiple mobile trophozoites and the diagnosis of Trichomonas species is made. Further examination of fresh wet smear from the lavage showed multiple mobile trophozoites and the diagnosis of Trichomonas tenax. The rest of lavage testing was otherwise unremarkable.

Therefore, the antibiotic regimen was modified by adding to metronidazole at a daily divided dose of 1500 mg for a total of fourteen days, with excellent clinical recovery.

Discussion: Trichomonas pulmonary disease is documented in the literature since the 19th century, affecting mainly patients with underlying medical diseases such as malignancy or lung disease. It is implicated in different types of pulmonary diseases, but the most common form is pleural effusion or empyema. Another form of presentation, which is very rare, is pulmonary hypersensitivity. Typically, the species of T. tenax has been involved in pulmonary infections, but other species were rarely implicated.

Conclusion: Pulmonary Trichomoniasis is a rare condition, although it appears to be underestimated. Clinicians and microbiologists need to be aware of this condition. Including it in the differential diagnosis of pulmonary infections and examining the respiratory specimens under microscope before fixation would probably unveil its true incidence, epidemiology and role in pulmonary infections.

AP296
A RARE CASE OF DISSEMINATED HYDATIDOSIS
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Background and Aims: Hydatidosis (Echinococcosis) is a parasitic infestation of humans by Echinococcus granulosus. The definitive hosts are dogs and humans are accidental intermediate hosts. We report a case of disseminated Hydatidosis involving lung, liver, mediastinum, peritoneum and spleen.

Methods: A 60 year old farmer presented with complaints of breathlessness for one month and abdominal distension for two weeks. Clinical examination revealed diminished breath sound in right lower hemithorax and mild hepatomegaly. Chest x ray showed a well defined oval shaped homogenous mass in right lower zone. Ultrasonogram abdomen showed multiple well demarcated cystic lesions with daughter cysts in right lobe of liver, peritoneum and spleen. CT chest and abdomen revealed multiple large cystic lesions with numerous daughter cysts in right lung, mediastinum, peritoneum, liver and spleen with calcifications. On detailed history evaluation, he told that he was having two dogs on his house for past three years.

Results: Hydatid disease is a parasitic infestation of humans by Echinococcus granulosus known as dog tape worm and rarely by E.multilocularis. Liver(75%) and lung (15%) are the common organs affected. Even though spleen is the third most common site of involvement, the incidence is 0.9% to 8%. Peritoneal involvement is 13% among abdominal hydatidosis. Clinical presentation depends on organs affected, size and number of the cysts, organ compression, blood flow obstruction, as well as rupture of the cyst. Diagnosis is by serology and radiological imaging. Radiological findings range from clear cystic lesions to solid masses.

Conclusion: The treatment of choice is surgical removal of the cysts combined with medical treatment using albendazole or mebendazole before and after surgery. If there is multi-organ involvement, surgery is not advisable.
Results: 14/23 (61%) cases were performed biological examination. Among them, 10/14 were by ultrasound-guiding needle aspiration, 2/14 were by bronchoscope, 2/14 were by percutaneous puncture aspiration. Culture of collected sample were positive in 11/14, rest were negative. Most of the detected bacteria are Streptococcus of the oral cavity and anaerobic bacteria. 9/23 (39%) cases were treated without sample collection. Common antibiotics used were Tazobactam/Piperacillin or Sulbac- tam/Ampicillin, followed by Amoxicillin/Clavulanate. There were no cases that antibiotics were changed by result of bacteriologic examination. One case of Nocardiosis was included, which bacteriological examination was useful and necessary for further treatment.

Conclusions: Bacteriological examination was expected to be useful and necessary for diagnosis and treatment of lung abscess, but it did not affect antibiotic selection in many cases. Moreover, without invasive examination such as needle aspiration, it seems possible to treat with empirical choice of antibiotics. However, as experiencing atypical case such as Nocardiosis, it still seems to be better to perform biological examination as much as possible for treating lung abscesses appropriately.

MAKING A CONNECTION: BRONCHOPLEURAL FISTULA AS A COMPLICATION OF HEPATIC ABDCESS
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Background and Aims: Secondary infection is a common complication of amebic liver abscess. Rupture of the abscess occur into the pleura, lung, pericardium or peritoneum. Abscesses which are located in the dome of the liver may rupture through the diaphragm and cause empyema, pleural effusion, bronchopleural fistula (4–7%) according to Sayek et al.

Methods: A 56-year old male presented in our center due to productive cough and difficulty of breathing. A month prior to admission, he had a generalized body weakness, upon work up, a hepatic mass was noted on abdominal ultrasound. He was admitted into another institution and underwent laparoscopic hepatectomy with right hemihepatectomy. Intraoperative finding was 8 x 6 cm mass at segment 7 extending to segment 8. Histopathology revealed marked acute and chronic inflammation with granulation content with organizing abscess. Patient was discharged stable with antibiotics. Two weeks prior to admission, patient sought consult in our institution due cough with rusty sputum and difficulty of breathing. CXR showed haziness in the right lower lobe and a suspicious air-fluid level. He was treated as a case of pneumonia and was started on antibiotic. A chest CT scan with contrast revealed a lung abscess and pleural empyema with bronchopleural fistula. Patient was referred to TCVS for further evaluation and management. However, patient refused further intervention.

Results: Our patient presented with cough which is a common symptom of bronchopleural fistula (BPF). One of the radiologic features suggestive of BPF include present air fluid level and a CT finding of fistulous communication which are present in our patient.

Patients who present with a BPF as a complication are initially managed medically such as drainage and reduction of the pleural space, antibiotics and nutritional supplementation.

Conclusions: BPF is associated with significant morbidity and mortality and treatment should be instituted as early as possible.

A CASE OF EMPYEMA CAUSED BY EDWARDSIlla TArDA
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Background: Edwardsiella tarda (E. tarda) is an infection that usually affects amphibious animals and is rarely found in humans. The most frequently reported manifestation of infection caused by E. tarda in humans is gastrointestinal disease although it has been reported to cause septicemia, meningitis and peritonitis. However, there have been limited reports of pleural empyema.

Case Report: An 80-year-old man who was diagnosed with bile duct cancer in 2012 underwent pancreatoduodenectomy at a different institution. The patient then visited our institution in May 2017, complaining of fever and fatigue.

On chest X-ray, a right pleural effusion was detected. Microscopic examination of the stained pleural fluid revealed neutrophils with Gram-negative rods, and E.tarda was cultured from the pleural fluid. These findings were consistent with empyema due to E.tarda.

We treated the patient with 4.5g of Piperacillin/Tazobactam intravenously 8 hours per day for 1 month, and thoracic drainage tube. His clinical course was benign and the patient recovered.

We believe the reason this patient was infected with E.tarda might be because of his weakened infection caused by his pancreatoduodenectomy and uncontrolled diabetes.

We describe this case in detail in light of the available literature.

THE ARGUMENT FOR A BRONCHIECTASIS SPECIFIC AR-DRG: ANALYSIS OF HOSPITAL DISCHARGE DATA (2012-2016) FOR PATIENTS REGISTERED TO THE AUSTRALIAN BRONCHIECTASIS REGISTRY
PITCHAYA KINGKAM1, SIMONE VISSER2, JAMES BROWN1, STEPHEN WOODCOCK1, TIM BAIRD3, DAN JACKSON3, LUCY MORGAN3
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Background and Aims: The Australian Refined Diagnosis Related Groups (AR-DRG) classification system classifies hospital inpatients into groups with similar case complexity and costs of care. The assigned AR-DRG contributes to determining funding for that episode of patient care. There is no bronchiectasis-specific DRG. Patients admitted with an exacerbation are variably assigned to other respiratory DRGs. DRG “outliers” are identified by discrepant length of stay (LOS) and/or cost and can attract additional funding. This project explores whether LOS during respiratory-related admissions for patients with a known diagnosis of bronchiectasis is consistent with the expected LOS for the assigned DRG.

Methods: Retrospective review of admissions, 2012-2016 at 3 centres (Concord Hospital, Royal Prince Alfred Hospital and Sydney Children’s Hospital). Single-day and/or non-respiratory admissions were excluded. Linear regression was used to establish the relationship...
between LOS of each admitted patient episode of care and the national average LOS for assigned DRG class.

**Results:** 257 patients with bronchiectasis were registered. 76 patients had 154 respiratory-related admissions of [32] days within the 5 year period. The mean LOS was 8.7 (± 8.48) days compared with the AR-DRG assigned expected mean LOS of 5.6 (± 4.15) days and an outlier classification mean of 15.5 (±10.24) days. The most frequent primary diagnosis was bronchitis and the most frequent DRG was COPD. Regression analysis reveals actual LOS for bronchiectasis patients is shifted significantly higher than expected national average LOS, but only 24 episodes would qualify for additional funding as system outliers.

**Conclusions:** The current AR-DRG classification underestimates the LOS. The outlier classification does not correct for the majority of episodes and therefore the costs for acute hospital admissions due to bronchiectasis are underestimated. There is an argument for the addition of a bronchiectasis-specific DRG.

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**THE ASSOCIATION WITH NON-TUBERCULOUS MYCOBACTERIA AND PULMONARY FUNCTION DECLINE IN PATIENTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS**

MENG-HENG HSIEH¹, CHEN-YU WANG²

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**Background and Aims:** Patients with cystic fibrosis are more susceptible to non-tuberculous mycobacteria (NTM). However, the role of NTM in patients with non-cystic fibrosis (CF) bronchiectasis remain unknown.

This study aimed to investigate the characteristics and clinical implication of NTM infection in non-CF bronchiectasis patients.

**Methods:** We retrospectively reviewed patients with high-resolution computed tomography (HRCT) diagnosed non-CF bronchiectasis from Jan 2011 to March 2014. Clinical presentation, pulmonary function, radiologic studies and a least 3 sputum samples cultured for mycobacteria were recorded. Every patient was followed at least 3 years.

**Results:** A total 83 patients were included for analysis. Thirty-one patients (37.3%) had NTM isolates and 52 (62.7%) patients had negative isolates. Mycobacterium avium complex (MAC) was the most common isolated pathogen (38.7%). None of them received anti-NTM medication. Patients with NTM isolates had a greater decline in both forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) than those with no isolates (-0.22±0.37 vs. -0.07±0.43L; -0.21±0.30 vs. -0.07±0.28L). Patients with NTM isolates also had more frequent exacerbations, emergency department visit and hospitalization than those with no isolates (4.68±1.13 vs. 0.80±0.21, p =0.0002; 3.61±0.93 vs. 0.46±0.17, p = 0.0002; 4.60±1.11 vs. 1.55±0.32, p = 0.0017). The total mortality rate was 8.4% without difference between groups.

**Conclusions:** NTM may have a role on pulmonary function decline in patients with non-CF bronchiectasis.

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**EFFECTS OF DAILY THREE-DRUG COMBINATION THERAPY FOR MILD NODULAR/BRONCHIECTATIC DISEASE ASSOCIATED WITH MYCOBACTERIUM AVIUM COMPLEX LUNG DISEASE: A LONG TERM PROGNOSIS**

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**Background and Aims:** Intermittent three-times-weekly treatment with clarithromycin or azithromycin, ethambutol, and rifampin is recommended in nodular/bronchiectatic disease associated with mycobacterium avium complex (MAC) lung disease. Daily administration is recommended as a more intensive treatment for patients with fibrocavitary disease or severe nodular/bronchiectatic disease. While, daily treatment is more common regardless of the severity of MAC lung disease in Japan. Here we report the long term efficacy of a daily treatment in patients with mild nodular/bronchiectatic MAC lung disease.

**Methods:** We retrospectively investigated 34 patients with nodular/bronchiectatic MAC lung disease whose treatment has been initiated between 2006 to 2011. Median age was 61 (35-77) yo, and 25 (73.5%) patients were female. Azithromycin was not used because it is unapproved for MAC disease in Japan. Data were updated on June 16, 2017. Median follow up time was 92.3 (10.5-131.0) months.

**Results:** The median dose of clarithromycin was 800 (400-800) mg/day, while the median dose of ethambutol was 500 (500-750) mg/day. The median dose of rifampin was 450 (300-450) mg/day, and the median duration of treatment was 18.5 (6.1-131.0) months. Radiological improvement was achieved in 29 (85.3%) patients. Conversion of sputum culture was achieved in 24 (70.6%) patients; however, 5 (14.7%) patients continued their treatment for a long time because of disease instability. Unfortunately, 16 (47.1%) patients became clinically or radiologically worsened after treatment in median duration of 17.9 (3.0-67.0) months, and 12 (35.3%) patients restarted treatment. Only 13 (38.2%) patients achieved long time disease stability.

**Conclusions:** The response rate for daily treatment of nodular/bronchiectatic disease was similar to rates seen in previous reports; however, the high rate of recurrence after treatment suggested that the treatment was insufficient even in mild nodular/bronchiectatic disease. A long term maintenance treatment would be needed in some patients with mild MAC lung disease.

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**ASSOCIATION BETWEEN LONG-TERM ERYTHROMYCIN MONOTHERAPY FOR MYCOBACTERIUM AVIUM COMPLEX AND CROSS-RESISTANCE TO CLARITHROMYCIN**

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**Background and Aim:** Multidrug chemotherapy is the standard treatment for moderate and severe Mycobacterium avium complex pulmonary disease (MAC-PD). Standard chemotherapy sometimes causes adverse effects and requires a long treatment period. Therefore, a more tolerable treatment is needed as both initial treatment for mild MAC-PD and subsequent standard chemotherapy. Macrolides show anti-inflammatory effects, and low-dose long-term erythromycin monotherapy has been reported to potentially suppress the exacerbation of MAC-PD with less toxicity. Although clarithromycin is a key drug for MAC, it is unclear whether erythromycin monotherapy induces cross-resistance to clarithromycin.

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Methods: A retrospective study was conducted on patients who met the microbiological diagnostic criteria for MAC-PD of the American Thoracic Society/Infectious Diseases Society of America of 2007 and had received erythromycin monotherapy for >6 months. This study was conducted between July 2008 and April 2017 at National Hospital Organization Toneyama National Hospital based on available data. We reviewed the clarithromycin minimum inhibitory concentration (MIC) of MAC tested twice: before and after initiating erythromycin monotherapy.

Results: A total of 110 MAC-PD patients received erythromycin monotherapy for more than 6 months, and 41 patients were tested twice for drug susceptibility to clarithromycin for MAC. Additionally, 19 patients received erythromycin monotherapy as initial treatment. Thirty-three and 5 patients showed susceptibility and resistance, respectively, to clarithromycin. Further prospective studies will be needed to verify this finding and to assess the efficacy of subsequent standard chemotherapy after erythromycin monotherapy.

Conclusion: This retrospective study shows that low-dose long-term erythromycin monotherapy for MAC-PD does not induce cross-resistance to clarithromycin. Further prospective studies will be needed to verify this finding and to assess the efficacy of subsequent standard chemotherapy after erythromycin monotherapy.

Background and Aim: Respiratory viruses constitute a major cause of acute respiratory illness worldwide. There is limited data on the prevalence and outcomes of respiratory viral illnesses in adults.

Methods: Patients aged ≥14 years with confirmed respiratory viral illness by multiplex real-time PCR at SQUH, reviewed retrospectively from September 2014 to August 2015. Data collection included demographics, clinical findings, management and outcome.

Results: Out of 1393 respiratory samples tested, 16.6% (231/1393) were positive. Out of 231 confirmed cases, 52.8% (122/231) were male. The median age was 40 years. 82.7% (191/231) patients had comorbidities (Table 1, Figure 1).

Table 1. Patient Characteristics

| Number of Cases | 231
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age</td>
<td>40 years</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>47.1% (n=109)</td>
</tr>
<tr>
<td>Male</td>
<td>52.8% (n=122)</td>
</tr>
<tr>
<td>Hospital Encounter</td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td>30.7% (n=71)</td>
</tr>
<tr>
<td>Inpatients</td>
<td>69.3% (n=160)</td>
</tr>
<tr>
<td>Median hospital stay of inpatients</td>
<td>7 Days</td>
</tr>
<tr>
<td>Co-morbid</td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>26.8% (n=62)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>19.9% (n=46)</td>
</tr>
<tr>
<td>Sickle Cell Disease</td>
<td>14.7% (n=34)</td>
</tr>
<tr>
<td>Chronic Renal Disease</td>
<td>12.1% (n=28)</td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td>11.7% (n=27)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>36.4% (n=84)</td>
</tr>
<tr>
<td>No comorbid</td>
<td>17.3% (n=40)</td>
</tr>
<tr>
<td>Site of Viral Specimen</td>
<td></td>
</tr>
<tr>
<td>Throat/Nasal swab</td>
<td>89.6% (n=207)</td>
</tr>
<tr>
<td>Sputum</td>
<td>6.9% (n=16)</td>
</tr>
<tr>
<td>Bronchoalveolar Lavage (BAL)</td>
<td>3.5% (n=8)</td>
</tr>
<tr>
<td>Influenza Vaccination</td>
<td></td>
</tr>
<tr>
<td>Received in last year</td>
<td>11.7% (n=27)</td>
</tr>
</tbody>
</table>
Among the 231 cases, we have identified 62 influenza A (of which 41 were H1N1), 61 rhinoviruses, 53 adenoviruses, 40 respiratory syncytial viruses (RSV), 22 influenza B, 8 enteroviruses, and 5 parainfluenza viruses. Virus dual-infection was seen in 17 cases, more with rhinoviruses (10/17). There were two viruses activity peaks, first from September to November attributed mainly to rhinoviruses, RSV, and influenza A. Second peak was seen from February to May, mainly due to influenza B, adenoviruses (Figure 2).

Cough was the main symptom (94%), followed by rhinorrhea (53.7%), and fever (35.5%) (Figure 3).

Pulmonary infiltrates were found on chest radiographs of 41.6% (96/231) patients (Figure 4).

77.5% (179/231) patients received oseltamivir (of whom 33% [77/231] had confirmed influenza) and 88.3% (204/231) patients received antibiotics; of whom 5.6% (13/231) had bacterial co-infection on admission. 70.3% (164/231) patients received empirical antibiotics without confirmed bacterial infection and 11.7% (27/231) patients received antibiotics for nosocomial infections. All-cause mortality was 9.1% (21/231) whereas absolute mortality related to viral respiratory illness was 2.2% (5/231); 3 patients infected with influenza A H1N1 and 2 with adenoviruses.

Conclusion: Marked seasonal variation was noted among respiratory viral infections. Most patients had pre-existing comorbidities. Majority of patients received empirical antibiotics for viral illnesses.

COMPARISON OF THE PATIENTS AFFECTED WITH RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA VIRUS: A SINGLE-CENTER PROSPECTIVE OBSERVATIONAL STUDY IN JAPAN

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Background and Aims: It has been reported that influenza virus (FLU) was a major cause of hospitalized adults with respiratory infections, however, the epidemiological data regarding with respiratory syncytial virus (RSV) in Japanese adults was scarcely reported until today due to the lack of commercially available rapid tests with high sensitivity. Our aim is to identify the RSV and FLU infection in the admitted adult patients using by a PCR-based method and characterized them.

Methods: A prospective observational cohort study was conducted in Kyorin University Hospital, Japan from 2012 to 2015. After an informed consent was obtained, respiratory samples were collected from hospitalized adult patients with respiratory distress by oro/nasopharyngeal swab or bronchoalveolar lavage to identify RSV and FLU by a PCR-based method. Enrolled patients' clinical data included age, sex, comorbid illnesses, and mortality.

Results: Among 429 hospitalized patients, 28 viruses (RSV A n=2, RSV B n=9, RSV unknown n=1, FLU N3N2 n=13, FLU H1N1 n=3) were detected. RSV infected patients (n=12, 2.8%) were characterized as follows, male 5 (42%), age 72.5 ± 12.8 years old, death 1 (8.3%), respiratory failure 11 (91.7%), ventilator use 2 (16.7%), pneumonia 3 (25%) and asthma/COPD exacerbation 9 (75%).

While, FLU infected patients (n=16, 3.7%) were as follows, male 6 (38%), age 70.3 ± 11.1 years old, death 1 (6.3%), respiratory failure 15 (93.8%), ventilator use 1 (6.3%), pneumonia 4 (25%) and asthma/COPD exacerbation 8 (50%). There was no significant difference between RSV and FLU patients in terms of age, sex, and respiratory failure.

Conclusions: Frequency of respiratory failure caused by RSV or FLU was comparable in admitted patients in our tertiary referral center, and almost all the infected patients were aged in both groups.

PULMONARY HISTOPLASMOSIS IN AN ASYMPTOMATIC AND IMMUNOCOMPETENT FILIPINO

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Background and Aim: Histoplasmosis, despite being a fungal disease occurring throughout the warm and humid areas of the world, is rarely reported in the Philippines and other South East Asian countries. There are only 10 reported cases of histoplasmosis in the Philippines, most of which are the progressive disseminated form and with immunocompromising comorbidities.
Primarily, this case report describes the pathophysiologic, clinical, radiographic and histopathologic features of pulmonary histoplasmosis in an immunocompetent adult. Secondly, this study reviews the documented cases of pulmonary histoplasmosis in the Philippines. Lastly, the paper tackles the approaches to pulmonary histoplasmosis, in which itraconazole therapy and video-assisted thoracoscopic surgery (VATS) played a pivotal role in this case.

**Case Report:** This is a case of a 47 year-old male who sought consult due to an incidental radiologic finding of right middle lobe mass during his annual check-up. The patient is asymptomatic, has no known comorbidities and is a non-smoker. As a photographer, he frequently crawled on grass fields while taking pictures in United States, Japan and Hong Kong few years before consult. Blood chemistries are normal. Rapid diagnostic test for pulmonary tuberculosis (e.g., Xpert MTB/RIF) and Human Immunodeficiency Virus antigen screening test are negative. The patient underwent VATS, wedge resection of the right middle lobe mass.

Histopathologic and immunohistochemical studies of the right middle lobe mass are consistent with *Histoplasma capsulatum*. Postoperatively, he was maintained on itraconazole 100 mg/capsule 2 capsules twice a day for 2 months, and was followed up regularly with noted clinical and radiographic improvement.

**Conclusion:** In conclusion, this case highlights the sporadic endemicity of pulmonary histoplasmosis in tropical and subtropical-ridden South East Asian countries such as the Philippines. Missing out this insidious disease in healthy patients with chest radiographic lesions mimicking tuberculosis and neoplasm may, in the long run, lead to poor outcomes.

**VARIABILITY OF VORICONAZOLE SERUM CONCENTRATIONS IN PATIENTS WITH CHRONIC PULMONARY ASPERGILLOSIS**

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**Background and Aim:** Voriconazole is the first line drug for the treatment of chronic pulmonary aspergillosis (CPA). Therapeutic drug monitoring is recommended by the IDSA guidelines for its clinical use. We often experience high variability of voriconazole concentrations, which cannot be explained by known factors. We examined the variability of voriconazole concentrations and investigated the factors associated with the variability.

**Methods:** A retrospective chart review study was performed for the patients who received voriconazole treatment for CPA and had voriconazole trough concentration measurement more than once with the same dosage between April 2014 and August 2016.

**Results:** A total of 218 samples from 69 patients were obtained in the study. The median age was 71 years. Pulmonary tuberculosis and nontuberculous mycobacteriosis were the most common underlying diseases. The median voriconazole trough concentration was 1.68μg/ml (range, 0.3 to 14.4). The median variability of voriconazole concentration with the same dose in a single patient was 1.83μg/ml (range, 0 to 10.94). Twelve patients revealed 3μg/ml or larger difference (17%). The voriconazole concentration exhibited a positive correlation with C-reactive protein (P=0.0001).

**Conclusion:** Voriconazole concentrations varied in correlation with CRP, suggesting inflammation may decrease voriconazole clearance. Therefore, multiple measurements of trough concentrations are recommended even with the same dose.

**LIFE THREATENING HEMOPTYSIS: A CASE OF CHRONIC CAVITARY PULMONARY TUBERCULOSIS COMPLICATED WITH ASPERGILLOMA**

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**Background:** Pulmonary Aspergilloma is a rare disease, usually presenting as secondary invasion of preexisting lung cavity. When a pre-existing lung cavity is colonized by Aspergillus fumigatus it forms a fungal ball known as Pulmonary Aspergilloma.

**Case Study:** This is a case of a 23 year-old female with past history of tuberculosis presented productive cough, respiratory distress, generalized body weakness and hemoptysis for two years. On initial investigation CXR revealed Cavitory PTB in the left upper lobe and Sputum AFB showed Positive. She was managed as case of Pulmonary Tuberculosis and was given Anti-Koch’s medication for 6 months. However there was recurrence of productive cough and hemoptysis. On subsequent investigation, repeat CXR revealed fibro-nodular density in the left upper lobe. Repeat Sputum AFB showed negative. Chest CT scan with contrast showed a radiological findings of a ball-like structure within preexisting lung cavity on the left upper lobe and a consideration of PTB versus Aspergilloma was made.

**Results:** On admission, CXR done revealed bilateral Koch’s infection with associated volume loss in the left; compensatory hyperaeration, left mid to lower and right lung; upper thoracic dextroscoliosis. Chest CT scan showed Chronic PTB with cicatrical volume loss in the left and bronchecstatic changes. A cavity is identified in the left upper lobe with mixed densities within, possibly representing an Aspergilloma (Figure 1). Lung scanning and Pulmonary Function test were done to assess suitability for lung resection. Following the preoperative evaluation for lung resection, she underwent Pneumonectomy, Left which was tolerated well. Histopathologic findings was fungal hyphae consistent with Aspergillus specie (Figure 2).

**Conclusion:** Surgical treatment of Pulmonary Aspergilloma is the most effective treatment; surgical resection of the cavity and removal of the fungus ball is the treatment of choice when indicated and in recurrent hemoptysis, if their pulmonary function is sufficient to allow surgery.

![Figure 1](image-url)
AN INTRIGUING CASE OF BONE MARROW TUBERCULOSIS
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Introduction: Tuberculosis is well known to be a great masquerader of various diseases and there are instances whereby it may cause hematological abnormalities especially with marrow involvement.

Methods: Case Report: We present a case of 81 year old Malay Male, known case of type II diabetes mellitus presented with intermittent low grade fever, loss of appetite, loss of weight and non productive cough for 2 months. Systemic examinations were unremarkable.

Blood investigation revealed pancytopenia (WBC -2.94 x10^3 u/L, Hb-7.7g/l MCV -71.4f, MCH 23.8pg, platelet 60x10^3u/l) with raised globulin and low albumin level. Both corrected calcium (2.63mmoll) and ESR (140) were elevated. His folate level was low (6.7 nmoll) with normal Vitamin B12 and iron level.

Chest X-ray showed a nodule on the left mid zone. Peripheral blood film revealed presence of target cell, tear drop cell, ellipocytes with pencil cells. Viral screenings, sputum for AFB, BFMP and leptospira serology were all negative.

Patient was treated for folate deficiency and provisional diagnosis of Myelodysplastic syndrome or lymphoproliferative disorders were given. BMAT reported as epithelioid granulomatous lesion with early caseation changes. However there were no acid fast bacilli seen on Ziehl Nelson stain. Thus, sputum for MTB culture and sensitivity was sent and it was negative. His folate level was low (6.7 nmoll) with normal Vitamin B12 and iron level.

He was then referred to pulmonology team and treated as disseminated tuberculosis. However he succumbed to hospital acquired pneumonia while receiving anti tuberculosis medication in the ward.

Conclusion: This case illustrates the importance of high index suspicion towards tuberculosis with hematological manifestation. Prompt treatment is utmost important and failure to diagnose can be fatal.

ANALYSIS OF THE IMPACT OF GASTRECTOMY ON MYCOBACTERIAL LUNG DISEASES
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Background and Aims: Mycobacterial infections are a global issue and that has not yet been resolved. The prevalence of nontuberculous mycobacteria (NTM) lung disease is increasing in many parts of the world. Gastrectomy has previously been reported to increase the risk of mycobacterial infections. The risk factors for NTM pulmonary disease have not been clearly elucidated, and no clear causal relationship has been found between gastrectomy and NTM in previous studies. The present study aimed to examine the effect of gastrectomy on NTM lung diseases retrospectively.

Methods: New cases of TB and NTM lung diseases were examined among patients who had undergone gastrectomy due to stomach cancer between January 1, 2009 and December 31, 2016 at a tertiary referral hospital in Busan, South Korea. The clinical history and information of eligible patients were retrospectively reviewed.

Results: This study included a total of 4,686 patients. New cases of TB and NTM lung disease were found in 92 (95%) and 5 (5%) cases, respectively. In a total of 5 NTM cases, 4 cases had Mycobacterium avium complex as the pathogenic organism and 1 case had Mycobacterium abscessus. Annualized crude incidence rates for TB, NTM lung disease were 348/100,000, 27/100,000, respectively. Standardized incidence rate of TB was higher in patients who undergone gastrectomy due to stomach cancer.

Conclusions: Gastrectomy seems to be a risk factor for increasing TB incidence but it does not appear to be a risk factor for NTM lung diseases. However, NTM lung disease should be considered as a differential diagnosis of TB in patients who undergone gastrectomy due to stomach cancer.

TUBERCULOUS EMPYEMA IN AN ADULT FILIPINO: A DIAGNOSTIC DILEMMA
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Background and Aims: Empyema thoracis remains a major problem in developing countries such as the Philippines. There is often a diagnostic challenge in differentiating tuberculous from non-tuberculous empyema.

Case Report: A 25-year old Filipino male with bicuspid aortic valve presented with chest discomfort associated with productive cough and undocumented fever. Physical examination revealed dental carries and decreased breath sounds on right mid to basal lung field on chest auscultation. Chest x-ray revealed an inhomogeneous opacity on the right base ascribed to effusion with concomitant pneumonia. Empyema was inserted on the right, however, drainage was minimal. Pleural fluid was foul-smelling and foul-smelling fluid was aspirated. Antibiotics were started and chest tube was inserted on the right, however, drainage was minimal. Pleural fluid culture did not grow any microorganism. He continued to have febrile episodes despite adequate antibiotics. Chest CT-scan showed ill-defined densities representing abscess with loculated effusion. VATS with decorticaiton was done. Abscess collected stained positive for acid-fast bacilli. He was started with anti-Koch's treatment.
**A CLINICAL STUDY ON RADIOLOGICAL LOWER LUNG ZONE PULMONARY TUBERCULOSIS IN A TERTIARY CARE TEACHING HOSPITAL OF BANGLADESH**

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**Background:** Lower lung field tuberculosis is atypical presentation of pulmonary tuberculosis which often causes confusion in diagnosis. HIV/AIDS epidemic & also Diabetes have considerably increased its incidence. Early diagnosis & treatment helps in the prevention of its complication.

**Objectives:** This study was designed to identify the proportion of lower lung field tuberculosis (LLFT) in different clinical conditions, its common clinical & radiological presentation, AFB status & outcome of treatment.

**Materials & Method:** This was a cross sectional study, was carried out in the department of Respiratory Medicine of National Institute of Diseases of The Chest And Hospital (NIDCH), Dhaka from 28.11.15 to 27.11.16. 91 patients with suspected tubercular lesions below an arbitrary line across the hila of their CXR, considered LLFT, were enrolled in this study purposefully according to inclusion & exclusion criteria. Baseline investigation, CBC, sputum for AFB, GeneXpert were done in all cases. In smear & GeneXpert – ve cases FOB was done to collect BAL fluid for AFB & GeneXpert study. HIV screening, blood sugar & other relevant investigations were done to exclude systemic diseases.

**Result:** Out of a total of 91 suspected TB patients, 51 patients (56%) had LLTB which was confirmed by investigation. The majority of the patients (45.1%) were 40-60 age group. It was more common in male (62.7%) than in female patients (37.3%). Cough (96.1%) & Fever (90.2%) were most common presenting clinical feature. Diabetes mellitus was most common risk factor (54.9%). Unilateral disease was more common (90.2%) & the right side was more frequently affected (60.8%). Cavitations (31.1%) & consolidation (13.3%) were the main radiological findings.

**Conclusion:** Lower lung field tuberculosis is fairly common in Bangladesh. Tuberculosis should be considered when lower lung fields are involved in elderly, Diabetes, CKD, HIV, immunocompromised and when the radiologic picture suggests unresolved pneumonia. These patients should be investigated further to exclude TB.

**CASES OF PULMONARY TUBERCULOSIS IN PATIENTS WITH COPD**

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Chronic obstructive pulmonary disease (COPD) triples the risk of tuberculosis. Cases of pulmonary tuberculosis in patients with COPD often have atypical imaging findings. We examined cases of tuberculosis in patients with COPD.

**Target and Method:** In patients with a history of smoking and images of emphysematous changes we examined cases of tuberculosis diagnosed at Showa University Hospital from April 2010 through March 2017.

**Results:** Of 220 cases of tuberculosis, 166 were pulmonary. We describe 6 cases with an interesting course. Case 1: In a patient with chronic renal failure, artificial nodules developed 3 months after a granular shadow was observed in the apex of the lung. Case 2: A lesion first appeared as a granular shadow of the pulmonary apex; it rapidly expanded through the upper lobe and formed a cavity. Case 3: The patient received prednisone because of chronic eosinophilic pneumonia, but the lesion of the apical patella expanded in both lungs, and a pneumatic image was observed. Case 4: Tuberculosis developed in the upper lobe of a patient with emphysema. A cavity lesion was observed 1 year after tuberculosis had been cured, but lesions spread further, and aspergillosis (due to Aspergillus niger) developed. Case 5: Because antibiotics had been administered for 5 months to treat refractory pneumonia, the symptoms repeatedly improved and worsened. Treatment for tuberculosis was started because of positive results of a Quantiferon-TB test and a family history of tuberculosis. Case 6: Because of negative results of an interferon-gamma release assay, a biologic agent was used to treat a patient with rheumatoid arthritis; tuberculosis developed 5 months later.

**Summary:** Cases of tuberculosis are common in elderly patients with emphysematous changes, progress rapidly, show no expanding granular shadow, and tend to expand via the airway.

**A RARE PRESENTATION OF COMMON DISEASE ENDOTRACHEAL -TUBERCULOSIS**

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**Background and Aims:** Tracheal tuberculosis is uncommon representing only 4% among those with endobronchial TB. So far less than 150 cases have been reported in literature.

**Methods:** We report a case of tracheal TB in a 65 year old male patient with complicated diabetes, who presented within weeks history of intermittent fever, productive cough, SOB and loss of weight. On presentation there was evidence of ongoing sepsis with low blood pressure, tachycardia, tachypnoea and a SpO2 of 90% on room air. Lung fields had bilateral coarse crepitations.

**Results:** Investigations on admission, WBC of 13 * 10^9/L, 65% neutrophils, 32% lymphocytes, 3% eosinophils, Hb 10g/dl, ESR 124mm, CRP 115, Mantoux 16mm. Creatinine 2mg/dl, FBS 18mmol/l, liver functions and electrolytes within normal limits. Sputum for AFB repeatedly negative. Chest x ray revealed no significant abnormalities. On follow up after discharge his symptoms improved except for the loss of appetite. He had persistently high ESR at 115 and a CRP of 55. This prompted further
investigations. Bronchoscopy showed normal larynx, pharynx and vocal cords. The trachea showed multiple white nodular infiltrates up to and involving the carina, but no involvement of the distal bronchial tree. Biopsy sent for Genexpert TB assay became positive for Mycobacterium tuberculosis. At the time of reporting he was showing good clinical response to anti tuberculosis medication and was awaiting a repeat bronchoscopy to assess the clearance of lesion.

Conclusion: This case illustrates the need for high index of suspicion and appropriate investigations of suspected tuberculosis. It helps to detect rare but important presentations of a common disease and to avoid irreversible and serious complications.

Background and Aim: The nature course of solitary or multiple lung nodules with histopathological findings suggestive of tuberculosis (TB) but lack of microbiologic confirmation remains unclear. Whether these patients require anti-TB treatment is currently unknown. This study compared outcome of untreated and treated patients with culture-negative histology-suspected TB presenting with either solitary or multiple lung nodules from a medical center in Taiwan and were followed for 2 years unless they died or developed active TB.Their medi-culture-negative histology-suspected TB within 2-year follow-up.

Method: From January 2008 to June 2013, patients with culture-negative histology-suspected TB presenting with either solitary or multiple lung nodules were identified from a medical center in Taiwan and were followed for 2 years unless they died or developed active TB. Their medical records, laboratory data, and image findings were reviewed.

Results: A total of 137 patients were identified. Among them, 69 (50.4%) were clinical asymptomatic. Tissue acid-fast stain (AFS) was positive in 29 (21.2%), and caseous necrosis was present in 82 (59.9%). Anti-TB treatment was prescribed in 66 (48.2%) patients; of them, 37 (56%) had adverse reactions. Multivariate analysis revealed that anti-TB treatment was favored in patients with positive tissue AFS and caseous necrosis, whereas observation was favored in those with malignancy or those received surgical biopsy. Only one case in the untreated group developed active pulmonary TB during 2-year follow-up (1 case per 139.3 patient-years).

Conclusion: In patients having culture-negative lung granulomas, the incidence rate of developing active TB was low. Regular follow-up sputum study and images instead of immediate treatment may be safe.

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OUTCOME OF UNTREATED LUNG NOODLES WITH HISTOLOGICAL BUT NO MICROBIOLOGICAL EVIDENCE OF TUBERCULOSIS

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Method: From January 2008 to June 2013, patients with culture-negative histology-suspected TB presenting with either solitary or multiple lung nodules were identified from a medical center in Taiwan and were followed for 2 years unless they died or developed active TB. Their medical records, laboratory data, and image findings were reviewed.

Results: A total of 137 patients were identified. Among them, 69 (50.4%) were clinical asymptomatic. Tissue acid-fast stain (AFS) was positive in 29 (21.2%), and caseous necrosis was present in 82 (59.9%). Anti-TB treatment was prescribed in 66 (48.2%) patients; of them, 37 (56%) had adverse reactions. Multivariate analysis revealed that anti-TB treatment was favored in patients with positive tissue AFS and caseous necrosis, whereas observation was favored in those with malignancy or those received surgical biopsy. Only one case in the untreated group developed active pulmonary TB during 2-year follow-up (1 case per 139.3 patient-years).

Conclusion: In patients having culture-negative lung granulomas, the incidence rate of developing active TB was low. Regular follow-up sputum study and images instead of immediate treatment may be safe.

AP318

CHARACTERISTICS OF TREATMENT OBSERVERS TO TAKE TUBERCULOSIS MEDICATION CONTRIBUTING TO BETTER TREATMENT OUTCOMES: A RETROSPECTIVE STUDY

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Background and Aims: Tuberculosis is a worldwide communicable disease and has high mortality rate. It remains endemic in developing country, as Indonesia ranked second globally. The incidence keeps increasing and leads to economic burden. DOTS strategy to counter tuberculosis is being executed, yet patient’s medication compliance is still a major issue. Thus, a treatment observer is required. This study was conducted in order to discover the characteristics of treatment observers contributing to better treatment outcomes in tuberculosis patients in Persahabatan Hospital, Jakarta.

Methods: The method used in this research was a retrospective study with once data retrieval (cross-sectional) from medical records of patient with tuberculosis patients who were cured and/or completed the treatment in Persahabatan Hospital, Jakarta in 2015-2016 which were selected through consecutive sampling method. The analyzed variables are the characteristics of the treatment observer (sex, age, relationship with patients, education, occupation, and observing method) and patient’s treatment outcome.

Results: Female (66.7%), adult aged 19-44 years old (43.1%), family member of patient (95.1%), well-educated or at least high school graduates (61.8%), a housewife (53.9%), and used verbal as observing method (77.5%) are common characteristics found in this study. Sex (P= 0.779), age (P = 0.238), relationship with patient (P= 0.680), education (P= 0.1), occupation (P= 0.207), and observing method (P = 0.776) are not significantly different between cured and completed treatment groups.

Conclusions: Female who aged 19-44 years old, a family member of the patient, well-educated, a housewife, and use verbal as observing method are the characteristics of treatment observers who leads to better treatment outcomes. The characteristics of treatment observers results from this study might be the basis of reference to develop people around the patient in order to succeed all tuberculosis treatments in developing countries by increasing the society participation, so that tuberculosis can be eradicated.

AP319

DESENSITIZATION THERAPY FOR ALLERGIC REACTIONS IN ANTITUBERCULOUS DRUGS

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Method:...
Background and Aims: We retrospectively evaluated the clinical usefulness of desensitization therapy for patients showing allergic reactions to antituberculous drugs (INH and RFP) according to the report by the Japanese Society for Tuberculosis (JST).

Methods: Desensitization therapy for antituberculous drugs was performed according the report by the JST for seventy patients (86 times) with mycobacterial disease in several hospitals between 1998 and 2016.

Results: Adverse reactions occurred as skin eruptions 36 patients, fever 25, and fever plus eruption 9. The causative drugs suggested by the clinical course or DLST were RFP 38 patients, INH 17, INH plus RFP 1, and unknown 14. The clinical effects of desensitization therapy for individual drugs were favourable 42 out of 54 times (78%) on receiving RFP, and 24 of 32 times (75%) on receiving INH. Twenty patients showing the failure of desensitization included 14 elderly patients and 2 patients with a history of drug allergies. The interval until the initiation of desensitization therapy ranged from 5 to 60 days after the disappearance of adverse reactions, and the interval until the appearance of adverse reactions during desensitization therapy ranged from 1 to 32 days. A comparative study between the patients group with successful desensitization therapy and that with failed desensitization did not show differences except for the age and interval until the initiation of desensitization therapy.

Conclusions: We confirmed the clinical effectiveness of desensitization therapy for antituberculous drugs according to the report of the JST in this multicentre study.

AP320

CUTANEOUS ADVERSE DRUG REACTION AND SUBSEQUENT RE-CHALLENGE WITH FIRST-LINE ANTI-TUBERCULOSIS DRUGS

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Background and Aims: Cutaneous adverse drug reactions (CADR) are a frequent cause of TB treatment interruption. Re-challenge with first-line drugs is usually attempted after resolution of non-life-threatening CADR because alternative regimens without rifampicin (RIF) and isoniazid (INH) are associated with poorer treatment outcomes. We aim to study the risk factors for CADR, culprit drugs and outcome of drug re-challenge strategies in patients with CADR.

Method: Retrospective case record review of patients with treatment interruption due to CADR identified from patients treated at the Singapore TB Control Unit in 2013 and 2014. A culprit drug was definite if rash resolved after withdrawal of drug and recurred after re-challenge or presumed if there was successful re-challenge of all but 1 (culprit) of the initial TB drugs.

Results: 2%(77/3860) had TB treatment interrupted due to CADR. HIV positivity (6.5% vs 2.3%, p=0.02) was a risk factor whereas gender and positive sputum AFB smear were not. Median rash onset was 15 days; 61%(47/77) CADR were serious (rash with fever +/- laboratory abnormalities/organ involvement). When rash resolved, first-line drugs were re-introduced in 96.1%(74/77) sequentially and additively in either escalating doses (group 1: 28.4%, 21/74; full doses (group 2: 32/74, 43.2%) or simultaneous introduction of 2 drugs (28.4%, 21/74). Successful re-introduction with both RIF and INH occurred in 13/18 (72.2%) using group 1 (p=0.44), 22/29 (75.9%) using group 2 (p=0.65) and 16/18 (88.9%) using group 3 strategies. The most common culprit drug was pyrazinamide (PZA) (33%, 23/77) followed by RIF (19%, 14/77). Diagnosis was presumptive in 74% PZA, 50% EMB 25% INH whereas for all RIF (100%), definite diagnosis was based on recurrence of rash when RIF was re-introduced. Significant risk factors for CADR in CHN were ethnicity other than Chinese/Malay/Indian (33.3%, p=0.04). PZA CADR patients had higher mean BMI (22.7 vs 19.9, p=0.01).

Conclusion: PZA was the most common drug responsible for CADR. Successful re-challenge was not affected by different re-challenge strategies.

AP321

THE EFFICACY AND SAFETY OF ADJUNCTIVE CORTICOSTEROIDS IN THE TREATMENT OF TUBERCULOUS PLEURISY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose: To evaluate the efficacy and safety of adjunctive corticosteroids in the treatment of patients with tuberculous pleurisy.

Methods: The PubMed, Cochrane, Medline, Embase, Web of Science and Chinese National Knowledge Infrastructure were searched. Clinical trials of corticosteroids compared with control were eligible for inclusion.

Results: Ten studies (6 randomized controlled trials [RCTs] and 4 non-RCTs) with 957 participants met the inclusion criteria. Compared to the controls (placebos or non-steroids), adjunctive corticosteroid use reduced the risk of residual pleural fluid after 4 weeks and the number of days to symptom improvement; however, there was no convincing evidence to support the positive effects of corticosteroids over the long term (8 weeks) on residual pleural fluid, pleural thickening, or pleural adhesions, and there was no statistical difference between the corticosteroid group and control group with respect to 7-days relief of the clinical symptoms or death from any cause. In addition, more adverse events were observed in patients who received corticosteroids than in those in the control group.

Conclusions: Our results suggest that adjunctive corticosteroid use did not improve long-term efficacy and might induce more adverse events, although the risk of residual pleural fluid at 4 weeks and the number of days to symptom improvement were reduced.

AP322

RAPID DESENSITIZATION TO ANTI-TUBERCULOSIS DRUGS

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Background and Aim: To overcome allergies to antituberculosis (anti-TB) drugs, desensitization in Japan usually begins at a dose of 25 mg/day, with a gradual increase every 3 days. This regimen is widely used with a high success rate of 75-92%, but a period of at least 2 weeks is required, and patients require careful monitoring during this time. The efficacy of rapid desensitization for 4 days to reach target doses of anti-TB drugs has been investigated.

Methods: This study included patients who underwent rapid desensitization between October 2015 and February 2017 in our hospital. These patients were unable to take anti-TB drugs because of drug allergies such as rash, fever, and liver dysfunction. Desensitization started with 0.1 mg on the first day, which was gradually increased at 15-min intervals and adjusted so that a near-target dose could be reached within 1 day. The target dose was then given in two divided doses daily for 3 days, followed by the standard once-daily dose.

Results: Fifteen patients were desensitized a total of 27 times. This included desensitization to multiple drugs in some patients, because often...
no single offending drug from a multi-drug regimen could be identified. Target drugs were isoniazid (INH) in 13 patients, rifampicin (RFP) in 12, and ethambutol (EB) in 2. The adverse reaction for which rapid desensitization was performed was a rash in 17 patients, liver dysfunction in 8, and fever in 2. Adverse reactions only recurred in 3 patients (4 events) after rapid desensitization therapy. The success rate was 67% for INH and 71% for RFP.

**Conclusion:** Rapid desensitization may lead to shorter overall treatment duration. The efficacy and safety of rapid desensitization should be evaluated in a larger number of patients.

### AP323

**ASSESSMENT OF THE TREATMENT EFFICACY OF TUBERCULOSIS PATIENTS WITH BIOMARKERS (SICAM-1, IP-10 AND QUANTIFERON GOLD-IN-TUBE)**

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**Background and Aims:** Tuberculosis (TB) is one of the world’s deadliest diseases. Inadequate case detection and failures to classify the disease progress impede TB control. Lacking of non-sputum based diagnostic test and objective auxiliary tools for monitoring TB treatment effectiveness and treatment completion confirmation delays optimal clinical management of patients. Biomarkers indicate initiation of successful treatment could facilitate development of alternative treatment strategies. Thus, the identification and validation of TB biomarkers is urgently needed to evaluate not only pathogen but also host of the response to infection. This study aims to evaluate responsiveness of biomarkers to tuberculosis and treatment.

**Methods:** Newly diagnosed TB patients without receiving any TB treatments before were included in the study group. We compared the biomarkers level of sICAM-1, IP-10, and IGRA in TB patients and normal subjects. Blood sample will be collected in TB patients at baseline prior initiation of medication, after two weeks, two months and six months of treatment or whenever they have completed their TB treatment. In control group, blood sample will be collected only once at baseline.

**Results:** A total of 95 TB patients were included in the study group, 51 non-TB subjects were recruited in the control group. Table 1 indicates that IGRA positive rate in experimental group was significantly higher than in control group.

Further, both sICAM-1(Figure1) and IP-10(Figure2) concentration level in experimental group was significantly higher than in control group with statically significant (p<0.001).

**Conclusions:** The primary endpoint of this study reveals that we may consider sICAM-1, IP-10 and IGRA act as potential biomarkers as an auxiliary tool for TB diagnosis. Further data collection and analysis are needed to validate responsiveness of these biomarkers to TB treatment and act as predictive biomarkers adequately once TB treatment has completed.

### AP324

**PLEURAL FLUID LACTATE LEVEL IN TUBERCULOUS PLEURAL EFFUSION AND THE RELATIONSHIP TO PARAPNEUMONIC PLEURAL EFFUSION IN HIGH TUBERCULOSIS SETTING – A PROSPECTIVE OBSERVATIONAL STUDY**

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**Background and Aim:** Tuberculous pleural effusion (TBE) and parapneumonic effusion (PPE) can present acutely. This leads to difficulty in initial management, as drainage remains the key for PPE while TBE
commonly requires pleural biopsy for diagnosis. Pleural fluid (Pf) lactate is higher in PPE, but data in TBE is limited. We postulate that Pf lactate will be lower in TBE as delayed hypersensitivity is the pathogenesis while PPE is secondary to pleural infection. Evaluate Pf lactate in TBE and its relationship to complicated (CPPE) and uncomplicated (UPPE) PPE. To define an optimal lactate level to discriminate TBE from CPPE.

**Methods:** Single institution study of all patients with pleural effusion that required diagnostic thoracocentesis over 18 months duration. Pf lactate was analyzed using blood gas machine along with Pf pH and glucose.

**Results:** 180 patients were included with 47 (26.1%) PPE, 56 (31.1%) TBE, 66 (36.7%) malignant and 11 (6.1%) transudate. Mean Pf lactate for TBE is 3.89 ± 1.57mmol/l, which was lower than PPE (8.29 ± 5.39mmol/l, p<0.001) and CPPE group (11.09 ± 4.37mmol/l, p<0.001). No difference between TBE and UPPE (p=0.149). In a subgroup analysis of CPPE and TBE whose pleural fluid pH was less than 7.2 and glucose less than 2.6mmol/l, we found that Pf lactate was higher in CPPE group (6.33 ± 0.51mmol/l in TBE and 11.72 ± 3.67 in CPPE, p<0.001). Pf lactate of more than 7.25mmol/l had a sensitivity of 79.3%, specificity of 100%, positive predictive value of 100% and negative predictive value of 90.3% in discriminating CPPE from TBE (AUC 0.942, p<0.001, 95% CI 0.89-0.99).

**Conclusion:** When suspecting TBE and CPPE, Pf lactate is significantly lower in TBE, even if Pf pH and glucose is low. Pf lactate of more than 7.25mmol/l can potentially aid clinician in discriminating CPPE from TBE, avoiding biopsy in this patient group.

**NEUTROPHIL-LYMPHOCYTE RATIO AND PROGNOSIS IN MILIARY TUBERCULOSIS**

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**Background and Aim:** It is difficult to predict the prognosis of miliary tuberculosis (TB) because its clinical course is variable and can be developed into fatal condition. The blood neutrophil–lymphocyte ratio (NLR) is an indicator of inflammatory status and is hypothesized to reflect independent prognostic significance in patients with miliary TB. The aim of this study is to investigate the relationship between NLR and outcome in miliary TB.

**Methods:** We retrospectively collected data from patients diagnosed with miliary TB in a tertiary referral hospital between January 1995 and January 2016. Logistic regression, Cox regression and Kaplan-Meier analysis were performed to evaluate the predictors for prognosis in patients with miliary TB. The area under the curve (AUC) was calculated from the receiver operating characteristic (ROC) curve to compare the predictability of inflammatory markers.

**Results:** A total of 96 patients were enrolled. Mean age of patients was 56 years (15–89), and 44 patients (46%) were male. Seventeen patients (18%) died during hospitalization due to miliary TB, and 9 (9%) died additionally during the 1-year follow-up period. Eighteen patients (19%) were diagnosed with acute respiratory distress syndrome (ARDS). In multiple logistic regression analysis, increased NLR was associated with ARDS (adjusted odds ratio 1.15; 95% confidence interval [CI], 1.03-1.28). By multivariate Cox regression analysis adjusting known prognostic factors including age, sex, body mass index, serum aspartate aminotransferase, and hemoglobin, NLR was an independent predictor of in-hospital mortality (adjusted hazard ratio [aHR] 1.08; 95% CI, 1.03-1.13) and 1-year mortality (aHR 1.08; 95% CI, 1.05-1.12). When AUC was compared to evaluate the usefulness of inflammatory markers in predicting 1-year mortality of patients with miliary TB, the AUC of the NLR (0.722) was the largest.

**Conclusion:** Pretreatment NLR at hospitalization may be a useful biomarker for mortality and the development of ARDS in patients with miliary TB.

**MULTIDRUG RESISTANT TUBERCULOSIS IN THE NORTHERN STATES OF MALAYSIA – A RETROSPECTIVE CASE SERIES FROM 2011 – 2016**

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**Background and Aim:** To describe the clinical characteristics, risk factors, diagnostic modalities, treatment, outcomes and complications of multidrug-resistant tuberculosis (MDR-TB) cases residing in northern states of Malaysia

**Methods:** A retrospective case series conducted for all patients treated for Drug Resistant Tuberculosis since 2011-2016. It is a pioneer study in analysing data pertaining to MDR-TB. Cases were identified by our Pulmonology Department with State Public Health Unit which is responsible for treatment of tuberculosis.

**Results:** Total of 6 MDR-TB patients were treated from 2011-2016. Formal drug susceptibility test and LPA test were done to confirm the diagnosis. Out of the total, there were 5 male and 1 female patients. The mean age of patient was 48years (ranging from 28 to 68 years) whereby 2 out of them were immigrants. Previous history of tuberculosis with exposure to treatment, and smoking status were most highly correlated with the current diagnosis of MDR-TB.

4 patients fulfilled WHO criteria of “treatment success”, 1 of them categorized under the criteria of “cure” and another patient belongs to “lost to follow up” category. Side effects of the therapy were far less than expected.

**Conclusion:** Although treatment regimes are complex, successful treatment outcomes (83.3%) are possible with coordinated and dedicated TB control programs.

**HYPOKALEMIA AMONG MULTIDRUGS RESISTANT TUBERCULOSIS PATIENTS**

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**Background and Aim:** Electrolyte imbalance, especially hypokalemia, is one of the adverse reactions mostly found in patients with multidrug-resistant tuberculosis (MDR-TB) who treated by injectable agent. To know the proportion of hypokalemia in MDR-TB patients receiving second line injection of antituberculosis drugs and the contributing factors.

**Methods:** This study is a cross sectional, retrospective, medical record based study among MDR-TB patients in Persahabatan Hospitals during intensive phase from July 2015 to June 2016 who received intensive phase treatment consist of kanamycin or capreomycin, pirazinamid, ethambutol, levofloxacin,cycloserine and ethionamide. Hypokalemia was defined as potassium level of <3.5 mEq/L.
Background and Aims: Tuberculosis is related with overproduction and bioactivation of Transforming Growth Factor Beta (TGF-β). There are some pulmonary alterations in post-tuberculosis patients, such as increasing amount of TNF-α, TGF-β and fibrosis. Smoking creates a mechanism that stimulate impairment in immunity and pathogen elimination. Smoking about 10 cigarettes daily significantly enhances tuberculosis relapses and declining FEV1/FVC value. This study aimed to reveal any correlation between TGF-β and FEV1/FVC value in post-tuberculosis patients with smoking history in Haji Adam Malik General Hospital Medan.

Methods: This cross-sectional analytical study involved 26 post-tuberculosis patients with smoking history. FEV1/FVC measurement was performed by using spirometry and TGF-β level was collected after collecting Enzyme-linked Immunosorbent Assay (ELISA) from venous blood sample.

Results: There were 26 people that involved in this study, about 96.2% of them were male. The average of TGF-β level was 6621.5 ± 4856.7 mg/ml. The average of FEV1, FVC and FEV1/FVC were 58.3 ± 23.7% and 77.6 ± 14.84% respectively. After performing analysis by using Spearman correlation test towards the data, there was no any correlations found between TGF-β and FEV1 (r=0.1, p=0.61), between TGF-β and FVC (r=0.14, p=0.48), and between TGF-β and FEV1/FVC (r=0.1, p=0.62).

Conclusions: There was no correlation between TGF-β with either FEV1, FVC or FEV1/FVC.

Background: Pulmonary tuberculosis is an infectious disease caused by Mycobacterium tuberculosis, which can attack various organs, especially the lungs. If it’s untreated or not complete treatment can create serious complications, even death. Post tuberculosis treatment may occur the lesions residual sequelae of tuberculosis, one of which is fibrosis. Transforming growth factor-β1 (TGF-β1) is a cytokine associated with lung inflammation, which plays a role in the occurrence of pulmonary fibrosis. However, only a few knows the serum level of TGF-β1 in patients with post pulmonary tuberculosis.

Aims: To determine the relationship between the level of TGF-β1 with pulmonary fibrosis in patients with post pulmonary tuberculosis treatment.

Methods: Examined level of TGF-β1 using ELISA in 51 patients with post ATT and declared cured (consist of 31 males, 20 females; 26 smokers; 25 males, 1 female), then associated with the chest x-ray of...
the patients which divided into lesions (+) and lesions (-). In this case, lesions (+) were defined as pulmonary fibrosis.

Results: Regardless of the smoking status, level of TGF-β1 with the presence of pulmonary fibrosis was significantly higher compared to the absence of pulmonary fibrosis. (mean ± SD, 7628.02 ± 4928.38 vs mean ± SD, 2315.11 ± 505.83; p = 0.001).

Conclusion: Level of TGF-β1 was significantly higher in post tuberculosis patients with pulmonary fibrosis.

Keywords: TGF-β1, post pulmonary tuberculosis, pulmonary fibrosis

CORRELATION OF SERUM TUMOR NECROSIS FACTOR-α LEVEL WITH PULMONARY FUNCTION IN POST PULMONARY TUBERCULOSIS PATIENTS
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Background and Aim: Post pulmonary tuberculosis are common problem especially in countries with high pulmonary tuberculosis prevalence. There are a large number of patients who recovered after completing TB treatment, but some clinically ill patients develop symptoms of shortness of breath associated with smoking habits. Inside the lungs, cigarette smoke have both, pro-inflammatory effect and immunosuppressive on the immune system, resulting in damage of the alveolus walls and also secreting various kinds of inflammatory mediators. Stress oxidation reactions from cigarette smoke or from inflammatory cells have the following effects: increasing TNF-α production and increasing isoprotanase which plays a role in bronchoconstriction.

The aim of this study is to investigate the level of TNF-α and its correlation with pulmonary function after post pulmonary tuberculosis.

Methods: A case series which examined level of TNF-α using ELISA in 43 patients with post pulmonary tuberculosis treatment and declare cured (male 25, smoker 20) then associated with pulmonary function that is FEV1 and FVC.

Results: In 43 patients who are predominantly male 58,10% with median age 39 (18-73). Among Smokers there is significant correlation between level of TNF-α with FEV1 (r: -0.593 p: 0.006), and TNF-α with FVC (r: -0.573 p: 0.008). Meanwhile among non smoker group there is no significant correlation between the level of TNF-α with FEV1 (r: -0.031 p: 0.888), TNF-α with FVC (r: -0.064 p: 0.771).

Conclusion: There is significant correlation between the level of TNF-α and pulmonary function FEV1 and FVC among smokers of post pulmonary tuberculosis patients.

Key words: Post pulmonary tuberculosis, Smoker, TNF-α, Pulmonary function, FEV1, FVC

LUNG FUNCTION AND QUALITY OF LIFE OF POST TB PATIENT- A PRELIMINARY STUDY
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Background and Aims: Indonesia has the second largest TB cases in the world (about 10% of whole world total cases). Until now there are no study about quality of life using standardize questionnaire. The aims of this study is to describe lung function and quality of life of post TB patient with a new TB cases.

Methods: This is preliminary result of a cross sectional study in the outpatient clinic of Persahabatan Hospital Jakarta. Seventeen patients were evaluated. We used generic questionnaire from medical outcome study short form-36 (MOS SF-36) to evaluate quality of life. Spirometry is done by using Chest multi functional spirometer HI-801.

Results: From all subjects, 9 (52.9%) were female. Mean of age is 32.41 years old. Acid fast bacilli (AFB) was positive in 10 cases (58.6%). Fifteen patients (88.2%) used Fixed Dose Combination (FDC) regimen. Duration of therapy was 6 month in 14 patients (82.4%), three patients get 9 month therapy. Spirometry is normal in 5 patients (29.4%), restriction in 8 patients (47.1%), obstruction in 1 patient (5.9%) and mixed in 3 patients (17.6%). In quality of life assessment 11 patients (64.7%) did not have disturbance in physical and mental health, three patients (17.6%) have a disturbance in mental health and 3 patients (17.6%) have a disturbance in physical and mental health. There was a weak correlation between spirometry result and quality of life of former TB patients in bivariate analysis (Pearson correlation -0.82).

Conclusions: In this small preliminary study, a majority of post TB patient have an abnormal spirometry with the most common result is restriction. In quality of life assessment using MOS SF36 only 6 patients (35.2%) have disturbance in quality of life. There is weak correlation between spirometry result and quality of life. We are currently awaiting result from bigger population.

POST-TREATMENT MORTALITY AMONG PATIENTS TREATED FOR TUBERCULOSIS IN VIETNAM
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Background and Aims: Tuberculosis (TB) is the leading infectious cause of death worldwide. Steep reductions in TB-related mortality are a central priority of the World Health Organization’s End TB Strategy. However, accurate mortality estimates are lacking in many countries endemic for the disease, particularly following discharge from treatment programs. This study aimed to establish the mortality rate among patients treated for pulmonary TB, and determine the excess mortality attributable to TB in this population.

Methods: We conducted a prospective cohort study among patients treated for smear-positive pulmonary tuberculosis in 70 Districts throughout Vietnam. Household contacts were also recruited. Participants were followed for at least two years after enrolment, and their vital status and disease outcomes ascertained. The relapse status of patients during follow-up was established using probabilistic data linkage with clinical records and self-report. Verbal autopsy were performed for a random sample of deceased patients, in consultation with household members.
Results: 10,964 patients with TB and their 25,707 household contacts were enrolled and followed for a median of 33 months. Among patients, 979 patients (8.9%) died during follow-up, of which just 342 (3.1%) had been notified to the National TB Program. The Standardized Mortality Ratio (SMR) was 4.0 (95% CI 3.7-4.2) among patients with TB compared to age and gender matched household contacts. Verbal autopsies indicated that 44.7% of deaths were likely to be caused by TB.

Conclusion: Patients treated for tuberculosis have a markedly elevated risk of death in the treatment and post-treatment period. Interventions during treatment to prevent post-treatment mortality may be beneficial for patients in high-burden settings.

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PLEURAL FLUID CYTOLOGY IN THE DIAGNOSIS OF MALIGNANT PLEURAL EFFUSION
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Background and Aim: It is reported that the sensitivity of pleural fluid cytology is about 60% for malignant pleural effusion (MPE). Immunohistochemistry staining and cell block cytology have been reported to individually improve the diagnostic yield. We postulate that a combination of both techniques will have a good diagnostic yield for MPE. This is a two-year analysis of the diagnostic yield of pleural fluid with immunohistochemistry and cell block cytology in the diagnosis of MPE.

Methods: We extracted patients admitted for pleural effusion that had pleural fluid sent for cytology from 2 January 2014 to 1 January 2016 from our registry of pleural diseases. Pleural fluids were collected via bedside ultrasound guided pleurocentesis. We looked at the final diagnosis of these patients. Patients were diagnosed with MPE when malignant cells were seen on pleural fluid cytology or subsequent pleural biopsy for those with negative cytology. Pleural biopsy was performed in patients who had negative cytology but clinical and radiological features to suggest MPE.

Results: 268 patients (171 males and 97 females) had pleural effusion at time of diagnosis. Ninety seven (36.2%) patients (34 males and 63 females) were diagnosed with MPE. Eighty two patients (84.5%) with MPE had positive pleural fluid cytology. This cytology method had a sensitivity of 84.5% (95% CI 75.8%-91.1%) and a negative predictive value of 91.9% (95% CI 87.7%-94.8%). Lung cancer is the most common primary cancer and was seen in 63 patients (64.9%) of which 57 (90.5%) had positive pleural fluid cytology. It is the most common primary cancer in both male (82.4%) and female (55.6%) patients.

Conclusion: Our study shows that immunohistochemistry staining and cell block cytology is a sensitive method with high negative predictive. It can be obtained by pleurocentesis and should be considered as an initial investigation in patients suspected of MPE.

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IS EVERYTHING CLEAR WITH PLEURAL EFFUSIONS IN PATIENTS WITH HEPATIC DISEASES?
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Background and Aims: Pleural effusions (PE) in patients (pts) with hepatic diseases on pneumology departments can be connected with some therapeutic problems. The portal hypertension, hypoprothrombinemia, hypoalbuminemia, immunodepression, and secondary infection can result in different PE: from transudates to empyema (EMP). Different types of PE require different management, particularly whether or not to perform chest drainage (CD). We share our experience in managing hepatic PE.

Methods: We analysed 28 pts (7.2%) with hepatic PE from 390 pts. Thoricentesis, blind pleural biopsy was performed. Biochemical, bacteriological, differential cells count in PE, and/or CT scan were performed. For diagnosis transudate/exudate Light’s criteria were used. CD was used in EMP and in large amount PE. Transudates was solved by the amount of PE and biochemical status. Only large PE with hypoprothrombinemia was drained. Smaller PE were solved with biochemical and clinical status.

Results: 25 M (53.51 years), 3 F (53.95 years), 18 pts had chronic hepatitis with failure, 9 toxic hepatitis, 1 cirrhosis. EMP was confirmed in 15 pts, PE in 12, TB in 1 pt. Serum hypoprothrombinemia was determined in 19/28 pts (67.8%), transudate was in 3/12 pts (25%). Ly 72.76±35.51, PMN 43.77±44.15, protein in PE 40.70±39 g/l in the PE analysis. Median CD was 11 (1-40 days). CD was successful in 15 EMP and TB, but from the last 13 pts, surgery was used on 3, and on 6 of them CD was unsuccessful.

Conclusions: CD is essential in empyema. In the big PE caused by hypoprothrombinemia and/or portal hypertension CD is problematic. CD in non EMP deepens hypoprothrombinemia, loss of minerals and hypoprothrombinemia causes retention of PE, oedema of the leg. Finally it caused weakened clinical status, and drainage failure. It would be better to firstly optimize pts nutrition status and then try to solve the problem of accumulated PE.

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PREVALENCE AND ASSOCIATED RISK FACTORS OF PLEURAL EFFUSION AMONG PATIENTS WHO UNDERWENT CARDIAC SURGERY IN CHONG HUA HOSPITAL
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Background and Aims: Respiratory complications remain a leading cause of post-cardiac surgical morbidity prolonging hospital stay and increasing costs. The high incidence of pulmonary complications is in part due to the disruption of normal ventilatory function that is inherent to surgery in the thoracic region. This study aimed to determine the prevalence and associated risk factors of pleural effusion after cardiac surgery.

Methods: This was a retrospective cross sectional chart review study design. The study involved 101 records of patients retrieved from January 2012 to December 2016 and were purposively selected with the following criteria, namely, cases aged ≥18 years old, who underwent post-cardiac surgery, and were assessed for pleural effusion. Also, excluded in this study were those whose pleural effusion was present at time of surgery and those patients diagnosed of pleural effusion caused by other disease including pulmonary embolism, drug reaction, malignancy or pleuro-pulmonary infection.

Results: The 5-year prevalence rate of pleural effusion at post-cardiac surgery was 84%. Pleural effusion was frequently seen in patients who are male (78%), aged 36-61 years old (M=60.8±9.99), overweight (26.61±5.02 kg/m²), and non-smokers (56.5%). The incidence of pleural effusion in CABG surgery only was 80.7% while the valve replacement with CABG surgery and valve replacement only both had 100%. Risk factors identified with pleural effusions were peripheral vascular disease (OR = 0.261 CI 0.07-0.92) and pre-operative proton pump inhibitor (OR = 3.081 CI 1.00-9.46). In the subgroup analysis, longer operation duration (p-value= 0.012), higher volume of total fluid given (p-value= 0.022), blood products transfused (p-value= 0.008), and blood loss (p value= 0.002) were statistically higher among patients with thoracostentesis.

Conclusions: The 5-year prevalence rate pleural effusion was 84% in post-cardiac surgery pleural effusion. The associated factors with pleural effusions were presence of peripheral vascular disease and use of proton pump inhibitors.
AN UNUSUAL CAUSE OF PLEURAL EFFUSION
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Background and Aims: Peritoneal dialysis (PD) is a rare cause of pleural effusion. It appears as a complication of PD in approximately 2% of patients. Hydrothorax in this situation is called “sweet hydrothorax” as hypertonic glucose solution fills the pleura.

Methods: 62-year-old woman with end stage renal disease presented with dyspnea on exertion and chest pain for about 4 weeks after initiation of PD six months back. A chest x-ray was done showed massive unilateral right-sided pleural effusion. She underwent small bore chest drainage for massive pleural effusion. Pleural fluid was crystal clear with high glucose concentration of 735 mg/dl. The pleural fluid protein was 0.2 g/dl. Cytological and microbiological examination of the pleural fluid showed no abnormalities. Pleural fluid analysis was consistent with transudate and pleural fluid glucose concentration was higher than patient serum glucose concentration suggestive of sweet hydrothorax. She was switched over to haemodialysis for 4 weeks. After 4 weeks she was started back on peritoneal dialysis with reduced fluid volume and reduced dwell time and increased frequency of fluid change without recurrence for six months under followup.

Results: Hydrothorax may develop several weeks or months after starting of PD. Diagnostic pleural tapping and pleural-fluid analysis are often diagnostic, revealing a crystal clear pleural fluid with a low protein and a high glucose concentration. In the patient presented here, glucose concentration in the pleural fluid was much higher than that in the serum drawn concomitantly.

Conclusions: It is advisable to keep sweet hydrothorax as a differential diagnosis while evaluating hydrothorax in patients on peritoneal dialysis.

A CASE REPORT ON PRIMARY CILIARY DYSKINESIA IN A FILIPINO MALE WITH BRONCHIECTASIS, NORMAL SITUS AND SPERM IMMOTILITY
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Background and Aim: Primary Ciliary Dyskinesia is a rare genetic disorder of the mottle cilia. This paper reports a case of a 16-year-old male came in with recurrent non-massive hemoptysis, secondary to bronchiectasis on the bilateral lower lobes via chest CT scan. He presented with perennial rhinosinusitis and history of neonatal pneumonia.

Methods: Patient was worked up for congenital causes of bronchiectasis where fiberoptic bronchoscopy, Fractional Exhaled Nitric Oxide (FENO) level using chemiluminescence analyzer, and sperm count and transmission electron microscopy (TEM) analysis that enable the attending physician to clinch on the final diagnosis.

Results: fiberoptic bronchoscopy revealed normal bronchial tree with suppurations and no obstruction, low FENO of 4ppb, and low sperm count with predominant non-motile population. The semen sample was sent for TEM analysis which revealed various ultrastructural defect such as missing central microtubules, and microtubular disorganization and missing both inner and outer dynein arms. These structural abnormalities in the spermatozoa flagella were associated with primary ciliary dyskinesia.

Conclusion: Primary ciliary dyskinesia may be considered among patients presented with bronchiectasis, with no definite infection cause, with predilection at the lower lobes with noted ciliary abnormalities on TEM.

WEGENER’S GRANULOMATOSIS - THE CHALLENGES IN ITS REVELATION AND TRIBULATION ON TREATMENT
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Introduction: Diagnosis of Wegener’s granulomatosis, a rare multisystem autoimmune disease remains a great challenge due to its clinical heterogeneity. Early commencement of immunosuppressive treatment is vital but often complicated by infection and sepsis. We present 2 cases which highlights different course of the disease.

Case series: Case 1: 25-year-old male presented with acute haemoptysis and fever. He had similar presentation 8 months ago and was treated as leptospirosis with pulmonary haemorrhage. He was discharged well till this admission. Upon presentation he was febrile, in respiratory distress and had right lower zone bronchial breathing. He also had leukocytosis, anemia and acute kidney injury with microscopic hematuria and proteinuria. Chest radiograph revealed diffuse reticulonodular shadowing. CT Thorax showed extensive ground glass changes and consolidation. Bronchoscopy revealed diffuse multiple bleeding spots. C-ANCA was positive. He was then treated with methylprednisolone, immunoglobulin and plasmapheresis. Once sepsis was controlled, he had cyclophosphamide. He responded well and was discharged with subsequent maintenance treatment.

Case 2: 43-year-old lady presented to multiple private center with 4 months history of tinnitus, epistaxis, bilateral lower limb weakness and haemoptysis. CT Thorax revealed bilateral lung consolidation. Unfortunately she took discharge against medical advice. 6 weeks later, she presented with similar symptoms associated with abdominal pain. She had acute kidney injury with anemia and urinalysis showed microscopic hematuria with granular cast. Her ANCA was positive and she was started on corticosteroid, plasmapheresis, immunoglobulins and cyclophosphamide. She then had massive lower GI bleed and caecal biopsy confirmed Cytomegalovirus infection. Unfortunately her admission was complicated with resistant CMV infection and nosocomial pneumonia of which she succumbed to the condition.

Conclusion: Both patients highlight clinical heterogeneity of the disease. Immunosuppressive treatment is vital to achieve remission (first case) but can be complicated by opportunistic infection and mortality (second case).
A 17- YEARS OLD BOY WITH FEVER AND MULTIPLE PULMONARY LESIONS

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Background: Behçet’s syndrome is a rare disease that causes vasculitis in various tissue and can be presented with different manifestations.

Clinical case: A 17-years old boy was admitted due to chest pain, nonproductive cough, fever and dyspnea that aggravated from 2 weeks ago. He did not have any past medical history. He had received oral antibiotics before admission with no improvement. On Physical examinations he has low grade fever and mild crackles in both lungs auscultation. Pustular skin lesions on his face and upper extremities were detected. Laboratory tests revealed WBC, 11800 /ml, with neutrophils %72, lymphocyte %24 and mix %4. ESR was 110. Renal and liver functions were within normal limits. Also rheumatologic test and serum galactomanan were negative.

Chest radiograph showed peripheral parenchymal opacities at the left lower lobe and CT scan was performed subsequently, which showed multifocal bilateral subpleural consolidation (Figure1). Sputum culture for bacterial and fungal infection and AFB were negative. Based on CT scan and laboratory findings the patient underwent open lung biopsy.

Result: Histopathological examination showed foci of infarct areas in lung parenchyma, thrombosis and occlusion of medium sized lung vessels; with recanalization and intraalveolar accumulation of hemosiderin-laden macrophage.

During the admission patient developed oral ophtosis and pathergy test was positive. The diagnosis of behçet’s disease was made. He treated with pulses of methylprednisolone and cyclophosphamide. After two weeks, chest radiograph was showed aneurysm with former parenchymal opacities. So pulmonary CT Angiography was down and revealed thickening and also aneurysmal dilation of right and left lower pulmonary artery branches, which could be suggestive of vasculitis and pulmonary emboli (Figure2).

Conclusion: Behçet’s syndrome presented with some various clinical manifestations. So in high prevalence areas this disease should be considered.

A CASE OF BLEEDING BRONCHUS

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Background and Aims: Endometriosis is the presence of functional endometrial tissue outside the uterus, most commonly in the ovaries, utero-sacral ligaments, and peritoneum. It affects 5% to 15% of women during their reproductive years. Thoracic endometriosis accounts for 2% of ectopic endometriosis. Catamenial hemoptysis is a rare complication of thoracic endometriosis, accounts for 7% of reported cases.

Methods: We report a case of endobronchial endometriosis with catamenial hemoptysis. This patient was a 23 years old girl who presented with periodic hemoptysis coinciding with first day of menstruation for six months. A chest computed tomography (CT) obtained during the first day of menstruation revealed ground glass opacities in the superior segment of the right lower lobe. Bronchoscopy was done on the first day of menstruation which showed bleeding from the superior segment of the right lower lobe bronchus. Follow up CT during the inter menstrual period demonstrated complete clearance of ground glass opacities without any active management. This clinched the diagnosis of catamenial hemoptysis. The patient was treated with Gonadotrophin-Releasing Hormone (GnRH) analogue therapy. The six months followup after hormonal therapy showed no recurrence or complications.

Results: Catamenial hemoptysis is a rare manifestation of thoracic endometriosis with < 50 cases reported in the literature. Diagnosis of catamenial hemoptysis is usually clinical, based on hemoptysis coincident with menstrual bleeding. CT scan often shows cavities, nodules, bullous formations, and ground glass opacities. Bronchoscopic findings in catamenial hemoptysis may be multiple bilateral purple-red mucosal lesions, single tiny red mucosal lesion or diffuse mucosal hyperaemia.

Conclusions: Catamenial hemoptysis a rare and complex condition, diagnosis is often delayed or missed by clinician. High index of suspicion is the key to diagnose any women of reproductive age group presenting with cyclical chest pain, dyspnea and or hemoptysis.
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UNUSUAL CO-OCCURENCE OF TRACHEOBRONCHEOPATHICA OSTEOCHONDROPLASTICA AND TRACHEOBRONCHIAL AMYLOIDOSIS

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Background and Aims: Co-occurrence of TBO and amyloidosis is not well documented in literature. We present an elderly male with chronic breathlessness, wheezing diagnosed as TBO and amyloidosis.

Methods/Case presentation: 72 year old man resident of India recently diagnosed case of Carcinoma prostate on chemotherapy (doce-taxel 9 cycles) had complaints of wheezing and breathlessness since last 25 years progressively increased in 2 months. Complete blood counts normal, Pulmonary function tests showed moderate airway obstruction with no reversibility. PET Scan done for screening of Carcinoma prostate showed bulky prostate with skeletal metastasis, computed tomography of chest showed irregular thickening of tracheal walls and right middle lobe bronchiectasis. Bronchoscopy revealed nodular lesions in trachea with sparing of posterior wall (image 1) however they were friable and easy to bleed, the right and left main bronchus showed nodular lesions nearly occluding the lumen. Bronchial lavage was negative for acid fast bacilli, pyogenic and fungus. Biopsy from endobronchial and tracheal nodule revealed subepithelial tissue acellular eosinophilic homogenous material (congo red positive) and Focal cartilagenous metaplasia/ destruction confirmed dual co-existance of TBO and amyloidosis. Protein electrophoresis, beta2 microglobulin & light chain detection in urine were negative

Conclusion: Although rare our patient manifested with both TBO and amyloidosis. The bronchoscopic picture showed lesions favouring features of TBO with sparing of posterior wall of trachea however they were easy bleeding and friable a feature seen with amyloidosis, although extensively evaluated cause of amyloid was not known. Noted here is nodular lesion in anterior trachea with sparing of posterior membranous part.

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AN UNUSUAL CASE OF SPONTANEOUS PNEUMOMEDIASTINUM

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Background and Aims: Spontaneous Pneumomediastinum (SPM) is defined as presence of free air within the mediastinum, not due to trauma. It is a uncommon condition with reported incidence between approximately 1 in 30000 and 1 in 44500. We report a case of SPM with bilateral pneumothoraces and subcutaneous emphysema due to vomiting.

Methods: A 55 years old farmer admitted with sudden onset of breathlessness after consuming a table spoon of rodenticide powder . On evaluation he admitted that he tried to empty the stomach by inducing vomiting by drinking soap water and the breathlessness developed after vomiting. He was dyspneic at rest with respiratory rate 34/min and SPO2 was 78 % in ambient air. His face and neck were swollen with extensive subcutaneous emphysema . Chest x ray showed pneumomediastinum and bilateral extensive subcutaneous emphysema. CT chest confirmed the same and also revealed bilateral subcutaneous emphysema. Esophageal rupture was ruled out by CT scan with oral contrast. The patient was managed conservatively with high flow oxygen and he improved drastically in 48 hours.

Results: SPM commonly follows intense coughing, vomiting and Val-salva maneuver, all of which can result in suddenly increased intraalveolar pressure without specific etiology such as trauma. The most common sign is subcutaneous emphysema especially over the neck.SPM is considered as a result of rupture of alveoli with tracking of air into the medias-tinum along the fascial planes. Usually SPM will have a benign clinical course and self limiting . Complications can occur including tension pneumomediastinum, pneumothorax and respiratory failure . Patients should be observed for at least 24 hours for monitoring complications and can be treated with high flow oxygen to expedite resolution .

Conclusion: If the patient develops subcutaneous emphysema or breathing difficulty after vomiting ,SPM should be suspected and esophageal tear should be ruled out.
DISSEMINATED ENDOMETRIOSIS PRESENTING AS HYDROPNEUMOTHORAX IN A YOUNG FEMALE

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Background and Aims: Thoracic endometrial syndrome (TES) hallmark presence of functioning endometrial tissue in pleura, lung parenchyma, airways, diaphragm presenting as catamenial hemoptysis/pneumothorax. We report a case of disseminated endometriosis presenting as hydropneumothorax.

Methods/case presentation: 35 year old female from Uganda with history of infertility presented with complaints of breathlessness and cough increasing since few weeks. She related the occurrence of symptoms during timings of menstrual cycles since few years (self resolving except for this time). She also gave history of recurrent dysmenorrhea and past history of oophorectomy (right) for ovarian cyst patient also had a nodular growth in umbilicus. Clinical examination on presentation suggested diminished breath sound on right hemithorax. Chest radiograph suggested Hydro-pneumothorax, Intercostal drainage tube was inserted and serosanguinous fluid drained. Pleural fluid was exudative, haemorrhagic, lymphocytic predominant, ADA 28.4 IU/L and Negative for acid fast bacilli, pyogenic culture. However the air leak was still significant and lung was not expanded. On further work up, USG abdomen showed uterine mass and ascites, transvaginal ultrasound confirmed presence of multiple uterine fibroids. Positron emission tomography showed enlarged uterus with multiple faintly FDG avid uterine fibroids. As per Multidisciplinary approach patient underwent Abdominal myomectomy, repair of uterus, biopsy of umbilical nodule & video assisted thorascoscopic surgery (VATS). VATS showed multiple haemorrhagic lesions/deposits in pleural cavity with large air leak from left upper lobe. Pleural deposits were fulgurated and upper lobe segment resection and stapling was done. Patient air leak resolved completely in 7 days and Intercostal drainage tube was taken out after full expansion of lung was achieved. Histopathology from uterus and umbilicus were consistent with endometriosis, pleural nodules showed endometrial invasions consistent with thoracic endometriosis

Conclusions: Hydropneumothorax is unusual to occur in thoracic endometriosis, multidisciplinary approach and VATS are beneficial in management.

EPITHELIOID HEMANGIOENDOTHELIOMA OF THE LUNG: A RARE VASCULAR TUMOR PRESENTING AS ASYMPTOMATIC BILATERAL PULMONARY NODULES

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Background and Aims: Epithelial Hemangioendothelioma (EHE) is a rare vascular tumor representing less than 1% of all vascular tumors, with only 248 cases currently officially reported in current registries. It may affect the lungs, pleura, liver, bone and other anatomic sites. It often misdiagnosed because of the heterogeneous presentation, noted to have low to intermediate grade malignancy with metastatic potential.

Methods: A healthy 62-year old female with no known comorbidities was admitted for a history of asymptomatic multiple bilateral pulmonary nodules noted as an incidental finding three years ago. Patient underwent extensive work-up including serial CT and PET scans, CT-guided biopsy and bronchoscopy with biopsy, all with inconclusive results. Patient was received at this institution for video-assisted thoracoscopic surgery (VATS) wedge lung biopsy with frozen section.

Results: Patient underwent such procedure where a portion of the right upper lobe adjacent to the minor fissure was wedged out. It revealed all lobes studded with numerous palpable hard tumors some of which were involving the visceral pleura with the parietal pleura having normal appearance. Gross examination showed cream hard rubbery nodules. Histomorphology revealed advancing micropolyloid tumor pattern growth with coagulative central necrosis and intracytoplasmic vacuoles. Immunohistochemical staining was positive for vascular markers CD34, CD31 and negative for CK, p63, MOC-31, TTF-1 and amyloid or Congo Red stains.

Conclusions: EHE is an unusual vascular tumor, often asymptomatic, presenting with multiple bilateral pulmonary nodules. The histomorphology and above immunohistochemical stain and Congo red stain results are consistent with pulmonary epithelioid hemangioendothelioma. Additional staining with ERG or CAMTA1 is ideally performed to further support the diagnosis but is currently not available in our country. A non-surgical treatment is being contemplated for the patient in a different country. There is currently no standard of treatment for EHE due to its rarity. Current therapeutic trials include anti-angiogenics, interferon and kinase inhibitors.
Background and Aims: Diffuse alveolar hemorrhage (DAH) is a life-threatening condition commonly seen with ANCA associated vasculitides, anti-GBM disease, and SLE. Early diagnosis and treatment is necessary for survival.

Methods (case report): A 32-year-old female presented with polyarthralgia, weight loss, hair loss, and oral ulcers for the past one month. Patient had progressive breathlessness and swelling over the right leg for one week. On examination, patient was tachypneic with room air saturation of 94%. Right leg was swollen, erythematous, tender, and ulcer seen. Investigations revealed anemia, neutrophilic leukocytosis, raised CRP, and bilateral patchy consolidation (CT thorax). Patient was initially started on antibiotics, oxygen support and planned to start on steroids after ANA profile reports. Next day patient had severe respiratory distress and hemoptysis. Patient was subjected for bronchoscopy under NIV support which revealed frank blood stained secretions in both bronchial tree suggesting alveolar hemorrhage. Patient was started on pulse methylprednisolone for 3 days, also antibiotics were escalated to meropenam and vancomycin. ANA, anti dsDNA, anti Sm Ab, anti SSB, Anti SSA, Anti Scl-70 were positive. Patient symptomatically improved, hence steroids tapered to 40 mg of prednisolone.

Results and Discussion: At the end of 20 days, there was complete radiologically resolution and right leg cellulitis healed well.

DAH is a life-threatening condition which manifests as hemoptysis, anemia, diffuse lung infiltration, and acute respiratory failure. The diagnosis of DAH relies on clinical suspicion combined with laboratory, radiologic, and pathologic findings. Demonstration of hemosiderin laden macrophages in BAL is suggestive of DAH. Treatment is pulse methylprednisolone. Other options were cyclophosphamide, plasmapheresis and rituximab in selective cases.

Conclusions: DAH should be suspected in any patient with B/L alveolar infiltrates, hypoxemia, anemia, and hemoptysis. Good clinical history with appropriate lab investigations (auto immune work up), imaging and bronchoscopy helps in diagnosis.

Clinical experience of neuromodulatory treatment against 2 cases with unexplained chronic cough whose sputa yielded Bjerkandera adusta

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Background and Aim: Although cough guidelines recommend the use of centrally acting neuromodulators in unexplained chronic cough (UCC) patients, the efficacy for chronic cough patients with fungal colonization in the sputum has not been investigated in detail. Here, we report therapeutic experience of 2 patients with UCC whose fungal culture of sputum yielded Bjerkandera adusta, which has attracted attention because of its potential role in enhancing severity of cough symptoms.

Method: Case 1: A 54-year-old female patient with UCC was visited our hospital on August 19, 2016. Antifungal drugs showed efficacy with increased score of Leicester Cough Questionnaire (LCQ) from 11.7 to 15.5. After the eradication of B. adusta colonization, pregabalin (300 mg, 14 days) demonstrated substantial reduction of cough symptoms with 17.0 of LCQ score.

Case 2: A 53-year-old male UCC patient was visited our hospital on March 1, 2016. He was sensitized to B. adusta. Though gabapentin (1200 mg, 14 days) did not show efficacy, subsequent itraconazole therapy (50 mg, 14 days) showed improvement in cough symptoms with increased score of LCQ from 7.1 to 11.3.

Results: Our cases demonstrated that pregabalin showed sufficient efficacy against cough symptoms after the eradication of fungal colonization; however, gabapentin which was prescribed before the usage of antifungal drugs didn’t show any efficacy against allergic fungal cough who had been sensitized to B. adusta.

Conclusions: Clinical trials to evaluate the efficacy of neuromodulatory treatment against UCC whose sputum yielded B. adusta would be required in near future.

Utility of Bjerkandera adusta specific real-time PCR method for detection of itraconazole responders in unexplained chronic cough patients

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Background and Aim: We have reported that filamentous basidiozymetes (f-BM) could be involved in some unexplained chronic cough (UCC) patients, and antifungal agents could improve cough symptom (the disease concept is called as fungal-associated chronic cough: FACC). The current diagnostic criteria of FACC advocated by our group needs the isolation of environmental fungi, especially f-BM, from respiratory specimens. However, the isolation of f-BM by a conventional culture-based method is difficult. The aim of this study is to develop a real-time PCR method for detection of Bjerkandera adusta (Bj), which is the most common pathogen of FACC, from clinical specimens of UCC patients.

Methods: Bj specific real-time PCR method (Bj-RTPCR) was developed with internal transcribed spacer region of rDNA. We have retrospectively examined the utility of the method using sputa from UCC patients diagnosed in accordance with cough guidelines. Sputa from 21 patients were cultured, and the remaining samples were used for the PCR analysis.

Results: 14 cases in 21 UCC patients needed itraconazole for improving cough symptom. In such patients (itraconazole responders), f-BM was isolated from one case (7.1 %). On the other hand, Bj-RTPCR was positive of 10 cases (71.4 %). In 7 cases whose symptoms were improved without antifungal agents, f-BM was not isolated, and Bj-RTPCR was positive of only 2 cases.

Conclusion: Most of UCC patients with positive result of Bj-RTPCR needed itraconazole for improving the symptom. The method would be useful for detection of the antifungal agent’s responders among UCC patients whose sputa could not yield f-BM by a culture method.
Background and Aims: In a tuberculosis endemic country unexplained clinical presentations get diagnosed and treated as tuberculosis often, particularly as tuberculosis is known to be a great mimicker. However this is not without pitfalls and sometimes important other diagnoses are missed. We report a case of Brucellosis presented to a respiratory unit as a TB mimic.

Results: A 57 year old previously healthy patient was referred to the chest physician to exclude the possibility of Tuberculosis as the patient was having a PUO with two months history of dry cough, fever and body aches. Other systemic inquiry was unremarkable. There was no contact or past history of tuberculosis. The patient is a police officer working in a rural area and a non smoker. A thorough examination revealed no abnormality. The septic work up was negative. Tuberculosis screen including quantiferon TB test negative.

Table 1: Investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full blood count</td>
<td>WBC 9.25, 10^9/l N52% L33% E2.5%</td>
</tr>
<tr>
<td>ESR</td>
<td>120 mm 1^st hr</td>
</tr>
<tr>
<td>CRP</td>
<td>29</td>
</tr>
<tr>
<td>ANA</td>
<td>Negative</td>
</tr>
<tr>
<td>HIV screen</td>
<td>negative</td>
</tr>
<tr>
<td>Blood picture</td>
<td>Evidence of viral infection, no evidence of haematological malignancy</td>
</tr>
<tr>
<td>Bone marrow aspiration and biopsy</td>
<td>No evidence of malignancy</td>
</tr>
<tr>
<td>Malaria screen</td>
<td>negative</td>
</tr>
<tr>
<td>CT chest abdomen and pelvis</td>
<td>Negative except small para aortic lymphadenopathy</td>
</tr>
<tr>
<td>Bronchoscopy and BAL</td>
<td>Negative</td>
</tr>
</tbody>
</table>

With extensive investigations not yielding a diagnosis before starting a trial of anti TB treatment as is the norm, patients history was revisited. This revealed that while working in a rural area he had contact with a deer that lives in his work place which the patient used to feed and pet. This prompted testing for brucellosis. Agglutination Test for Brucella abortus became positive confirming a diagnosis of brucellosis.

The patient was treated with Doxycycline 100 mg bd for 6 weeks and Streptomycin 1g daily for 2 weeks, resulting in complete clinical and biochemical improvement.

Conclusions: This case illustrates the importance of keeping an open mind even when demographic and epidemiological data points towards a common illness, as rare diseases can also have common presentations. Conforming to a good clinical approach with meticulous history taking and a high index of suspicion leads to diagnosing rare yet significant diseases.
THE DASH PROJECT - AN INTERVENTION AIMED AT CHANGING PHYSICIANS’ PRACTICE OF INPATIENT OBSERVATION FOLLOWING ANTIBIOTIC DE-ESCALATION IN UNCOMPLICATED COMMUNITY ACQUIRED PNEUMONIA
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Background: Anecdotally, we have observed the practice of 24 hour in-hospital observation following de-escalation from intravenous (IV) to oral antibiotics in the management of community acquired pneumonia (CAP). This practice has a limited evidence base and can unnecessarily prolong length of stay.

Aims: We aimed to determine the prevalence of in-hospital observation following antibiotic de-escalation in uncomplicated CAP

Promote an early discharge policy following antibiotic de-escalation

Determine effect of this intervention on clinical practice in CAP for the subsequent year

Methods: An audit of uncomplicated CAP was performed using an E62C Diagnosis Related Group (DRG) across Eastern Health for June-September 2015 excluding hospital acquired, aspiration pneumonia, and residential facility patients. Patient records were retrospectively analysed to determine whether discharge was delayed for inpatient observation following antibiotic de-escalation. In April 2016, an education program was implemented to promote safe and early discharge on the day of de-escalation in clinically stable patients. A repeat audit was performed using the E62C DRG, for June-September 2016 to determine the effect on practice of our intervention.

Results: There were 62 (June-Sept 2015) and 110 (June-Sept 2016) admissions for the relevant DRG that met the inclusion criteria. Between audit periods, there was a non-significant trend to reduction in number of admissions where discharge was delayed following antibiotic de-escalation (18 (29%) vs. 21 (19%) admissions; p=0.18). There were no differences in bed days lost between audit periods (23 vs. 21 days; p=NS), or readmission rates.

Conclusion: For uncomplicated CAP, our results confirm that in-hospital observation following de-escalation to oral antibiotics occurs in one fifth of admissions. We observed a non-significant trend to improvement in this practice following an education program. This reduction did not result in bed day savings. Future work will concentrate on understanding clinician reasoning for this practice to inform education programs.

Background and Aims: Massive haemoptysis is defined as expectoration of large amount of blood, volumes ranging from 100ml-1000ml per day. We encountered an unusual scenario of a patient coughing out a lung tissue along with haemoptysis. We report the first case in literature of coughing out of lung parenchyma along with blood.

Methods: A 70 year old female presented with the history of breathlessness, cough with expectoration for past 6 months and history of fever for past 1 month. She had haemoptysis of around 50ml, frank blood, 3 episodes in last 6 hours, no past history of pulmonary TB, no history of trauma. On examination, she was poorly built and nourished, anaemic, tachypenic with Spo2 of 95% on room air. Rest of the examination was normal apart from crackles heard over bilateral infra scapular and infra axillary area. Suddenly patient had a bout of haemoptysis of around 500ml. While intubating the patient had another bout of haemoptysis of around 250 ml, along with that she coughed out a dark grey, spongy tissue. Patient immediately developed cardiac arrest and could not be revived. Medical autopsy was planned however patient’s bystanders denied consent. Gross specimen and histology pictures are below.

Results: Histopathological examination of tissue showed lung tissue with most of the alveoli dilated, ruptured and confluent.

Conclusions: To the best of our knowledge this is the first case ever reported on coughing out of one’s own lung tissue, which we wish to term as PNEUMOPTYSIS.
EFFECT OF NASAL HIGH FLOW SYSTEM ON OXYGENATION DURING SEDATION UNDER SPINAL ANESTHESIA IN ELDERLY PATIENTS

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Background and Aims: Intravenous sedation (IVS) is widely used to relieve patient’s anxiety during various procedures including surgery. IVS attenuates autonomic activation, which results in hemodynamic stability. However, the application of IVS carries some complications such as hypoxia and pulmonary aspiration. The application high flow nasal cannula (HFNC) in oxygenation of ICU or emergency patients with respiratory failure has significantly increased. In addition, HFNC has been reported to be effective measures of oxygenation in sleep apnea syndrome. This study investigated the effect of the HFNC on oxygenation in elderly surgical patients under spinal anesthesia combined with IVS.

Methods: Fifty patients were scheduled for the randomized controlled study. The interim analysis was done with first twenty enrolled patient. Twenty patients, age over 70, undergoing orthopedic or urologic surgery with spinal anesthesia combined with IVS were randomly allocated to mask oxygenation of 5L/min with spontaneous breathing (LF group, N=10) or HFNC system (Optiflow THRIVETM ) with oxygen administration rate of 50L/min (HFNC group, N=10). Intravenous sedation was induced by dexametomidine. Non-invasive mean blood pressure, heart rate, oxygen saturation (primary outcome parameter), and bispectral index values, arterial blood gas analysis were statistically analyzed. Incidence of below 93 % of oxygen saturation was check during sedation

Results: Compared with the LF group, HFNC group showed significantly high SpO2, and BIS was significantly low at 10 minutes after IVS (100.0±0.0 % vs. 96.6±1.5 %)(P<0.01). Incidences of below 93 % of oxygen saturation were frequently observed in the LF group (0 vs. 1.6 average-incidence per person).

Conclusions: This study suggests that use of the HFNC system can be effective in oxygenation and reduces the frequency of hypoxia during spinal anesthesia with intravenous sedation in elderly patients.

THE CLINICAL FEATURES OF PNEUMOTHORAX ARE COMPLICATED BY EATING DISORDERS

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Background: Eating disorders (EDs) involve extreme dietary restrictions or overeating, and include anorexia nervosa (AN) and bulimia nervosa. EDs are characterized psychologically by insufficient resistance to psychological stress, poor social adaptability and communication difficulties, and also physically by complications associated with the poor nutrition and tissue fragility, including emphysema and bullae. Pneumothorax (PTx) can also develop in EDs.

Aim: To evaluate the prevalence and prognosis of pneumothoraces in EDs.

Methods: We reviewed the medical records of ED patients that were hospitalised between April 2013 and March 2016. Results: 195 patients were admitted during the period, 3 of whom had PTx.

[Patient A] A 17-year-old woman with a 1-year history of AN (restricting type) was diagnosed with right pneumothorax with chest pain and dyspnea. The pneumothorax improved with 3-weeks rest without hospitalisation.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>Duration (days)</th>
<th>Subtype of EDs</th>
<th>Location of PTx</th>
<th>Degree of PTx</th>
<th>Complications</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>17</td>
<td>11</td>
<td>1</td>
<td>Restricting</td>
<td>Right</td>
<td>II° Rest</td>
<td>Osteoporosis</td>
<td>Improved</td>
</tr>
<tr>
<td>B</td>
<td>17</td>
<td>10</td>
<td>2</td>
<td>Binge eating/ purging</td>
<td>Right</td>
<td>II° Rest</td>
<td>Acute Pancreatitis</td>
<td>Deceased</td>
</tr>
<tr>
<td>C</td>
<td>35</td>
<td>15</td>
<td></td>
<td>Restricting</td>
<td>Left</td>
<td>II° Therapeutic thoracentesis</td>
<td>Hypoglycemic Coma</td>
<td>Improved</td>
</tr>
</tbody>
</table>

[Patient B] A 17-year-old woman with a 2-year history of AN (binge eating/purging type) was admitted to hospital with aspiration pneumonia, pulmonar y oedema, acute pancreatitis, intravascular coagulation and pancytopenia. Right pneumothorax developed but chest tube drainage was not performed due to her critical condition. The patient died 4 months later due to multi organ failure.

[Patient C] A 35-year-old woman with a 15-year history of AN (restricting type) was admitted to hospital with hypoglycemic coma and liver dysfunction.

THE CLINICAL FEATURES OF PNEUMOTHORAX ARE COMPLICATED BY EATING DISORDERS
dysfunction. Left pneumothorax occurred and progressed gradually. Therapeutic thoracentesis was performed successfully. No recurrence was observed.

Conclusions: In each case, the severity of the pneumothorax was grade 2, which, according to clinical practice guidelines, would ordinarily be an indication for chest tube drainage. Instead, each case was managed conservatively by prescribing rest or by performing therapeutic thoracentesis to remove the excess of air in the thoracic cavity.

Background and Aims: The occurrence of Acute Respiratory Distress Syndrome (ARDS) with Paroxysmal Nocturnal Hemoglobinuria (PNH) has been rarely if not encountered in literatures. Lung protective strategies for ARDS cannot be readily done due to patient's refusal to intubation.

Results: A case of a 79-yr-old male who came in with difficulty of breathing. He is a diagnosed case of PNH. On PE he was to be drowsy, febrile, in cardiopulmonary distress, no note of hypotension, with intercostal retractions, coarse crackles on both lung fields. There’s combined respiratory and metabolic alkalosis with mild hypoxemia at oxygen inhalation of 5 liters nasal cannula. He was advised intubation, but patient refused. Non-invasive ventilation (NIV) was given with settings of FiO2 of 50%, pressure support of 12 cmH2O and PEEP of 6 cmH2O, repeat ABG was combined respiratory and metabolic alkalosis with adequate oxygenation, and pH ratio was 180. X-ray showed bilateral confluent infiltrates.

Background: Pulmonary alveolar proteinosis (PAP) is a rare lung disease characterised by the accumulation of lipoproteinaceous material within alveoli, resulting in impaired gas exchange, and in some cases, respiratory failure. PAP occurs in three forms: congenital, autoimmune, and secondary, associated with haematological malignancies, toxic inhalational exposures and various opportunistic infections. Here, we present the case of a 65-year-old lady with progressive hypoxaemic respiratory failure and dense bilateral airspace consolidation due to secondary PAP on a background of advanced myelofibrosis. Initially, with uncertain diagnosis, she was treated with high dose steroids and broad-spectrum antibiotic therapy. Following inpatient referral to a tertiary hospital, she had progressive deterioration and the requirement for intensive care support and high-flow nasal prong oxygenation. A diagnosis of PAP was established after multi-disciplinary review of previous transcutaneous and transtracheal biopsies. She proceeded to bilateral whole lung lavage (WLL) under general anaesthesia with veno-venous extra-corpooreal membrane oxygenation (ECMO) support, leading ultimately to marked subsequent clinical and radiological improvement.

Results: Each lung was lavaged with five litres of normal saline, in conjunction with manual percussion delivered by a physiotherapist team. Subsequent to the procedure, she was able to wean to low-flow oxygen via nasal cannulae, with significant clearing of the dense radiographic infiltrates. In conjunction, her underlying myelofibrosis was treated with ruxolitinib and intermittent hydroxyurea. She subsequently had two further admissions over the next six months with disease relapse and respiratory failure, each time successfully treated with WLL with ECMO.

Conclusion: Whole-lung lavage with veno-venous ECMO represents a novel approach to management of this rare and complex lung disease. Recurrent lavage was effective and led to improved symptoms and quality of life for this patient with severe pulmonary alveolar proteinosis. The use of veno-venous ECMO support enabled the procedures to be carried out more safely without producing worsening, life-threatening hypoxaemia.

Background: Intestinal lung disease (ILD) is a serious side effect that can be caused by a wide range of drugs including antineoplastic agents and associations with biological products. We investigated drug-induced lung injuries, including drugs to be treated, image patterns, treatments, etc.

Methods: Some reported cases of drug-induced lung injury suggest new anti-neoplastic agents and associations with biological products. We investigated drug-induced lung injuries, including drugs to be treated, image patterns, treatments, etc.

Results: There were 20 cases, ages 43 to 85 years old, 9 males and 11 females. As suspected drugs, 9 anticancer drugs were the most common, and others were HMG-CoA reductase inhibitors and traditional Chinese medicines. The period from the start to the onset of symptomatic treatment ranged from 10 days to 1461 days, but most occurred within 3 months. DLST measurement was 35%, and bronchoscopy was performed 45%. There was no characteristic tendency in peripheral eosinophil ratio or eosinophil ratio in bronchoalveolar lavage fluid. Although image findings were observed for NSIP pattern, OP pattern, AEP pattern, some were difficult to judge. Treatment was carried out in 13 patients with steroid pulse therapy, and 3 cases were improved only with cessation of...
drugs to be treated. Although outcome was improved in response to treatment in the majority of cases, two cases of death were also observed.

Conclusion: Drug lung injury has been reported in recent years, cooperation with each department is indispensable, and further examination such as a pattern which is difficult to treat is reported and reported.

PROPORTION AND CLINICAL CHARACTERISTICS OF ASTHMA-COPD OVERLAP (ACO) IN CHINA: A NON-INTERVENTIONAL STUDY

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Background and Aim: As Asthma-COPD Overlap (ACO) is a relatively new term and it’s still poorly recognized in China, further research is needed to improve clinical understanding and optimize the disease management. This study aims to investigate the distributions and characteristics of patients with ACO over age 40 with airflow limitation in China.

Methods: A total of 2,003 patients over age 40 with airflow limitation (post-BD FEV1/FVC<0.7) in China tier 3 hospitals were included in this multicenter (20 sites), cross-sectional non-interventional study (NCT02600221) from December, 2015 to October, 2016. Disease diagnosis and management were under routine practice. The evaluation was based on GOLD 2015.

Results: Of 2,003 patients, 37.4%, 48.5% and 14.1% were evaluated as ACO, COPD and asthma, respectively. The diagnostic rate of ACO patients was only 6.0%(45749), and 65.3%, 37.7%, 25.4% and 17.5% of ACO patients had been diagnosed as asthma, COPD, chronic bronchitis and emphysema, respectively. The exacerbation rate of ACO in previous 12 months was as high as 42.6% (319749) with average 2.2±2.2 times/person-year compared to COPD (40.7%; 2.0±1.6 times/person-year) or asthma (33.9%. 2.1±1.9 times/person-year). The proportion of patients classified into high-risk group (group C+D) with ACO and COPD was 57.2% and 66.5% according to GOLD 2015. About 33.0% of ACO patients did not receive pharmaceutical treatments. Among 749 ACO patient, only 51.1% were treated with ICS/LABA, while 25.1%, 14.8% and 14.4% were treated with anticholinergics, leukotriene receptor antagonists and methylxanthines (overlapping prescriptions were presented).

Conclusion: Nearly two-fifths of patients over age 40 with airflow limitation in this study were ACO patients with higher exacerbation rate. However, ACO patients did not receive adequate treatment due to low diagnostic rate. Therefore, ACO patients in China are in great need of accurate diagnosis and standard management.

A COMPARATIVE EVALUATION OF DLCO IN PATIENTS OF ACOS, ASTHMA, AND COPD

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Background and Aim: ACOS (Asthma-COPD overlap syndrome) is relatively new clinical entity and has common features of both asthma and COPD. Measurement of DLCO (diffusing capacity for carbon monoxide) helps to distinguish between emphysema and other causes of chronic airway obstruction. Emphysema lowers the DLCO and asthma frequently increases the DLCO. In this study we have tried to evaluate and compare the DLCO in ACOS patients with that in asthma and COPD patients.

Methods: This study was conducted in the department of TB and respiratory Diseases, J.N.Medical college, AMU, Aligarh. A total of 219 patients were included in this study. There were 115 patients of ACOS, 54 patients of asthma and 50 patients of COPD. They were diagnosed as per GINA and GOLD guidelines. DLCO of patients was measured using Easy One Pro System developed by Easy One Pro medical technologies, Switzerland. Statistical analysis of results was done using SPSS version 21. The mean values of DLco of the three groups were compared with ANOVA test.

Results: DLCO (mean±SD) was maximum, 97±12.60 in asthma patients, minimum 58±14.50 in COPD patients while it was 61±16.59 in ACOS patients. DLCO in 74.8% patients of ACOS was found below normal (41-80% of predicted). Very low values (21-40% of predicted) were found in 14.6% ACOS patients. In most of the asthma patients DLCO was above 80% of predicted. It was more than 100% in 44.4 patients of asthma patients. In 78% COPD patients DLCO was low in the range of 41-80% of predicted. A very low DLCO 21-40% was found in 14% COPD patients.

Conclusion: Though ACOS has features of asthma but as far as the DLCO of lungs is concerned it is not increased as in cases of asthma. There is no significant difference in DLCO values in ACOS and COPD.

IMPACT OF CORRECT INHALATION TECHNIQUE ON SEVERITY OF OBSTRUCTION AND QUALITY OF LIFE IN PATIENTS OF OBSTRUCTIVE AIRWAY DISEASE

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Background and Aim: The aim of this study was to evaluate the impact of rectification of inhalation technique on severity of obstruction (FEV1) and quality of life measured by Asthma Control Test (ACT) and COPD Assessment Test (CAT) in patients of Asthma and COPD respectively.

Methods: Patients who were symptomatic (from outside our institute) despite being already diagnosed as Asthma/COPD and prescribed inhaled steroids/bronchodilators in optimal dosage were included. Severe persistent asthma and GOLD stage D COPD were excluded as they needed stepping up of treatment immediately. Enrolled patients underwent spirometry and filling up of ACT/CAT questionnaire in asthma and COPD respectively at 0 weeks and then at 4 weeks after rectifying the inhalation technique. Inhalation technique was cross checked as per steps laid down in National Asthma Council Australia. The patients who lost to follow up during the 4 weeks were excluded.
Results: In 33 Asthma patients, mean FEV1 improved from 2.01±0.41 L (at 0 weeks) to 2.09±0.43 L (at 4 weeks). Mean difference was -0.08 (CI -0.12 to -0.04) and p value was <0.001 (significant). Mean ACT score was 17.85±2.13 (at 0 weeks) which improved to 20.82±1.79 (at 4 weeks). Mean difference was -0.29 (CI -3.62 to -0.3) and p value was <0.001 (significant). In 21 COPD patients, mean FEV1 improved from 1.51±0.37 L (at 0 weeks) to 1.54±0.43 L (at 4 weeks). Mean difference was -0.03 (CI -0.08 to -0.018) and p value was 0.211 (not significant). Mean CAT score was 20.00±3.87 (at 0 weeks) which improved to 18.17±4.03 (at 4 weeks). Mean difference was 1.9 (CI 0.676 to 3.13) and p value was <0.001 (significant).

Conclusion: Demonstration and cross checking of correct inhalation technique is an indispensable part of prescription of inhaled medication.

EARLY INTERVENTION OF PULMONARY REHABILITATION FOR ELDERLY PATIENTS WITH ACUTE RESPIRATORY FAILURE OR EXACERBATION OF CHRONIC RESPIRATORY DISEASE : A RETROSPECTIVE ANALYSIS
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Background and Aims: Effects of pulmonary rehabilitation (PR) is established in improvement of exercise tolerability, health-related quality of life and symptoms of chronic respiratory disease. Aging of the population and increase of burden for insurance associated with it, are serious issues nowadays in Japan. However, the effect of early intervention of PR for elderly patients with acute respiratory failure (ARF) or exacerbation of chronic respiratory disease (ECRD) is unclear. We hypothesized that early intervention of PR for elderly patients with ARF or ECRD would improve physical function and conduct this retrospective analysis.

Methods: Clinical data were obtained from medical records between April 2015 and May 2017. Patients aged 75 years or more with ARF or exacerbation of ECRD were evaluated. Patients who were started PR within 48 hours from admission were defined as the early PR group, whereas patients who were started PR after 48 hours of admission were defined as the usual care group. Barthel index (B.I.) as a scale of physical function, hospital days, mortality were compared and analyzed between two groups.

Results: 36 (34.0%) patients were assigned to the early PR group and 70 (66.0%) patients were assigned to the usual care group. No significant difference was seen in improvement of each B.I. before and after PR between two groups (20.0 vs. 26.0, p=0.35). Mortality was not significantly different (1 (2.8%) vs. 5 (7.1%). OR, 0.35, 95% C.I. 0.04-3.16, p=0.31), however duration of hospital days was significantly decreased in the early PR group (22.0 vs. 26.0, p=0.025).

Conclusions: Early PR for ARF or ECRD in elderly patients decreased duration of hospital days without increase of mortality although it could not improve physical function compared with usual care.

Clinical Relevance Between Respiratory Muscle Strength and Postoperative Morbidity in Patients with Non-Small Cell Lung Cancer
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Background and Aims: Since surgical resection is the treatment of choice for localized non-small cell lung cancer (NSCLC), developing an effective strategy to reduce the risk of postoperative complications caused by insufficient preoperative preparation is important. As such, we have implemented a comprehensive preoperative pulmonary rehabilitation program aimed at strengthening body and respiratory muscle through intensive nutritional support. Since the clinical implications of respiratory muscle strength in patients scheduled to lung resection has not yet been clearly elucidated, we explored whether respiratory muscle strength relates to postoperative morbidity in NSCLC patients.

Methods: From 2011 to 2016, 207 patients underwent standard lobectomy for NSCLC. Clinical characteristics and perioperative factors (including respiratory muscle strength) were assessed to evaluate for clinical relevance between respiratory muscle strength and postoperative morbidity.

Results: The average age in 130 men (63%) and 76 women (37%) was 68.4±7 years. The median %predicted maximal expiratory pressure (%predicted-PExmax) and %predicted maximal inspiratory pressure (%predicted-PInmax) were 101.2–1.24, 169.39–7.43, respectively.

Conclusions: The results of this study indicate that PExmax is significantly related with postoperative morbidity in patients scheduled to undergo pulmonary resection for NSCLC. Future studies are required to investigate the clinical efficacy of preoperative interventions intended to strengthen respiratory muscle with special emphasis on creating a clinically beneficial preoperative rehabilitation program.

Table: Univariate and multivariate logistic regression analyses for postoperative morbidity

<table>
<thead>
<tr>
<th></th>
<th>Odds 95%CI</th>
<th>P value</th>
<th>Odds 95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.95</td>
<td>0.91-4.57</td>
<td>0.0884</td>
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</tr>
<tr>
<td>Gender</td>
<td>3.19</td>
<td>1.50-7.34</td>
<td>0.0020</td>
<td>1.78</td>
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<tr>
<td>Approach</td>
<td>0.27</td>
<td>0.08-0.77</td>
<td>0.0150</td>
<td>0.66</td>
</tr>
<tr>
<td>Operative time</td>
<td>3.54</td>
<td>1.60-7.76</td>
<td>0.0020</td>
<td>1.38</td>
</tr>
<tr>
<td>Blood loss</td>
<td>3.53</td>
<td>1.60-7.76</td>
<td>0.0020</td>
<td>2.27</td>
</tr>
<tr>
<td>%VC</td>
<td>2.72</td>
<td>1.41-5.38</td>
<td>0.0027</td>
<td>1.75</td>
</tr>
<tr>
<td>FEV1%</td>
<td>3.05</td>
<td>1.56-6.01</td>
<td>0.0012</td>
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<tr>
<td>%predicted-PExmax</td>
<td>3.21</td>
<td>1.66-6.37</td>
<td>0.0005</td>
<td>2.22</td>
</tr>
<tr>
<td>%predicted-PInmax</td>
<td>1.24</td>
<td>0.65-2.39</td>
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</tbody>
</table>

Abstracts
Background and Aims: Although daily physical activity and respiratory muscle strength has been intrinsically measured objectively in non-small cell lung cancer (NSCLC), these markers may be useful for predicting morbidity and short-term outcome after pulmonary resection for NSCLC. Thus, we aimed to investigate the relationship between daily physical activity and respiratory muscle strength in patients scheduled to undergo surgery for NSCLC.

Methods: This prospective observational study included 59 individuals with NSCLC. The number of steps and energy consumption per day (daily physical activity) were recorded 2–4 weeks preoperatively. Respiratory muscle strength (maximal expiratory pressure (PEmax) and maximal inspiratory pressure (Pinmax)) was measured before starting to record daily physical activity. The clinical relevance between daily physical activity and respiratory muscle strength was evaluated.

Results: The mean age in 29 men and 30 women was 73 years. The average number of steps and energy consumption per day were 5,396 ± 250 steps and 117.0 ± 6.6 kcal per day, respectively. A statistically significant relationship was detected between age and daily physical activity. PEmax was marginally related with number of steps (r = 0.24, p = 0.0656), and there was no statistically significant relationship between other values of pulmonary function (VC, %VC, FEX1.0, FEV1.0%) and daily physical activity. Additionally, there was no significant relationship between other values of pulmonary function (VC, %VC, FEX1.0, FEV1.0%) and daily physical activity.

Conclusions: The results of this study indicate that daily physical activity is significantly related with PEmax in patients who are scheduled to undergo surgery for NSCLC. Future studies are required to investigate the efficacy of interventions to increase physical activity and respiratory muscle strength to reduce morbidity after pulmonary resection for NSCLC.

Figure: Relationship between PEmax and energy consumption

CLINICAL RELEVANCE BETWEEN DAILY PHYSICAL ACTIVITY AND RESPIRATORY MUSCLE STRENGTH IN PATIENTS SCHEDULED TO UNDERGO SURGERY FOR NON-SMALL CELL LUNG CANCER

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COMPREHENSIVE PREOPERATIVE PULMONARY REHABILITATION INCLUDING INTENSIVE NUTRITIONAL SUPPORT DECREASES POSTOPERATIVE MORBIDITY RATE IN THE ELDERLY, LOW BODY WEIGHT, SARCOPENIA-RELATED PATIENTS WITH LUNG CANCER

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AUDIT OF CT PULMONARY ANGIOGRAM OVER 6 MONTHS AT WAGGA WAGGA RURAL REFERRAL HOSPITAL (WWRRH)
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Background and Aims: Venous thromboembolism (VTE) is a feared and well recognised complication of hospitalisation and pulmonary embolism (PE) can result in death. The incidence is one hundred-fold higher than in the community. Computed tomographic pulmonary angiography (CTPA) is the diagnostic method of choice for PE, and is often employed due to its availability after hours, in addition to the information it can give regarding alternative diagnoses. There are however potential disadvantages including radiation exposure, contrast administration reactions and cost. The Royal College of Radiologists (UK) recommend that for referral for CTPA there should be assessment of pre-test probability of PE (using a validated clinical score such as WELLS) and use of d-dimer. The accepted yield of CTPA for PE is 15.4-37.4% with alternative diagnoses in up to 56%. Prevention of hospital VTE is the focus of a 2015 Clinical Excellence Commission Focus report and assessment of VTE risk and appropriate thromboprophylaxis prescription is NSW Health Policy (PD2014_032). It is also the subject of multiple national and International guidelines and regular monitoring of compliance with VTE prescribing is recommended.

Methods: A retrospective clinical audit of CTPA over a 6-month period at a Rural Referral Hospital.

Results: This study will provide local audit data on the yield of CTPA and also provide information on the rates of VTE risk assessment and prescribing practice in those patients with proven PE.

Conclusions: Clinical audit is an essential component of quality assurance, can lead to an understanding of local practice, and guide future quality improvement.

THE EFFECTS OF ANTHOCYANIN OF PURPLE CASSAVA ON THE LEVEL OF SPUTUM MDA AND NO IN ASYMPTOMATIC SMOKERS
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Background and Aim: Cigarettes consist of 4000 substances which can induce oxidative stress. The high free radical level in blood of smokers leads to various diseases, such as COPD, lung cancer, and asthma exacerbation. In lung, oxidative stress causes lipid peroxidation which produces MDA, which in tum leads to DNA damage, gene mutations, and loss of repair. Cigarettes also reduce the activity of endogenous Nitric Oxide (NO) which results in pulmonal abnormalities. This damage can be prevented with antioxidant supplements. Anthocyanin of purple cassava is antioxidant that can prevent oxidatif stress. The aim of this study were to determine the effects of anthocyanin of purple cassava to sputum MDA and NO of asymptomatic smokers.

Methods: This experimental randomized pre-post control group design study was conducted in dr. Soetomo Hospital Surabaya, Indonesia. The subjects were male, 20-50 years old with asymptomatic moderate smokers and met the inclusion-exclusion criteria. Subjects were divided into treatment group receiving 15 ml purple cassava juice twice/day, and control group receiving 15 ml placebo twice/day. The effects were evaluated on the next 14 days

Results: This study demonstrated that sputum MDA level in treatment group decreased significantly (pre 418.43 ng/ml; post 250.91 ng/l, p 0.000) compared to that of the control group (pre 544.15 ng/l; after 574.21 ng/l). The sputum NO level increased but did not significantly (p>0.05) in the both treatment groups (pre 93.77 ng/l; post 131.57) and the control group (pre 104.14 ng/l; post 126.91 ng/l). Compared to the control group, the treatment group had a higher level of NO (38.3 ng/dl and 22.76 ng/dl, respectively).

Conclusion: Administration of anthocyanin of purple cassava significantly increased sputum MDA level of asymptomatic moderate smokers. There was no significant increase of NO level in treatment and control groups.

THE EFFECTS OF ANTHOCYANIN OF PURPLE CASSAVA ON THE LEVEL OF SPUTUM MDA AND NO IN ASYMPTOMATIC SMOKERS

USEFULNESS OF QSOFA WITH LACTATE TO PREDICT MORTALITY IN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA IN THE EMERGENCY DEPARTMENT
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Background: Community-acquired pneumonia is a major source of sepsis, and sepsis-related acute organ dysfunction determines patient’s mortality. Therefore, early risk stratification using clinical scores and subsequent evaluations for organ dysfunction to identify high-risk patients should be the standard of care. qSOFA is a new screening system for sepsis that exhibits prognostic performance equal to the full SOFA for patients with suspected infection outside the ICU, but the predictive value of qSOFA for mortality in patients with pneumonia is not clear. We investigated the predictive value of qSOFA and other severity scores relative to in-hospital mortality in patients with CAP in the emergency department.

Methods: From January to June 2015, we retrospectively analyzed 443 patients clinically diagnosed with CAP in the ED. We compared the performances of various predictors and qSOFA for the prediction of inhospital mortality.

Results: Of the 443 patients, 44 (9.9%) died. In ROC analysis, the areas under the curves of qSOFA, CURB-65 and PSI class for mortality were 0.720, 0.652 and 0.686, respectively. There were significant differences among qSOFA and SOFA (AUC, 0.720 and 0.845, respectively). The AUC of qSOFA with lactate was 0.828, which was not significantly different from that of SOFA. The sensitivity of qSOFA with lactate was 71.4% and the specificity was 83.2%.

Conclusion: Determination of lactate levels at admission significantly improved the prognostic value of qSOFA scores in CAP patients similar to that of SOFA. Therefore, qSOFA with lactate should be considered rapid and broadly available additional criteria for risk assessments in patients with CAP.

THREE CASES OF ACUTE CORONARY SYNDROME DURING BRONCHOSCOPY
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Bronchoscopy and Interventional Techniques
Background and Aims: Bronchoscopy (BS) is generally considered safe. Pneumothorax is reported to be a major complication with the rates of 3.5-7.5% and cardiovascular complications are rare. A aim of this study is to investigate the clinical characteristics of the patients who developed acute coronary syndrome (ACS) during BS.

Methods: We retrospectively analyzed the clinical feature of the cases who developed ACS during BS. Between 2013 April and 2016 March, we performed 1608 BSs. Of those, fluoroscopy was concur- rently used in 794 cases.

Results: Three cases of ACS during BS were observed in this period.

Case 1: The patient was a never smoker 74-year-old male with hyperlipidemia referred to our hospital for evaluation of pulmonary nodule. After termination of trans bronchial biopsy (TBB), he developed sudden hypotension and bradycardia with elevation of ST in electrocardiogram (ECG). ACS was suspected and transferred to emergency room (ER). Coronary angiography (CAG) showed normal study and his symptoms was sup- posed to be transient vasospasm.

Case 2: A 59-year-old, ex-smoker, hyperlipidemia, male was sus- pected of lung cancer. TBB was performed and he felt anterior chest pain with bradycardia. She was suspected to acute myocardial infarction because ST elevation was observed in multiple ECG leads. CAG demon- strated coronary stenosis of 50-75%.

Case 3: A 73-year-old, current-smoker, hypertensive, hyperlipidemic, female detected abnormal shadow on chest X ray. TBB was performed and she developed chest pain and bradycardia. ST elevation and com- plete A-V block were observed in multiple ECG leads. Percutaneous coro- nary intervention was performed because CAG showed significant stenosis to coronary arteries.

Conclusions: ECG before TBB is not routinely recommended, once ACS is suspected, the ECG is helpful for following treatments. Although the rate of ACS was only 0.4% in this study, the ECG before TBB might be considered.

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CLINICAL ANALYSIS OF COMPARISON BETWEEN FLEXIBLE BRONCHOSCOPY AND VIRTUAL BRONCHOSCOPY IN FOREIGN BODY ASPIRATION

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Background: Foreign body aspiration is an uncommon entity in adults, but it is sometimes life-threatening condition. It requires immediate intervention. Virtual bronchoscopy (VB) is a noninvasive technique which provides an intraluminal view of the tracheobronchial tree. We investi- gated the cases with foreign body removed by flexible bronchoscopy and its findings were compared with VB findings.

Methods: We evaluated adult foreign body cases which underwent flexible bronchoscopy between June 2010 and May 2017 by using data of bronchoscopy database. Demographic, clinical, and bronchoscopy data were analyzed. From these data collected, we also represented VB through three-dimensional analysis with Zostation2 based on multidetector computed tomography (MDCT) images to evaluate its use- fulness by comparing with actual bronchoscopy findings.

Results: During the study period, total of 3022 flexible bronchos- copies were performed. Of these, 8 subjects (average age of 74 year old, 7 males) who had undergone bronchoscopy for foreign body aspiration were identified. Foreign bodies were located at right bronchus in 5 cases, and at left bronchus in 3 cases. Foreign bodies were dental materials (2 artificial teeth and 2 teeth) in 4 patients, food aspiration (tuna sushi, sliced raw yellowtail, antenna of lobster) in 3 patients, and tablet form aspiration in one patient. In all cases bronchoscopy were performed safely without adverse events and alligator forceps or straight grasping forceps or snare were used to remove foreign body.

Three cases underwent MDCT and were conducted to VB. VB could be helpful to identify the exact location and approximate feature size as foreign body.

Conclusion: Flexible bronchoscopy was useful and tolerable tool to remove foreign body. VB images were proved to be a valuable method for diagnosis of the patients with suspected foreign body. VB provided accurate information for the diagnosis and treatment due to foreign body, which was useful in decision making.

AP370

TRANSCUTANEOUS MONITORIZATION OF COMBINED CARBONDIOXIDE PRESSURE AND OXYGEN SATURATION DURING FIBEROPTIC BRONCHOSCOPY

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Background and Aims: The aim of the present study was to assess the effects of interventions during bronchoscopy to the ventilation and the risk factors related to both interventions and patient’s anthropo- metric measures with a device measuring both oxygen saturation and car- bodioxide tension transcutaneously (probe placed to ear lobe) during fiberoptic bronchoscopy which is frequently used in pulmonology practice.

Methods: 81 patients were included in the study, 7 patients were excluded because of insufficient recordings. Basal, mean, peak and min- mum measures of SaO2 and PaCO2 during bronchoscopy were analyzed and we tried to determine the risk factors for hypoventilation.

Results: Mean PaCO2 was 37.09±5.6; mean difference was 3.25±2.12 (increased during bronchoscopy). Mean SaO2 was 95.95±2.27; mean difference was 5.11±3.17 (decreased during bronchoscopy). Measured mean and peak CO2 were much higher in men. In whole group, in the patients with the smoking history of 20 packages-year and more, similarly PCO2 measures were higher compared to non- smokers or less smokers. In the patients with endobronchial lesion and mass, SaO2 measures were lower during bronchoscopy. There was no significant relationship between ventilation measures and existent pleural effusion and COPD history. We also determined that, duration of FOB over than 15 minutes and complex interventions like biopsy, brushing are related with lower SaO2 measures.

Conclusions: Ventilation changes during fiberoptic bronchoscopy are multifactorial issues. The best indicator for ventilation is CO2 and it is obvious that especially monitorization of PaCO2 is so important to detect hypoventilation. In order to predict ventilation problems in the patients planning to get in FOB, we determined some risk factors as a result to our study. We recommend that in the male patients with endobronchial lesion, smoking history, and in case longer duration of FOB, saturation together with CO2 must be monitored.
A NEW SERVICE MODEL TO ENHANCE SERVICE DEMAND OF PATIENT RECEIVED INTERVENTIONAL BRONCHOSCOPY

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Background: Interventional Bronchoscopy (FOB) is the most widely used invasive tool for diagnosis and treatment of bronchopulmonary diseases. A new service model—Fiber-optic-Bronchoscopy Preparation Nurse Clinic (FPNC) was established since 2013 to coordinate and facilitate patient’s care scheduled for FOB.

Aims: To evaluate the efficiency and effectiveness of FPNC.

Methods: It’s a retrospective study to evaluate the FPNC from 1st January 2013 to 30 September 2016. An individual consultation interview was offered after a group-educational session which includes 1) Indication and benefit of FOB 2) Preparation, assessment and observation before and after FOB 3) Possible complication and attention after discharge

During consultation interview, we perform respiratory assessment, educate symptom management and offer emotional support. Consent form, imaging and blood investigations prior FOB would be arranged. Instruct with a note to withhold certain drugs would be given. A help-line was provided for enquiry or procedure refusal. Those defaulted FPNC would be followed and reconfirmed for attendance. Multidisciplinary FOB conference (MDFC) will be attended and discussed to coordinate the further specific care prior or after FOB.

Results: 656 patients attended FPNC and 8.5% either refused (45%) or performed FOB in private hospitals. 9% of the scheduled appointments were advanced earlier into the defaulted time-slot. 2.1% eventually agreed for FOB after attending FPNC. 25.8% and 13% were admitted or performed FOB in private hospitals. 9% of the scheduled appointments were advanced earlier into the defaulted time-slot. 2.1% eventually agreed for FOB after attending FPNC. 25.8% and 13% were admitted or performed FOB in private hospitals.

Conclusion: FPNC is a new service model to enhance patient-centered focus and lead to improvements in healthcare quality and outcomes.

ENDOBRONCHIAL OBSTRUCTION CAUSED BY A FOREIGN BODY ASPIRATION

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Background and Aims: Foreign body aspiration causes lethal acute respiratory failure (asphyxia) when the obstruction near the throat at the level of the trachea occurs. On the contrary, foreign bodies that can advance to lower levels of the tracheobronchial tree may cause respiratory system problems due to deterioration of airway due to endobronchial obstruction distal to the obstructed region and preparation of infection.

Methods: A 79-year-old woman presented to our clinic for complaints of wheezing and coughing for a month. She told a history of swallowing a bone in the soup one month ago.

Results: Thorax CT revealed a calcified dendrite with a diameter of 12 mm in the right lower lung lobe bronchus (picture 1, 2). Fiber optic bronchoscopy showed an organized structure with a white colour that narrowed to the right intermedia bronchus. This tissue was not removed with aspiration and forceps, and a large number of biopsies were taken from this area. For example, pathology was interpreted in favour of fibrinous exudate and granulation tissue. The patient was directed to the external center for rigid bronchoscopy for foreign body. As a result of rigid bronchoscopy, the foreign body was removed (figure). In the patient who had no radiopaque dancing on the chest X-ray of the control, the complaints of coughing and wheezing were completely gone.

Conclusions: The possibility of foreign body aspiration should come to mind and considered, especially in children and elderly patients with a long-standing cough, and detailed history should be taken. The presence of localized monchus on physical examination may be indicative of endobronchial obstruction. Rigid bronchoscopy in such cases, where foreign body aspiration is suspected, should be considered as the first choice in terms of both diagnostic and foreign body removal.
A CASE REPORT OF STRIDOR AND RESPIRATORY FAILURE
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Background and Aims: Tracheobronchomalacia (TBM) results from structural and functional abnormalities of the respiratory system. It is characterized by excessive dynamic expiratory airway collapse at least 50% of the cross-sectional area of the trachea and main bronchi.

Methods: A 81 year old man was referred to emergency department with cough, purulent sputum, dyspnea and stridor since one week. He had a medical history of Chronic obstructive pulmonary Disease (COPD) on inhaler medications. On examination he had dyspnea, tachypnea, central cyanosis and reduced air entry on bilateral lower lobe. The arterial blood gas analysis showed hypercarbia with respiratory acidosis. (pH7.23, pCO2=78mmHg, pO2=65mmHg, HCO3=38mmol/l, sO2=90%). He was intubated and started on mechanical ventilation followed by tracheostomy in view of difficult weaning. Computed tomography (CT) of the chest revealed marked dynamic expiratory airway collapse. He underwent bronchoscopy which revealed marked expiratory collapse, with contact between the anterior and posterior walls of the trachea, and extending into both main bronchi. These characteristics were compatible with TBM. Subsequently, a Dumon Y stent was placed by means of rigid bronchoscopy. After the procedure, he was gradually improved and discharged.

Results: TBM in adults can be classified into primary (congenital) and secondary (acquired) forms. Congenital causes include polychondritis, Mounier-Kuhn Syndrome while acquired causes include post-traumatic, chronic infection and inflammation and extrinsic from aneurysms, tumours, cysts and abscesses. The TBM is considered mild if the obstruction is one-half of the lumen, moderate if it is three-quarters and severe if the anterior and posterior walls touched. Silicone stents were preferred to metallic one to keep the malacic airway patent.

Conclusions: TBM is a rare and sometimes under-diagnosed disease. In COPD patients, stridor and dyspnea due to acute respiratory failure might be considered as important signs relating to TBM.

ENDOBRONCHIAL LEIOMYOMA: A RARE FORM OF BRONCHIAL TUMOR
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Background and Aims: An endobronchial leiomyoma is a rare benign tumor of the bronchial tree. It occurs from the smooth muscle along the tracheo-bronchial tree or within the lung parenchyma. It presents less than 2% of all benign lung tumors. To date almost less than 60 cases have been reported in the world literature. In this paper, we present a case report of a rare benign lung tumor in younger individuals.

Methods: This is a case report of a 24 year old female, known asthmatic and a 10-pack year smoker, with no family history of malignancies, presenting with acute onset fever, productive cough and shortness of breath, with no resolution despite 7 day course of oral antibiotics.

Results: Chest radiograph showed hazy density of right lower lung. Plain high resolution computed tomography of the chest, showed mucus plugging/impaction in the right bronchus intermedius causing obstructive atelectasis of the right middle and lower lobes. Patient underwent flexible bronchoscopy which showed a sessile endobronchial mass at the right bronchus intermedius, attempt to remove the mass by forceps extraction was unsuccessful. Endobronchial mass biopsy was done which revealed a Spindle cell tumor. Further, immunohistochemical stains showed negative for S-100 and positive for SMA consistent with Leiomyoma. She underwent rigid bronchoscopy with endobronchial mass excision. On follow-up, patient reported symptom improvement.

Conclusions: Endobronchial Leiomyoma is a rare and benign tumor that can occur in younger individuals, awareness and prompt diagnosis can lead to a very good clinical outcome.
NEW RISK FACTORS FOR DIAGNOSTIC FAILURE OF CT-GUIDED PERCUTANEOUS CORE NEEDLE BIOPSY OF THE LUNG
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Background and Aim: Percutaneous core needle biopsy (PCNB) of the lung is a well-established method for diagnosis of pulmonary nodules. Diagnostic accuracy for lung lesions by CT-guided PCNB ranges from 84% to 97%. The purpose of this study was to evaluate risk factors influencing the diagnostic failure of CT-guided PCNB of the lung.

Methods: Two hundred thirty-eight cases of lung nodules that received CT-guided percutaneous core needle biopsy were included in this study. We classified the cases into a “diagnostic success” group (true-positive and true-negative) and a “diagnostic failure” group (false-positive and false-negative) to evaluate the factors affecting diagnostic failure in CT-guided PCNB of the lung.

Results: The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy for the diagnosis of malignancy by CT-guided PCNB were 94.4% (152/161), 100% (77/77), 100% (152/152), 89.5% (77/86), and 96.2% (229/238). To evaluate the factors contributing to diagnostic failure, patient age, sex, pulmonary function tests, final diagnosis, lesion location, size, distance from skin to target lesion, distance from pleura to target lesion, and number of tissue sampling were analysed. The significant risk factors for diagnostic failure were as follows: male sex (p=0.029), lesions in the lower lobe (p=0.035), malignant lesions (p=0.033), and shorter distance from skin or pleura to target lesion (p=0.001).

Conclusion: Our results suggest that male sex and shorter distance from skin or pleura to target lesion can serve as new risk factors to predict the probability of diagnostic failure in CT-guided PCNB of the lung.

CORRELATION BETWEEN MAGE-A3 EXPRESSION WITH HISTOPATHOLOGIC FINDING FROM CORE BIOPSY SPECIMENS
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Background and Aim: Most of cancer patients seek the treatment in already advanced diagnosis with high mortality rates. This diagnostic delay is due to difficulty in determining the tumor type and staging. Tumor markers has promising diagnostic method for lung cancer. The expression of Melanoma Associated Antigen (MAGE) is reported about 30-50% in lung cancer and MAGE A-3 occupies the highest expression in Non-Small Cell Lung Cancer (NSCLC). This study analyze association between the expression of MAGE A3 and histopathology type of core biopsy specimens in NSCLC patients. The aims of this study were to determine correlation between Mage-A3 expression with histopathologic finding from core biopsy specimen

Methods: A total of 13 patients with lung tumors who fulfilled the criteria were included in this study. All the subjects underwent core biopsy with ultrasonography guiding in the pulmonology surgery unit of Dr. Soetomo. The data was analyzed by fisher’s exact test.

Results: There were 9 out of 13 positive subjects of NSCLC (69.3%). MAGE-A3 expression was positive in only 4 of total 9 NSCLC subjects (44.4%).

Conclusion: There was no significant association between MAGE-A3 expression and histopathologic type.

Keywords: MAGE-A3, Core biopsy, NSCLC

ABILITY OF TRANSPBRONCHIAL SAMPLING FOR PULMONARY METASTASIS USED BY NEW MIDDLE-RANGE BRONCHOSCOPE WITH LARGE CHANNEL
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Background and Aims: T790M detection after EGFR-TKI resistance in EGFR mutation-positive NSCLC became essential for subsequent treatment policy determination. The recurrence pattern of lung cancer is determined by the features of the lesion, such as primary tumor...
growth/ lymph node metastasis/ pulmonary metastasis/ distant metastasis/ cavity fluid retention. Currently, bronchoscopic sampling from pulmonary metastases is considered difficult because of negative bronchus sign, and VATS or percutaneous needle biopsy are the first choice. We previously reported new middle-range bronchoscope with large channel (outer diameter 5.1 mm/ inner diameter 2.6 mm/ new BF) can obtain enough tissues with large diameter instrument from peripheral pulmonary lesion. We retrospectively assessed diagnostic utility for pulmonary metastasis using new BF.

Methods: Twenty-four patients with pulmonary metastasis of various cancer who underwent bronchoscopy between March 2013 to March 2015 were enrolled in this study, median age 65 years old (range, 48-82 years), male/ female 12/12, median size 23.5 mm (range, 11-64 mm). The used BF was new BF/ current BF (1T260, P260, LF-TP) 17/7, used GS was K203 (large)/ K201 (small) 22/2 and TBNA through a guide sheath (GS-TBNA) was performed in 16 cases.

Results: The overall diagnostic yield was 83.3% (20/24), the results for each BF were 93.8% (15/16) in new BF group and 62.5% (4/8) in current BF group, respectively. The EBUS findings prior biopsy was within 7/ adjacent to 14/ invisible 3, but after doing TBNA and biopsy, within 14/ adjacent to 8/ invisible 2 and 7 cases confirmed the improvement of reachability. There were no serious complications.

Conclusions: The combination of new BF and GS-TBNA for pulmonary metastasis improves accessibility and enables sufficient specimen collection. This method can be an effective and safe modality for the sampling of pulmonary metastasis.

AP379
FALSE POSITIVE FDG-AVID THORACIC LYMPH NODES DUE TO ANTHRACOSILICOSIS
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Background: Silicosis and anthracosis can present with isolated hilar lymphadenopathy in the absence of interstitial findings. Fluorodeoxyglucose (FDG)-avid thoracic lymph nodes on positron emission tomography-computed tomography (PET-CT) in suspected or confirmed anthracosis and/or silicosis obtained by endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (EBUS-TBNA).

Aim: To identify characteristics of false positive FDG-avid positive hilar and mediastinal lymph nodes with cytological evidence of anthracosis and silicosis obtained by endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA).

Methods: Retrospectively 26 consecutive patients from Sir Charles Gairdner Hospital, Western Australia with false positive FDG-avid thoracic lymph nodes on PET-CT that yielded anthracosis and/or silicosis on cytology from 1/7/2009 to 31/12/2013 were reviewed. All PET-CT images were individually reviewed for maximum and mean standardised uptake value (SUV) of each target lymph node.

Results: Median (interquartile, IQR) age was 72 (61-74), majority were male (21, 81%) and ever smokers (23, 88%). Seven (27%) had confirmed silica exposure, 5 (19%) had probable exposure and 14 (46%) had no significant exposure. PET-CT was primarily used for staging of possible/confirmed cancer (17, 65%). Fifty five hilar and mediastinal lymph nodes (mean 2.12 per patient) were sampled; most frequent stations were 1R (35%), 7 (25%) and 4R (20%). The mean (standard deviation, SD) SUVmax was 5.11 (±3.89) of lymph nodes exhibited SUVmax of more than 2.5. Twelve patients (46.2%) had symmetrical FDG-avid hilar lymph nodes, 15 (50%) were asymmetrical and one without any hilar activity. Symmetrical FDG-avid mediastinal lymph nodes were observed in 16 (61.5%) and no mediastinal activity in 5 (19%). In patients with symmetrical mediastinal FDG-avidity, there were equal numbers (8, 30.8%) of asymmetrical and symmetrical hilar FDG-avidity.

Conclusion: False positive FDG-avid lymph nodes due to anthracosis are seen in patients with no history of significant exposure. More than half have symmetrical FDG-avid mediastinal lymphadenopathy.

AP380
ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL BIOPSY FOR GROUND-GLASS OPACITY-PREDOMINANT NODULES IN THE LUNG PERIPHERY
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Background and Aims: Peripheral lung nodules containing ground-glass opacity (pure GGO and mixed GGO) are difficult to diagnose by conventional transbronchial biopsy (TBB) because they are not visible by fluoroscopy. Recently developed endobronchial ultrasound (EBUS)-guided transbronchial biopsy is useful for diagnosing these nodules. This study aimed to clarify the contribution of EBUS to the diagnostic yield of TBB for peripheral lung nodules containing GGO.

Methods: Medical records of 41 patients (21 males; 20 females; median age, 72 years) with lung peripheral pure GGO or mixed GGO nodules who underwent EBUS-guided TBB were retrospectively reviewed.

Results: The median diameter of target lesions was 18.6 mm (8.8–46.7 mm). There were seven pure GGO lesions and 34 mixed GGO lesions. The total diagnostic yield was 65.9% (27/41). EBUS images could be obtained (positive) for 30 (73.1%) cases. Among clinical factors, only a positive EBUS finding was significantly associated with a higher diagnostic yield (p=0.018). Diagnostic yield was higher in cases with a positive CT bronchus sign (recognizable responsible bronchus into the lesion) and increased consolidation-to-tumor rate.

Conclusions: EBUS-guided TBB is useful for diagnosing GGN or mixed GGO. Obtaining positive EBUS findings is important for successful TBB for lesions containing GGO.

AP381
A PROSPECTIVE, RANDOMIZED TRIAL OF COMPARING THE NEEDLE GAUGE USED TO OBTAIN SPECIMENS DURING ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION
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Background and Aim: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive modality for sampling of mediastinal and hilar lesions. Two dedicated aspiration needles are used for EBUS-TBNA. The relative utility of 21- versus 22-gauge needles remains controversial. The aim of this study was to evaluate the...
was associated with either procedure.

Background and Aim: Radial probe endobronchial ultrasound (R-EBUS) is a novel technique in localizing peripheral lung mass with overall diagnostic yield of 70%. Conventional biopsy techniques using forcep or fine needle aspirates guided by R-EBUS occasionally resulted in small sample which may not be suitable for immunohistochemical or molecular studies. R-EBUS guided transbronchial cryobiopsies in peripheral lung mass is a feasible technique to obtain larger tissue samples without affecting safety. We described our initial experience with three consecutive patients who underwent R-EBUS guided transbronchial cryobiopsy in our unit in May 2017.

Methods: Therapeutic flexible bronchoscope with a 2.8mm working channel, 2.0mm 20 Hz ultrasound probe (UM-S20-20R, Olympus Medical) within a 2.2mm flexible guide sheath and 1.9mm flexible cryoprobe (1150mm ERBE, Medizintechnik, Germany) was used in all cases.

Results: The mean age was 60±11.6 years (range 47-68 years). Two cases were performed under conscious sedation and one under total intravenous anaesthesia. Mean procedural time was 48±3.1±15.9 minutes. All lesions were located in right upper lobe. Two patients had non-diagnostic computed tomography (CT) guided biopsy prior. Mean lesion size was 2.6±0.4cm with mean distance to the pleural of 1.2cm. All lesions were able to be identified via R-EBUS with two lesions orientated within the radial probe while one adjacent to it. Cryobiopsy was obtained by freezing the tip of cryoprobe for 5 seconds. Three attempts were performed in Case 1 and 3, two in Case 2. First two cases were guided with cryoscopy. All patients had minimal intra-procedure post biopsy bleeding which was easily managed. Mean specimen size was 10.6mm. All biopsies yielded adenocarcinoma of lung with immunohistochemistry positive for CK7 and TTF-1.

Conclusion: Our initial experience shows that R-EBUS guided transbronchial cryobiopsy is safe and can potentially increase the diagnostic yield of peripheral lung mass. Our center anticipate further experience with this technique in the future.
the correlation between the %CSA<5 and the radionuclide uptake rate visualized by pulmonary perfusion scintigraphy.

Results: The %CSA<5 in the obstructed side of the lung after treatment displayed significant improvements after intervention (p = 0.04). Among the 5 cases that underwent pulmonary perfusion scintigraphy before and after the treatment, the radionuclide uptake rate of the obstructed side improved in all patients, whereas the %CSA<5 improved in 4 of the 5 patients.

Conclusion: Measurement of the %CSA<5 might be useful to assess the outcome of interventional bronchoscopy.

AP384

A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY OF HIGH-FLOW NASAL CANNULA OXYGEN AND NON-INVASIVE VENTILATION IN HYPOXEMIC PATIENTS UNDERGOING DIAGNOSTIC FLEXIBLE BRONCHOSCOPY

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Background and Aim: The diagnostic bronchoscopy in acute hypoxemic patients might result in profound hypoxemia requiring intubation. We aimed to study the effectiveness of non-invasive ventilation (NIV) compared with high-flow nasal cannula (HFNC) in those patients requiring the diagnostic bronchoscopy. The primary end point was the lowest oxygen saturation during the procedure.

Methods: The prospective, randomized-controlled trial was conducted in patients with acute hypoxemia requiring the diagnostic bronchoscopy from September 2015 to December 2016. They were randomized into either the NIV with the setting of EPAP of 5 cmH2O and IPAP to achieve the tidal volume of 8 mL/kg, or HFNC group with the setting of inspiratory flow 40 L/min, and FiO2 of 0.6 in both groups. The vital signs and gas exchange parameters during the procedure were recorded and analysed.

Results: Of 20 patients in NIV and 18 patients in HFNC, the baseline PaO2 and SpO2 at ambient air were 51 mmHg and 85% versus 56 mmHg and 89% (P=0.14 and 0.10, respectively). Other demographic data were comparable in both groups. The lowest SpO2 during the procedure between NIV and HFNC group were not different (94.1±4% vs 92.7±7%, P=0.41). In addition, the secondary outcomes in terms of the vital signs and gas exchange parameters were not different during peri- and post-procedure. Five patients in NIV group (25%) and two patients in HFNC group (11%) were intubated within 24 hours post-bronchoscopy (P=0.27). The 7-day mortality rate was not different in both groups (10% in NIV vs 6% in HFNC, P=0.61).

Conclusion: In acute hypoxemic patients undergoing diagnostic bronchoscopy, NIV and HFNC provided the similar effectiveness in prevention of hypoxemia and respiratory failure peri- and post-procedure. Accordingly, we should consider either one of them as an adjunct to bronchoscopy in those patients in order to reduce the risk of acute respiratory failure needing invasive mechanical ventilation.

AP385

HIGH-FLOW NASAL CANNULA OXYGEN DELIVERY FOR BRONCHOALVEOLAR LAVAGE IN ACUTE RESPIRATORY FAILURE PATIENTS: ANALYSIS OF 33 CASES

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Background and Aim: Fiberoptic bronchoscopy during bronchoalveolar lavage (BAL) may cause significant hypoxemia to be followed by the endotracheal intubation (ETI). To prevent hypoxemia during BAL, non-invasive ventilation can be used, but it was not widely used in clinical practice because of technical difficulties. Recently, high-flow nasal cannula (HFNC) oxygen delivery has been used to various hypoxemic situations. However, role of HFNC during bronchoscopy with BAL in acute respiratory failure (ARF) patients has not yet been demonstrated. We evaluated effectiveness and safety of HFNC oxygen delivery during BAL in ARF patients.

Methods: We retrospectively reviewed patients undergoing bronchoscopy with BAL who admitted in Daegu Catholic University Hospital, between March, 2013 and May, 2017. Among these patients, we investigated the patients who had PaO2/FiO2 ≤ 300. Patients who had BAL after ETI were excluded. We analyzed 33 cases of BAL of 32 patients (18 men, 14 women, age 23-83 years). During BAL in ARF patients, Optiflow or AIRVO (Fisher&Paykel, New Zealand) was applied as a HFNC oxygen delivery system. Oxygen saturation was measured by pulse oximeter (SpO2). Both fraction of inspired oxygen (FiO2) and SpO2 was measured before during/after BAL and complications also examined within 24 hours after BAL.

Results: Baseline FiO2/PaO2 was 166.1± (46.7). Oxygen devices were all replaced by Optiflow or AIRVO, just before bronchoscopy. Before BAL, FiO2 was 0.45±0.1 and then SpO2 was 94.8±2.9%. During BAL, applied Flow of HFNC system was 49.0± (7.2) L/min and FiO2 was increased to 0.74±0.2 and then SpO2 was 94.6± (3.5)%. After BAL, FiO2 was 0.57±0.1 and then SpO2 was 95.2±2.8%. BAL was successfully performed in all patients. Several complications were found such as transient hypotension or hypoxemia but there was no ETI.

Conclusion: HFNC oxygen delivery can be applied effectively for bronchoscopy with BAL in ARF patients without subsequent ETI.
Background and Aim: Loculated effusions are most commonly due to complicated parapneumonic effusions, followed by tuberculosis, hemothorax, and malignant effusions. Surgery such as VATS or invasive thoracotomy is often needed to physically break down the septations in order to facilitate drainage. These measures are effective, but are expensive and not easily accessible. Intrapleural fibrinolytics such as streptokinase and alteplase lyse pleural adhesions by activation of plasmin, aiding drainage of the effusion by breaking down fibrinous septations. The objective of this study is to determine significant factors which affect outcomes of intrapleural fibrinolysis among adult patients with loculated pleural effusion.

Methods: The study design was an observational cross sectional study involving adult inpatients in the Cardinal Santos Medical Center from January 2008 to June 2016, with loculated pleural effusion (n=43). Patients who received either streptokinase or alteplase were then compared in time to resolution of effusion, time to recurrence of effusion, and subsequent need for VATS.

Results: This retrospective study in 43 patients admitted in our institution with loculated pleural effusion reveals the following patient profile: mean age of 53.8 years, mostly males (60.5%), 79.1% with at least 1 comorbid condition, and the most common etiology of the loculated effusion was malignancy (51.2%), followed by tuberculosis and pneumonia. Chest tube thoracostomy (CTT) alone was inadequate in resolving the effusion, as 62.7% of the patients needed to undergo subsequent intrapleural fibrinolysis or VATS. We found that age, etiology of effusion, and comorbid conditions were not factors that predict treatment failure. However, it was noted that initial volume of effusion more than 1,000cc was positively associated with need for additional surgical intervention in our study population.

Conclusion: The use of fibrinolytic agents streptokinase and alteplase may potentially obviate the need for VATS but the findings are not statistically significant.

SUCCESSFUL CLOSURE OF BRONCHOPLEURAL FISTULA BY ADMINISTRATION OF CYANOACRYLATE GLUE IN A PATIENT WITH RIGHT SIDED SECONDARY SPONTANEOUS PNEUMOTHORAX AND PNEUMOMEDIASTINUM

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Background and Aims: Bronchopleural fistula (BPF) is a sinus tract between the bronchus and the pleural space. Clinically, it may be best described as a persistent air leak or a failure to re-inflate the lung despite chest tube drainage for 24 hours. The management of BPF is one of the most complex challenges encountered by the chest physicians. We here reporting a case of successful closure of BPF using cyanoacrylate glue.

Methods (case report): 55 year old gentleman, smoker, diabetic, presented with right sided pleuritic chest pain and breathlessness for 4 days. On examination GCS was 15/15, tachypneic (RR-24/min), tachycardic (HR-106/min), BP-130/80 mmHg, Spo2-92% at room air and breath sounds were absent over the right hemi thorax. Chest X ray revealed bilateral right upper lobe with right pneumothorax with chest drain insitu and pneumomediastinum. As the air leak (BPF) was persisting even after 1 week, proceeded with bronchoscopic intervention for BPF closure. Air leak was identified at right upper lobe anterior segment using balloon catheter. Cyanoacrylate glue was injected at right upper lobe anterior segment. The very next day after the procedure, air leak settled and there was no pneumothorax, even after clamping the ICD tube, then pleurodesis was done using povidone iodine.

Results and Discussion: Patient symptomatically improved, COPD medications were optimized and was discharged in stable condition. BPF may occur after pulmonary resection, necrotizing pneumonia, persistent spontaneous pneumothorax, thoracic trauma. In acute presentation, BPF can be life threatening due to tension pneumothorax. Clinical manifestation can be sudden dyspnea, hypotension, subcutaneous emphysema or cough with expectoration (BPF secondary to necrotizing pneumonia/empyema). Diagnosis of BPF is obvious in patient with chest drain. CT thorax can sometimes demonstrate the fistulous communication in addition to parenchymal abnormalities like bulla/bleb. Several methods like methylene blue instillation technique, bronchography, ventilation scintigraphy using radioactive xenon helps to demonstrate BPF. Bronchoscopy is an important tool in the diagnosis and management of BPF. Distal BPF require use of balloon to locate the fistula, where sealing agents like cellulose, cyanoacrylate glue, blocking coils and silver nitrate has been tried.

Conclusions: BPF leads to significant morbidity, prolonged hospitalization and even mortality. Recognizing this condition and proceed with Bronchoscopic interventions for distal BPF <8mm. Larger or central BPF requires cardiothoracic surgical intervention.

CT showing bilateral extensive subcutaneous emphysema with pneumomediastinum and right pneumothorax with ICD insitu.
OUTCOME OF PATIENTS WITH NON-DIAGNOSTIC PLEUROSCOPY
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Background and Aims: Previous studies showed that patients with non-diagnostic pleuroscopy usually have a favorable outcome with low risk of harboring a malignant disease. The 2010 British Thoracic Society guidelines considered a watchful waiting approach appropriate for patients with non-diagnostic pleuroscopy. The aim of the study is to assess the outcome of patients with non-diagnostic pleuroscopy in our institution.

Methods: We retrospectively analysed the outcome of patients who underwent pleuroscopy for undiagnosed exudative pleural effusion between May 2009 and September 2016.

Results: 88 patients underwent pleuroscopy with flexi-rigid instrument performed under moderate sedation and local anesthesia. The procedure was diagnostic in 60 (68.1%) patients (malignancy = 35; tuberculosis = 25). The procedure was failed in 7 patients due to the presence of dense adhesions. Amongst these 7 patients, 3 (42.9%) were found to have malignant disease and 4 (57.1%) had benign conditions.

Twenty-three procedures were successfully performed in the remaining 21 patients but with non-diagnostic histology findings. Malignant condition was later diagnosed in 7 (33.3%) of these 21 patients and benign condition in 12 (57.1%) patients. The diagnosis was uncertain in the remaining 2 (9.6%) patients.

Conclusions: About one-third of our patients with non-diagnostic pleuroscopy were later found to have malignancy. This is much higher than that reported which ranged from 5% to 15.4%. Our finding suggested that the excellent result reported in the literature may not be reproducible in the setting of a community hospital. With the advent in the treatment of advanced malignancy, early diagnosis of an underlying malignant condition may have a positive impact on the prognosis and quality of life of the patients. We suggest that for patients with undiagnosed pleural effusion after pleuroscopy, close monitoring is required and further investigatory procedures for undiagnosed exudative pleural effusions should be considered if the clinical suspicion of a malignant condition is high.

BACKGROUND AND AIM: Liquid sclerosants, such as mistletoe extract, have been sprayed evenly into the pleural cavity during semi-rigid pleuroscopy. We conducted a retrospective study of a prospectively collected database to identify the usefulness of pleurodesis with a mistletoe extract delivered via a spray catheter during semi-rigid pleuroscopy for symptomatic malignant pleural effusion (MPE).

Methods: All consecutive patients with symptomatic MPE who underwent semi-rigid pleuroscopy from October 2015 to September 2016 were registered. The responses were evaluated with chest X-rays or computed tomography 4 weeks after pleurodesis. According to World Health Organization criteria, no replenishment of effusion at the time of the response evaluation was classified as a complete response. Partial response was defined as replenishment of MPE < 50% of pre-treatment effusion and no symptoms. The response was classified as no response when additional treatment was needed, such as insertion of an intercostal tube, for recurrence of MPE within 4 weeks after chemical pleurodesis.

Results: The study included 43 patients who underwent pleurodesis and received mistletoe extract via a spray catheter. Complete and partial responses were seen in 21 (49%) and 19 (44%) patients, respectively. The median duration of chest tube placement after pleurodesis was 7 days (range: 6–8 days) in the 40 patients with complete or partial responses. No cases of severe hemorrhage, empyema formation, respiratory failure, or procedural-related mortality were observed in the subjects at 4 weeks after semi-rigid pleuroscopy.

MEDICAL THORACOSCOPY VERSUS BLIND PLEURAL BIOSY IN UNDIAGNOSED EXUDATIVE PLEURAL EFFUSIONS - SERIES OF 22 CASES
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Background and Aim: Medical thoracoscopy (MT) has a great diagnostic yield, quoted to be 93.2% versus 84.5% with blind pleural biopsy (BPP) by Muturu et.al (2015). We aim to look at the outcome of MT versus BPP.

Methods: This is a retrospective analysis of patients with pleural procedures for undiagnosed pleural effusions (UPE) done by single operator.

Results: A total of 22 patients presented with UPE were studied (9 had BPP and 13 had MT). The mean age was 48.4 and 48.2 years old respectively. There were seven males and two females in the BPP group, nine males and four females in the MT group. Bedside ultrasound was used to guide the procedures. Majority of procedures were done for suspected pleural tuberculosis while the rest were done to rule out carcinoma. The diagnostic yield from BPP was 55.6% (one had unsatisfactory result due to presence of fat cells only and three had unremarkable results). The diagnostic yield of MT was higher, 76.9% (two patients had inconclusive findings due to crushed samples and one had unremarkable results). Pleural tuberculosis and carcinoma were diagnosed in three and two patients respectively through BPP. Pleural tuberculosis and carcinoma were diagnosed in eight and two patients respectively through BPP. Pleural tuberculosis and carcinoma were diagnosed in three and two patients respectively through MT.

Conclusion: MT is associated with higher diagnostic rates compared to BPP in investigating exudative effusions, hence should be the procedure of choice. However, in circumstances where MT is not feasible, BPP should still be performed prior to starting empirical treatment. These procedures are generally safe. The diagnostic yield can be further enhanced by the use of bedside ultrasound.
AP392
REBIOPSY IN NON-SMALL CELL LUNG CANCER PATIENTS WITH ACQUIRED RESISTANCE TO EGFR-TKI
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Background and Aims: Transbronchial tissue rebiopsy (TBTrB) is performed in Japan to confirm the presence of secondary epidermal growth factor receptor (EGFR) mutation. Several retrospective Japanese studies showed that rebiopsy was successful in approximately 80% of patients, while the rebiopsy-associated complication rate was over 5% which was higher than that at the first biopsy. We aimed to investigate the current safety of rebiopsy at the Institute of Jichi Medical University Hospital. We studied the frequency of bleeding after transbronchial lung rebiopsy (TBLrB).

Methods: We retrospectively screened electronic medical records of patients with EGFR mutation positive NSCLC who underwent TBTrB at our institute after April 2016. We investigated the rebiopsied organ, success rate, type of EGFR mutation, age, and tumor size. Success was defined as being able to obtain tumor cells by TBLrB. We also investigated the safety of rebiopsy and the inspection time of bronchoscopy. We estimated rebiopsy-associated bleeding at the amount of hemostatic drugs.

Results: All 19 patients harbored EGFR mutation; 63% (12/19) had L858R mutation, 32% (6/19) had exon 19 deletions and 5% (1/19) had G719A mutation. The age at the time of rebiopsy was 64.9±8.7 [mean±standard deviation (SD)] years. Maximum diameter of the rebiopsy target was 35.9±10.8 mm. We succeeded in rebiopsy in 68% (13/19), and T790M genotype was found in 37% (7/19). Eight patients underwent both TBLB and TBLrB. The mean amount of hemostatic drugs was 0.8ml vs 9.4ml (TBLB vs. TBLrB, p<0.01) and the inspection time of bronchoscopy was 29 minutes vs. 36 minutes (p=0.01), which may indicate that bleeding tends to occur more frequently during TBLrB than TBLB.

Conclusions: When we succeed in TBLrB, bleeding is the most common complication and tends to occur more frequently than during the first biopsy. It is important to pay attention to bleeding tendency during TBLrB.

AP393
MANAGEMENT OF AIRWAY STENOSIS IN ENDOBRONCHIAL TUBERCULOSIS
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Background and Aims: Endobronchial tuberculosis (EBTB) is often misdiagnosed and mistreated, such as asthma. More than 90% of EBTB cases present with tracheobronchial stenosis. Interventional bronchoscopy provides good outcome for the management of EBTB with airway stenosis if prompt diagnosis is made before fibrotic process finished.

Methods: Case report: A 34-year-old female was admitted into emergency department for worsening breathlessness for last 3 days. Patient was previously diagnosed with moderate persistent asthma without improvements following two months of treatment. Chronic cough, hoarseness, decreased appetite and weight loss also present along with expiratory stridor, bronchial breath sound and expiratory wheezes. Blood gas analysis showed normal results. Acid-fast bacilli smear was negative. Computed tomography (CT) scans showed distal trachea narrowing and right lung tree-in-bud and ground glass opacity. Bronchoscopy revealed distal trachea and right main bronchus fibrotic narrowing. The working diagnosis of this patient was fibrostenotic EBTB based on Chung classification. The tracheal stenosis was managed with balloon-dilation using rigid bronchoscopy to improve the symptoms along with administration of anti-tuberculosis chemotherapy and inhaled long-acting β2 agonist- corticosteroid (LABACS). One-month bronchoscopic re-evaluation showed tracheal diameter was satisfactory and subjective improvement was found.

Results: Discussion: Diagnosis of EBTB in this patient was established from CT and bronchoscopy findings. Principles in management of EBTB are eradication of tubercle bacilli and prevention of airway stenosis which is performed through bronchoscopy including mainly interventional bronchoscopy technique such as balloon dilatation. Balloon dilatation provides minimal invasive approach for this case and granulation formation in airway can be avoided.

Conclusions: Prompt and early diagnosis and treatment of EBTB are required to prevent the disease progression such as tracheobronchial stenosis due to fixed fibrotic process. Balloon dilatation performed in this EBTB case shows to relieve airway stenosis and inhaled LABACS shows to minimize the occurrence of granulation and inflammation.

AP394
FULLY COVERED SELF-EXPANDABLE METALLIC STENTS FOR MALIGNANT AIRWAY DISORDERS
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Background and Aims: The use of fully covered self-expandable metallic stents (SEMSs) (AERO®; Merit Medical Systems) was approved in Japan in 2014. The aim of the present study was to evaluate the clinical efficacy and safety of fully covered SEMSs for treating malignant airway disorders.

Methods: We retrospectively reviewed all stenting procedures done using a fully covered SEMS at Nagoya Medical Center from February 2015 to April 2017.

Results: We inserted 35 fully covered SEMSs (trachea insertion, n = 22; left main bronchus insertion; n = 11, and right main bronchus insertion, n = 2) in 30 patients. All procedures were performed using both rigid and flexible bronchoscopes under general anesthesia. The main purpose was to treat airway stenosis in 30 cases and a tracheoesophageal fistula in 5 cases. Stents were successfully inserted in all except one case (97%), in whom the stent could not be expanded because of a small airway diameter. Supplemental oxygen was reduced immediately after stenting in 14 of 19 patients (74%) who required supplemental oxygen before stenting. Pulmonary function measurements taken before and after stent removal, which were available in 16 patients, were as follows: forced vital capacity, 2.57 ± 0.90 and 2.73 ± 0.91 L (p = 0.02); forced expiratory volume in 1 sec, 1.60 ± 0.57 and 1.95 ± 0.73 L (p = 0.03); and peak expiratory flow, 2.72 ± 1.25 and 3.85 ± 1.58 L/s, respectively (p < 0.01). Stent-related complications included migration in four cases, granulation tissue formation in two cases, obstruction with fibrinous membrane in one case, stent collapse in two cases, and mucus impaction in two cases.
Conclusions: Bronchial artery embolization (BAE) is ideal treatment for hemoptysis due to BE because bronchial artery (BA) anatomically covers ectatic bronchi. We examined to reveal that BAE is effective for controlling hemoptysis in patients with BE.

Methods: We performed BAE using coil for 511 patients at our hospital from 2011 to 2016. Among them, 105 patients (20.5 %) were diagnosed with BE. Twenty-eight patients were excluded due to loss of follow-up or diagnosis of nontuberculous mycobacterial pulmonary infection after BAE etc. We retrospectively reviewed medical records of 77 BE patients who underwent BAE and evaluated efficacy of BAE in BE patients.

Results: The median age was 69.0 (22-85) years and 57 (74.0 %) were female. Chest CT revealed bilateral bronchiectasis in 53 (70.7 %) patients. Pseudomonas, the most common pathogen, was detected in 23 patients and 49 patients were treated with macrolide. Only BA were embolized in 54 cases and non-bronchial systemic arteries were additionally embolized in the other cases. The median number of embolized vessels was 2.3 per case. Among the patients, rebleeding developed in 10 cases (13.0 %) within a mean follow-up period of 18 months. The cumulative hemoptysis control rates were 96.5 % and 80.5 % in one and two years, respectively. In rebleeding 10 cases, the second BAE was performed in 9 cases. Besides, the third BAE was performed in 2 cases with second rebleeding. In only 1 case, operation was performed.

Conclusion: BAE using coil, minimally invasive intervention, can control hemoptysis in patients with BE.

Effectiveness and Safety of Bronchial Thermoplasty

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Background and Aim: Bronchial thermoplasty (BT) is a bronchoscopic intervention for patients with severe persistent asthma using maximal medical therapy. In Japan, about 300 patients with severe persistent asthma have received BT.

Methods: Eleven patients with severe persistent asthma as defined by Japanese guidelines that were poorly controlled despite step 4 therapy were enrolled. BT was performed in operation room. The purpose of this study is the evaluation of the effectiveness and safety of BT.

Results: BT was successfully performed in 10 patients. In only 1 patient, third procedure could not be performed, because eosinophilic bronchitis developed. In 3 of 4 subjects, the AQLQ score significantly increase before and one year after BT. Other 1 patient developed osteonecrosis of the femoral head 1 year after BT and this event affected AQLQ score. Except the AQLQ score, the number of ER visit decreased and air-trapping disappeared in chest CT. In complications, all subjects presented mild to moderate symptoms of asthma and developed acute lung injury. Only 1 patient developed atelectasis every procedures and non-invasive positive pressure ventilation was effective after third procedure of BT. All patients improve acute lung injury and atelectasis without any complications.

Conclusion: The results of bronchial thermoplasty after 1 year show promise in patients with severe asthma patients during general anesthesia.

Patient Characteristics and Procedure Details of Patients Undergoing Bronchial Thermoplasty for Severe Persistent and Poorly Controlled Asthma in the United Arab Emirates

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Background: A proportion of patients with severe persistent asthma remain poorly controlled despite optimal medical therapy. Bronchial thermoplasty is a three-stage one-off treatment which aims to reduce airway smooth muscle mass improving airway diameter and reducing bronchospasm.

Aims: To describe patient characteristics and procedure details of patients who have undergone Bronchial thermoplasty (BT) at our institution.

Methods: Retrospective review of demographic, lung function, quality of life, and procedural data from all patients who underwent BT at our institution to date.

Results: Nineteen patients underwent BT procedures from February 2016 to date (53 procedures with four procedures pending). Proportion of females was 79%. Median age of female patients 37 (range 29 to 62) years, males 47.5 (range 29 to 62) years. Mean (SD) BMI was 32.5 (8.9) kg/m² (females 33.8 (9.6) kg/m²; males 26.1 (1.27) kg/m²). Pre-treatment median post-bronchodilator FEV1 was 73 (range 58 to 91) % predicted. Pre-BT median ACT score was 14 (range 6 to 20) points. 16/19 patients had eosinophil counts >300 x10^6/mL pre-BT. 9/19 patients had IgE levels >100 IU/mL, with seven patients on Omalizumab therapy and 2 others having discontinued therapy. All patients were on combination LABA/ICS therapy, 14 on LAMA, 17 on montelukast and three on continuous maintenance oral corticosteroids. Mean (SD) number of activations administered to the right lower lobe was 61.6 (17.7), left lower lobe 63.1 (27.2), and upper lobes 83.8 (31.0). Of the 53 procedures, 11 were followed by a 3 day admission for treatment of mild exacerbations, and 3 patients had severe exacerbations requiring longer admissions (4, 6, and 17 days). No other adverse events occurred.

Conclusions: Females formed a higher proportion of all patients treated, were younger with a higher BMI, and had a similar degree of airways obstruction compared to the AIR2 and other published BT trials/registries.

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THE REAL-WORLD EVIDENCE IN TAIWAN: DATA FROM 251,398 ACOS AND 514,522 COPD ALONE PATIENTS

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Background: Based on the guideline, asthma–COPD overlap syndrome (ACOS) is identified in clinical practice by features and there is an urgent need for more research to guide appropriate treatment for ACOS.

Methods: Using Taiwan’s National Health Insurance Research Database, we conducted a nationwide population-based study to evaluate medication effects in patients with ACOS. Patients diagnosed with both asthma and COPD between 1997 and 2012 were enrolled as the ACOS cohort. Patients followed for <1 year were excluded. Patients were categorized as non-users and users of long-acting beta 2 agonists (LABAs), long-acting muscarinic antagonists (LAMAs), inhaled corticosteroids (ICSs), and ICS/LABA combinations. The primary endpoint was acute exacerbation. The definition of COPD and asthma was validated using the claims database of Taipei Veterans General Hospital.

Results: Validation study confirmed the accuracy of the definition of COPD (sensitivity, 94.0%) and asthma (sensitivity, 95.3%). The study included 251,398 ACOS patients and 514,522 COPD alone patients with a mean follow-up period of 9.85 years. The ACOS cohort had fewer comorbidities, but more medical services than did the COPD alone cohort. After adjustment, hazard ratios (HRs) for LAMA and ICS/LABA combinations were lower [time-dependent model, 1 year: LAMAs, HR 0.51, 95% confidence interval (CI) 0.49–0.54; ICS/LABA combinations, HR 0.61, 95% CI 0.60–0.62; time-dependent model, 90 days: LAMAs, HR 0.23, 95% CI 0.21–0.25; ICS/LABA combinations, HR 0.24, 95% CI 0.23–0.25; all p<0.0001] compared with non-users in ACOS patients.

Interpretation: LAMA or ICS/LABA combinations use was associated with a lower risk of acute exacerbation in ACOS patients in this study.

Figure 1. Flow diagram summarizing the process of enrollment.

Figure 2. Kaplan-Meier curve of acute exacerbation-free probabilities in patients with ACOS and COPD alone. There was a statistically significant difference between the two curves (log-rank test, p < 0.001).
Abstracts

Background: Asthma COPD overlap (ACO) is widely gaining recognition as separate phenotype of chronic airway disease with distinct treatment and prognosis. A paradigm shift in first line management of COPD (GOLD 2017 guidelines), poses an important challenge of accurately diagnosing ACO.

Aims: To estimate the prevalence of ACO among patients previously diagnosed as COPD and compare their clinical, biochemical, radiological and pulmonary function profile

Methods: This was retrospective study of 101 patients with COPD admitted at our center between 2015-2016. A detailed chart review including demographic, clinical, laboratory investigations, spirometry, chest Xray and HRCT findings was recorded in prestructured proforma. The diagnosis of ACO was based on GINA/GOLD criteria2014 and aforementioned parameters were compared between ACO group and COPD group.

Results: Of the total(n=101), ACO was diagnosed in 22(21.8%) patients. Mean age of patients in ACO was 63.0±9.6years with male preponderance. Age of onset of symptoms was significantly lower in ACO group than COPD(50.4±9.6 vs. 58.5±9.6years, p=0.001). Presence of trigger was the most sensitive parameter for defining ACO(n=100%). There was a significantly higher incidence of wheeze, nasal symptoms, family history of atopy, peripheral eosinophilia(8/22 vs 6/79, p=0.002) and mean serum IgE levels (p=0.002) as compared to COPD. On spirometry, there was no statistically significant difference in severity of airflow obstruction but bronchodilator reversibility was significantly more in ACO(22.72% vs 2.53%,p=0.005). COPD patients had higher reduction in respiratory muscle pressure(predominantly inspiratory)(70%vs36%, p=0.037). There was no significant difference in various radiological findings on X-ray and HRCT between two groups.

Conclusion: ACO represents a large proportion (20%) of COPD patients with younger age of onset, higher bronchodilator response, and better respiratory muscle strength. IgE and AEC are important biomarkers to differentiate ACO from COPD with limited role of chest imaging. The study results have implications for earlier identification and appropriate treatment of this distinct clinical phenotype.

AP401
LEVELS OF FRACTIONAL EXHALED NITRIC OXIDE (FENO) IN ASTHMA-COPD OVERLAP (ACO) PATIENTS COMPARED WITH THOSE IN COPD PATIENTS AND IN HEALTHY PERSONS IN VIET NAM
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Background and Aims: FeNO has been used as a marker for Th2-mediated airway inflammation in asthma. This type of inflammation has been proposed plays an important role in ACO. However, little is known about the FeNO levels in patients with ACO in comparison with those with COPD alone or healthy persons.

Methods: A cross-sectional study conducted in Asthma and COPD clinic at University Medical Center, Hochiminh City, Vietnam from 6-12/2016. We recruited 50 stable ACO patients (aged 23-75 years), 50 stable COPD patients (aged 41-81 years) and 30 healthy persons (aged 17-64 years). COPD was diagnosed and classified based on GOLD 2016. ACO patients were those got asthma with or without smoking but had FEV1/FVC<0.7 for at least 6 months of treatment and had been diagnosed as ACO by doctors in this clinic. Healthy persons were those who had no history and current symptoms of any respiratory disease, had no other diseases being treated, and had normal plasma C-reactive protein and normal FEV1/FEV6 measured by COPD-6 devices. FeNO was measured by Niox Mino device from Aerocine company and spirometry done using KoKo PFT Spirometer.

Results: The mean age (±SD) of ACO, COPD patients and healthy persons were 54 (±12.5), 65 (±9.4) and 37 (±9.6) years respectively. The mean of FeNO level was higher in subjects with ACO compared with those with pure COPD (31.1 vs 18.8 ppb; difference, 12.4 ppb [95% CI, 4.0 to 20.7]; P=0.004) and compared with those in healthy persons (31.1 vs 15.7 ppb; difference, 15.4 ppb [95% CI, 7.6 to 23.3]; P=0.001). There was no significant difference in means of FeNO between COPD group and healthy persons (p=0.2).

Conclusions: The increased FeNO level could be found in ACO and that may be one of the characteristics to distinguish ACO from COPD alone.

AP402
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN WOMEN VERSUS MEN: CHARACTERISTICS OF AN EMERGING GENDER-SPECIFIC PHENOTYPE
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Background and Aims: The prevalence and mortality of chronic obstructive pulmonary disease (COPD) in women is increasing. In the Philippines, COPD ranked as the 7th leading cause of mortality in 2009, which may be due in part to increase in number of female smokers, who numbered approximately 2.8 million in a nationwide survey in the same year. The female sex is being tagged as a new phenotype for COPD, due to epidemiologic observations that women developed the disease at a younger age and with less pack years. This study aims to compare disease expression of male and female patients with COPD: baseline characteristics, pack years, spirometry findings, and determine if there is a significant difference between the two.

Methods: The study design is a cross-sectional study involving men and women who had Spirometry done in CSMC from Jan 2012 until June 2015, with finding of post bronchodilator FEV1/FVC < 0.7. The T test was used to compare numerical data while chi square test was used to detect associations between categorical data sets. Pearson correlation was used to measure the degree of correlation between risk factors and %FEV1 values. A p-value of <0.05 was used to estimate if there is a significant difference between the said variables.

Results: Our study showed that compared to men, women with COPD were younger, had less number of pack years, and had a greater proportion of non-smokers who developed the disease. Number of pack years was positively correlated to number of symptoms in both sexes. Gender differences were detected at the 41-50 pack year group, with males having more severe COPD (%FEV1) than females with the same amount of cigarettes smoked.

Conclusion: No association between age, BMI, and symptoms were noted. Possible explanations include sex difference in airway anatomy, genetics, and susceptibility to cigarette smoke.

AP403
SPIROMETRIC REFERENCE VALUES FOR TIBET RESIDENTS AGED 15–98 YEARS
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Background and Aim: Normal spirometric values and prediction equations are largely unknown for Tibet residents. This study aimed to determine spirometric values and establish prediction equations for healthy Tibet residents.

Methods: This prospective cross-sectional study enrolled 2909 healthy, non-smoking Tibetans aged 15-98 years. A multistage cluster sampling strategy was used for sample selection. Anthropometric and spirometric data from six different urban and rural areas were obtained. Age stratification and the male to female ratio were highly considered. Student’s t-Test was used to obtain normal reference values based on sex and altitude. Multiple linear regression was used to establish prediction equations.

Results: The study was conducted between February 2015 and August 2016 in Tibet. Normal reference values of anthropometric data, such as age, height, and weight based on sex and altitudes, showed significant differences (P<0.01). Additionally, prediction equations with age, height, and weight were established for FVC and FEV1 between different genders and altitudes, respectively. Height and weight had positive effects on the equations, while age had negative relationships.

Conclusion: This study firstly provides reference values for demographic characteristics and spirometry data for healthy Tibetans, with spirometry reference prediction equations based on sex and altitude.

Acknowledgements: The authors thank all cooperators and local administrations for great cooperation on the field in this study.

PREVALENCE AND RISK FACTORS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AMONG TIBETANS

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Background and Aim: Chronic obstructive pulmonary disease is a leading cause of public health problem in China. Because of geographic and financial diversity, the prevalence of COPD and its risk factor pattern in Tibet region is limited. The aim was to obtain the prevalence of COPD and investigate the potential risk factors for COPD among Tibetans.

Methods: This prospective cross-sectional study involving six urban and rural Tibet regions was performed via stratified cluster random sampling. All subjects interviewed using a revised questionnaire, examined by chest radiograph and underwent pulmonary function tests. Post-bronchodilator forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) of less than 70% was the diagnostic criteria of the Global Initiative for Chronic Obstructive Lung Disease.

Results: Among 6000 subjects sampled for the study, 3871 participants completed the questionnaire, chest radiograph and spirometry. The overall prevalence of COPD was 11.06%. The prevalence of COPD was 14.86% for people aged more than 40 years and 7.64% for less than that (P=0.01). The prevalence was 9.26% (OR=1.40, 95% CI=1.04-1.21), lower body mass index (OR=1.08, 95% CI=1.04-1.12) and indoor exposure for cooking (OR=1.14, 95% CI=1.32-1.54) were positively associated with the increased risk of COPD among Tibetans.

Conclusion: COPD in Tibetans aged over 15 years old was prevalent and an important health burden in China.

Acknowledgements: The authors thank all cooperators and local administrations for great cooperation on the field in this study.

CORRELATION OF COMPOSITE INDICES AND COPD ASSESSMENT TEST (CAT) IN THAI COPD PATIENTS

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Background and Aims: The BODE Index is a composite marker of disease for prognostication. The BODE is correlated with COPD patients survival. CAT score is used for assessing symptoms and personalize treatments. The correlation of BODE and CAT was investigated in Thai COPD.

Methods: Retrospective study was done by clinical reviewing in chest clinic between January and December 2016. BODE was calculated (BMI, post-bronchodilator FEV1, modified MRC scale and 6-MWT). SPSS version 22 was used for analysis. P value of 0.05 indicates statistical significance.

Results: Total 82 consecutive COPD patients were recruited. There were 19 (23.2%), 34 (41.5%), 25 (30.5%) and 4 (4.5%) of COPD patients were classified GOLD stage 1, 2, 3 and 4 respectively. There was association between CAT score and GOLD stages classified by post-bronchodilator FEV1 (p =0.016). There was significant difference of 6-MWT distance between GOLD stages (p 0.017). BODE was calculated and categorized to 4 quartiles according to summed BODE score. Hence COPD patients were classified BODE quartiles. There were 50 (61.0%), 20 (24.4%), 7 (8.5%) and 5 patients (6.1%) in quartiles 1 (BODE score 0-2), quartile 2 (BODE score 3-4), quartile 3 (BODE score 5-6) and quartile 4 (BODE score 7-10) respectively. There was significant difference of CAT between 4 BODE quartiles in Thai cohort (P <0.003).

Conclusions: GOLD stages significantly correlated with symptoms either assessed by CAT score or MMRC scale and exercise tolerance (6-MWT). CAT score correlated with composite indices of BODE in Thai COPD patients.

WHICH IS THE BEST TOOL TO EVALUATE THE RESPONSIVENESS TO THE THERAPY IN EXACERBATION OF COPD: CAT, LUNG FUNCTION OR FENO?

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Background and Aims: The COPD Assessment Test (CAT), fractional exhaled nitric oxide (FENO) and lung function (FEV1% predicted) are all widely used to access the responsiveness to therapy in AECOPD. However, it is unknown which is the best tool among them. Thus, this article was about to compare these measurements and provide a best way to evaluate the curative effect.

Methods: This study assessed CAT’s changes in health status of 123 patients with AECOPD during the first 24 hours and the seventh day after admission. Among then, 55 patients completed FENO and lung function measurement twice. After 7 day’s treatment, their health status were...
Abstracts

Background and Aims: There are many risk factors that are known to cause or are significantly associated with COPD. Presence of multiple risk factors can contribute to the progression and severity of COPD. Our aim was to identify the risk factors for COPD and analyze their relationship with COPD severity.

Methods: A descriptive cross sectional study. Patients with COPD were staged according to GOLD criteria. Demographic data and exposure to known risk factors were recorded using an interviewer administered questionnaire. Data were analyzed using Microsoft Excel.

Results: A total of 101 male patients, mean age 67yr; mean FEV1 42.7%. There were 18 (17.8%), 41 (40.59%), 41 (40.59%), 01 (0.99%) patients between 50-59, 60-69, 70-79, 80-89 yrs age groups respectively and 23 (22.7%), 52 (51.4%), 21 (20.7%), 5 (4.9%) with very severe, severe, moderate and mild COPD respectively. 5 (4.9%) were non smokers. 75(74.2%) had exposure to indoor air pollution. 14(13.8%) had agricultural dust exposures. 4(3.9%) were exposed to timber dust. 2(1.9%) had industrial dust exposures. 9 (8.9%) had a past history of tuberculosis. Out of the non smokers 3 were exposed to indoor air pollution and 2 did not have an identifiable risk factor.

Conclusions: 74% of this study group had severe to very severe COPD. Majority were smokers and also had exposure to one or more other known risk factors. Highest number of patients had indoor air pollution as the main risk factor other than smoking. Exposure to multiple risk factors may have contributed to the majority having severe COPD.

AP106

DESCRIPTIVE STUDY ON THE PATTERN OF COPD ACCORDING TO GOLD GROUPS OF SEVERITY IN A COHORT OF COPD PATIENTS IN CENTRAL SRI LANKA

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Background and Aim: The grading of severity of COPD depending not only on spirometry criteria but also on symptoms and risk of exacerbations was introduced in 2011 through the GOLD guidelines. It had been noted in day to day clinical practice that a vast majority of the patients managed through COPD clinics in Sri Lanka are of category D indicating severe disease. However due to lack of published data regarding local statistics, there is no documented evidence to prove this fact. Our objective is to describe the pattern of patients with COPD in Sri Lanka in the form of severity groups described by the GOLD guidelines.

Methods: A random sample of 105 patients were selected from a COPD clinic in central Sri Lanka and were subjected to an assessment by trained interviewers. The information gathered included the mMRC grade of shortness of breath on exertion and a detailed assessment regarding the number of exacerbations including the ones requiring hospital admission. The data were analysed using Microsoft Excel.

Results: A vast majority of patients 65.714% (n= 69) were of category A and there were no patients in category D. There were 35 patients in category B which amounts to 33.33%. Only one patient belonged to category C and there were no patients in category D.

Conclusion: The majority of patients being followed up in central Sri Lanka for COPD are of category D indicating severe disease with increased symptoms and high risk of exacerbation. This is most likely due to late presentation, due to lack of facilities to identify early disease or lack of awareness among the general public.

AP407

DESCRIPTIVE ANALYSIS OF RISK FACTORS IN A COPD COHORT IN CENTRAL SRILANKA

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Background and Aims: Cigarette smoking is the most commonly encountered and readily identifiable risk factor for chronic obstructive pulmonary disease (COPD). However, it is not clear which quantitative factors related to smoking influence the prognosis of COPD patients.

Methods: A total of 204 patients with a long-term history of smoking were enrolled into this study and followed up for 5 years. Patients were divided into a “death” or “survival” group based on follow-up results, and a “quitting smoking” or “continuing smoking” group based on whether they gave up smoking.

Results: Patients in the death group had a longer smoking time, lower prevalence of quitting smoking, lower onset of COPD symptoms, older age at quitting smoking, lower forced expiratory volume in one second (FEV1) % predicted, and lower ratio of FEV1/forced vital capacity. Age, age at quitting smoking, and FEV1 %predicted were independently associated with mortality from COPD. Compared to the continuing-smoking group, the quitting-smoking group had a lower mortality rate, longer course of COPD, earlier onset of COPD symptoms, and lower residual volume percentage predicted. During the 5-year follow-up, 113 deaths were recorded (quitting-smoking group: n = 92; 40 deaths; continuing-smoking group: n = 112; 73 deaths). The mortality rate remained significantly higher in the continuing-smoking group than the quitting-smoking group (log-rank test, 13.59; P = 0.0002).

Conclusions: Smoking time may be related to the mortality rate from COPD. Smoking cessation has the greatest capacity to influence the natural history of COPD.
MORTALITY OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A POPULATION-BASED COHORT STUDY

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a major cause of mortality in the world. There are no population-based studies on the long-term mortality of COPD patients in Korea.

Methods: Using the National Health Insurance Service-National Sample Cohort (NHIS-NSC), which is a large population-based cohort, we identified COPD patients using the International Classification of Disease-Tenth Revision (ICD-10) and prescription details in NHIS-NSC during 2003-2013. We analyzed the survival curves of COPD patients by sex and age and the causes of death.

Results: A total of 14,127 individuals were diagnosed with COPD. Total deaths in COPD patients were 3,695 (26.2%) during 2003-2013. The 5-year mortality rate was 25.4% (29.9 % in males and 19.1 % in females). The mortality rate increased rapidly with age. The most common cause of death in COPD was chronic lower respiratory disease.

Conclusions: This study showed that the long-term mortality of COPD patients in general population was relatively high. The higher mortality was observed in males, and it was closely related to the age.

RISK FACTORS OF INCREASING LUNG FUNCTION DECLINE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A REAL-WORLD ANALYSIS

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Background and Aim: Lung function decline is a hallmark in chronic obstructive pulmonary disease (COPD) even under treatment. Increasing decline in lung function had been observed in some patients. Associated risk factors were investigated.

Methods: A retrospective study was performed since January to December, 2013. All COPD patients who had a post-bronchodilator forced expiratory volume in first second/forced vital capacity (FEV1/FVC) less than 70 were included for review. Patients were divided into two groups: increasing and normal FEV1 decline from followed lung function test. Increasing FEV1 decline was defined as more than 30ml decreasing per year. Demographic data, clinic characteristics, underlying co-morbidities, and complication were analyzed to explore associated risk factors.

Results: Four hundred and four COPD patients were included for review. 176 patients had followed, qualified, and post-bronchodilator lung function for analysis. The mean age was 68.3 with male predominant (88%). The mean post-bronchodilator FEV1% of predicted value was 62.1%. Mean duration of followed lung function for calculation was 2.3 years with mean declined FEV1 9.7ml per year. There were 78 patients

CUT-OFF VALUE OF FEV1/FEV6 TO DETERMINE AIRFLOW LIMITATION USING HANDHELD SPIROMETRY

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Background and Aims: Postbronchodilator FEV1/FVC less than 0.7 using spirometry is the golden standard to diagnose COPD. Recently, measuring the FEV6 has been suggested as an alternative to measuring FVC. Studies about the cut-off value for FEV1/FEV6 to diagnose airflow limitation showed variable results, with values between 0.7 and 0.8. The purpose of this study was to determine the best cut-off value of FEV1/FEV6 to detect airflow limitation using handheld spirometry.

Methods: We recruited subjects over 40 years of age with smoking history over 10 pack-years. The participants underwent the handheld spirometry and conventional spirometry. We calculated the sensitivity and specificity of the value of FEV1/FEV6 using receiver-operating characteristic (ROC) curve analysis. We evaluated the diagnostic accuracy of handheld spirometry to detect airflow limitation. We further compared the clinical characteristics according to the cut-off value obtained by ROC curve.

Results: A total of 290 subjects were enrolled. The mean age and smoking amount were 63.2 years and 31.8 pack-years, respectively. There were 135 subjects with COPD defined by postbronchodilator FEV1/FVC <0.7 using conventional spirometry. According to our ROC curve analysis, sensitivity and specificity were maximal when the FEV1/FEV6 ratio was ≥73%. The area under the ROC curve was 0.93. The sensitivity, specificity, positive predictive value, and negative predictive value were 86.7%, 89.7%, 88.0%, and 88.5%, respectively. The diagnostic accuracy was calculated to 88.3%. The subjects with FEV1/FEV6 ≥73% had lower FEV1 predicted value compared to subjects with FEV1/FEV6 <73% (62.5% vs. 85.1%, p<0.0001). However, other characteristics such as age, smoking amount, and symptoms were not different between the groups.

Conclusions: We demonstrated the value of ≥73% in FEV1/FEV6 using handheld spirometry has the best sensitivity and specificity to detect airflow limitation. Further studies are necessary to verify this cut off value.
Introduction: The St. George’s Respiratory Questionnaire (SGRQ) is an instrument to assess health status in patients with COPD. Although the longitudinal changes in health status and aggravation factors are well described, the researches confined to aggravating factors on mild-moderate COPD patients are still limited. Our study aimed to investigate the baseline characteristics of aggravating SGRQ group and to identify the factors associated with aggravating change in SGRQ scores in early COPD patients (FEV1<50%).

Methods: We analyzed 827 patients who completed one year SGRQ and were followed up in Korea COPD Subgroup study cohorts. We collected the information of demographic data, spirometer parameters and clinical data. Based on the difference between the baseline SGRQ score and the score after one year follow-up, patients were categorized into a non-aggravation group (≥4 point increase in SGRQ) and an aggravation group (≥4 point increase in SGRQ). We analyzed the related factors using a logistic multivariate analysis.

Results: 130 of a total 827 patients (15.7%) were belonged to the aggravation group. Comparing baseline characteristics between two groups, FEV1/L and FEV1/FVC% of the deteriorating group were lower than those of the other groups (p=0.007, p=0.004), but there are no significant difference in 6MWT, CAT, mMRC and the acute exacerbation history. The risk factors of the deteriorating SGRQ group were the decrease of FEV1/L (p<0.001) in a year and an acute exacerbation (p=0.03). From the analysis of 1-year changes of the parameters, we found that FEV1, FEV1/FVC, BMI and 6MWT decreased and CAT, mMRC increased significantly in the deteriorating group. The ratio of the current smoker is higher and an acute exacerbation was more frequent in the group.

Conclusion: The baseline predictors of SGRQ aggravation in early COPD patients were the lower FEV1 (p=0.007), the lower FEV1/FVC (p=0.004), an acute exacerbation (p=0.03) and the FEV1 decline (P=0.001).

AP411

CLINICAL UTILITY OF THE DYSPNEA-12 QUESTIONNAIRE ON PREDICTING ACUTE EXACERBATION OF COPD

PATIENTS
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Rationale: The Dyspnea-12 Questionnaire (D-12) measures the current level of a patient’s breathlessness severity with 12 descriptors and consists of two components: physical and emotional. It is short and easy to use. The purpose of our study is to examine association between D-12 scores and occurrence of acute exacerbation of COPD (AECOPD).

Methods: A total of 65 patients (4 females) with stable COPD completed the D-12 and the COPD Assessment Test (CAT) on their regular outpatient visits. During 2-year observation period after evaluations of those tests, episodes of AECOPD and hospitalizations of respiratory diseases were evaluated.

Results: The average age and %FEV1 were 73 years and 48.5%, respectively. Out of 65 patients, 14 patients had at least one episode of AECOPD, and 12 were hospitalized due to respiratory diseases including AECOPD. Average CAT scores of 14 patients with AECOPD and 51 without AECOPD were 16.2 and 14.7 with no significant difference. The D-12 score of 14 patients with AECOPD were significantly higher than that of 51 without AECOPD (6.4 vs 3.4). The D-12 emotional scores skewed strongly: 52 patients scored 0. Thirteen patients with the D-12 emotional score of more than 0 demonstrated high prevalence of AECOPD (6 patients). Forty-seven patients scored more than 9 points of CAT and 11 patients (23%) of them experienced AECOPD. Among 11 patients who scored in both the CAT of more than 9 and the D-12 emotional score of more than 0, five patients (45%) suffered from AECOPD.

Conclusions: COPD patients with AECOPD tended to score worse in the D-12. Although the D-12 emotional scores skewed with floor effect, patients with any points of D-12 emotional demonstrated high prevalence of AECOPD. In addition to the CAT, evaluating COPD patients with the D-12 could be useful in predicting AECOPD.
CORRELATION BETWEEN BODY MASS INDEX, GOLD STAGE AND FEV1 PERCENTAGE PREDICTED IN A COHORT OF COPD PATIENTS IN CENTRAL SRI LANKA
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Background and Aim: Poor nutrition and low body weight are known factors that contribute to severity of COPD. It is also a significant predictor of survival and mortality in COPD patients. We looked for a possible correlation between BMI and COPD severity by FEV1 and according to COPD GOLD stage.

Methods: A random sample of 90 patients attending the COPD clinic were selected and their lung functions were assessed using COSMED Software Version 2013. BMI was assessed using standard methods. This group included a total of 6,11,50, and 23 patients in GOLD stages 1, 2, 3 and 4 respectively. Data were analysed by MINITAB 17 statistical software. Correlation between BMI and FEV1 percentage was assessed by Pearson’s correlation coefficient. An association between COPD GOLD stage and BMI was assessed using ANOVA.

Results: The mean BMI of the group was 19.64 kg/m2. The mean FEV1 was 0.926 l and the average of percentage predicted was 40.86%. Pearson correlation coefficient between BMI and percentage predicted of FEV1 was 0.196 and this does not show a significant correlation (p=0.064). One way ANOVA between GOLD stages and BMI, similarly did not reveal a statistically significant result (p=0.629).

Conclusion: There was no significant correlation between BMI and COPD stage or the FEV1 demonstrable by statistical analysis. However, this may be due to an over representation of the more severe stages of COPD in this cohort.

ANALYSIS OF TRANSCRIPTOME SEQUENCING DATA IN THE LUNG TISSUE OF EMPHYSEMA SUBJECTS
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Background and Aims: To date, the precise genetic mechanism of chronic obstructive pulmonary disease (COPD), including emphysema is not fully understood. We aimed to explore the molecular pathogenesis of COPD with and without emphysema, using gene expression profiling of lung tissues by RNA sequencing method.

Methods: RNA was isolated and processed from lung tissues obtained from smokers with history of more than 10 pack years. We classified subjects to three groups to elucidate differentially expressed genes or pathways related to emphysema or COPD without emphysema: Emphysema COPD, Airway COPD and control group. RNA samples were isolated and processed with RNA-seq using the GiSeq 2000 system. One-way ANOVA test was performed to identify different genes between three groups.

Results: A total of 110 subjects included in final analysis. Emphysema COPD, Airway COPD and control group was noted in 29, 21 and 60 subjects respectively. Among 16,676 genes evaluated, 649 up-regulated and 577 down-regulated genes were differentially expressed in Emphysema COPD group but not in Airway COPD group compared to control. And 318 up-regulated and 116 down-regulated genes were differentially expressed in Airway COPD but not in Emphysema COPD compared to control. Pathway analysis represented by DAVID results showed mitochondrial genes related pathways decreased in expression both Airway COPD and Emphysema COPD, but not in Emphysema COPD compared to control.

Conclusions: Our study identifies difference in gene expression and pathway annotations between patients with Emphysema COPD and Airway COPD by RNA-seq transcriptome analysis. These findings may have clinical implications in COPD.
Background and Aim: Vitamin D may be affecting the lung function in patients with Chronic Obstructive Pulmonary Disease (COPD). We compared 25 Hydroxy Vitamin D (25OH Vit D) level in COPD patients with healthy control subjects.

Methods: A case-control study was conducted among the patients referred to the pulmonology clinic of Shahid Beheshti Hospital of Hamadan in the west of Iran. We enrolled 136 persons who were equally divided into two groups (68 persons with COPD in case and 68 healthy persons in control group). All subjects were evaluated by history, physical examination and pulmonary function tests in terms of lung function especially FEV1 (Forced Expiratory Volume in First Second) by spirometer. The serum level of 25 OH Vit D was measured by ELIZA method.

Results: Mean age of participants was 58.83 years old; there were 2 females in each group. Case group were older and had lower BMI than control group (P-Value<0.05). Mean serum level of 25 OH Vit D was 22.22±15.83 and 27.47±21.43 ng/ml in COPD and control group, respectively (P-Value<0.01). There was a positive correlation between FEV1 and 25 OH Vit D level in case group.

Conclusion: Vitamin D deficiency in COPD patients was more prevalent than control group. Due to the high prevalence of 25 OH Vit D deficiency, we suggest measurement of 25 OH Vit D in such patients.

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Keywords: COPD, 25 OH Vit D, FEV1, BMI, GOLD Criteria

Prognosis of Common Myeloid Cells Deficiency in Chronic Obstructive Pulmonary Disease

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Background and Aim: Little is known the deficiency of common myeloid cells (red cells, platelets, and white cells) in COPD. The aim of the study was to explore their relation to mortality in patients with COPD.

Methods: In this study, participants enrolled from the National Health Research Institute Database (NHIRD) of Taiwan, and we reviewed 53503 patients with their sequential clinically diagnosed COPD with or without anemia, thrombocytopenia or leukopenia data between 2005 and 2009.

Results: There were 1724 COPD patients with common myeloid cell defect. 1629 patients with anemia, 82 in thrombocytopenia and 13 in leukopenia. The mortality rate in each myeloid cells deficiency was 4.8%, 8.5%, 7.7% respectively. Our results show that COPD patients show significantly (p < 0.001) increased mortality accompany with anemia (95% CI, 1.53(1.21-1.92)) and thrombocytopenia (95% CI, 2.15(1.02-4.52)) but not leukopenia(95% CI, 1.08(0.15-7.67)).

Conclusion: In the present study, variant prognosis was noted in COPD patients with deficiency of common myeloid cells. COPD with anemia or thrombocytopenia was high risk for the mortality if compared to COPD only. Identification of those most at risk, and attempts early correct the myeloid cells deficiency should be encouraged.
could predict poor outcomes in exacerbation of COPD including serum albumin, hemoglobin, white blood cell count, serum sodium on the first day of admission and previous history of exacerbation. Binary logistic regression was used to identify factors associated with respiratory failure.

**Results:** A total of 349 admission records were reviewed. The subjects' mean ± SD age was 74.2±11.6 years, and 274 (78.5%) were male. During the admission, a total of 87 patients (24.9%) had respiratory failure and required ventilatory supports. In-hospital mortality rate was 8.0%. The only factor that associated with respiratory failure was low serum albumin level on the first admission day, 3.40±0.62 g/dL (in respiratory failure group) compare to 3.67±0.57 (in non-respiratory failure group), P=0.003. The other factors such as hemoglobin level, while blood cell count, serum sodium and history of previous exacerbation were not significantly associated with respiratory failure.

**Conclusions:** Serum albumin on the first day of admission could predict respiratory failure in COPD patients with acute exacerbation.

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CARBOCISTEINE INHIBITS THE EXPRESSION OF MUC5B IN COPD MOUSE MODEL

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**Background:** Chronic mucus hypersecretion and airway inflammation induced by cigarette smoke (CS) contribute to the pathogenesis of COPD. MUC5B and MUC5AC were the major secreted mucins which were strongly expressed in respiratory diseases with mucus hypersecretion. Carbocisteine, which could reduce viscosity and elasticity of mucus via decreasing mucins such as MUC5AC, was widely used in COPD. However, it is unknown whether carbocisteine can affect the expression of MUC5B in COPD.

**Aim:** We investigate the levels of Muc5b in COPD and carbocisteine intervention model.

**Method:** C57BL/J mice were used to develop COPD model by instilling intratracheally with lipopolysaccharide on days 1 and 14 and were exposed to CS for 2h twice a day for 12 weeks. Low and high doses carbocisteine 112.5 and 225 mg/kg/d, respectively, given by gavage administration were applied for the treatment in COPD models for the same duration, and carboxymethylcellulose were used as control (n=12 in each group). Pulmonary function and the mean linear intercept (MLI), pro-inflammatory cytokines and the production levels of Muc5b and Muc5ac were measured.

**Results:** Carbocisteine significantly attenuated inflammation in BALF and pulmonary tissue, improved pulmonary function and defended against emphysema. High dose carbocisteine significantly decreased the overproduction of Muc5b and Muc5ac in model group (0.85±0.13 vs 2.0±0.47, 0.61±0.12 vs 5.4±2.9, respectively, p<0.01), and prevented the decrease of the Muc5b/Muc5ac ratio in model group (1.46±0.33 vs 0.46±0.22, p<0.001). Moreover, the relative levels of Muc5b negatively correlated with pro-inflammatory cytokines, MLI, functional residual capacity (FRC) and airway resistance (Ri), but positively correlated with dynamic compliance (Cdyn).

**Conclusions:** Carbocisteine alleviated inflammation infiltration, reduced the secretion of Muc5b and Muc5ac, and inhibited the relative decrease of Muc5b, thereby improving lung function, which may further improve mucus clearance and affect the process of COPD.
of mice of the control group and experimental group in 14, 21, 28 days was tested with immunohistochemical method.

Results: A small amount of the above-mentioned three subtypes of LPA receptors expressed on the airway epithelium cell membranes in the control group, indicating normal pulmonary tissue has such expression. Compared with the control group, the expression of the three subtypes of LPA receptors of PF in the experimental group, namely LPA1, LPA2, LPA3, gradually increased and reached the highest in the 21-day period. The results were statistically significant. The intra-group comparison in the experimental group, which indicated that the three subtypes of LPA receptors expressed more and more along with each week, was also statistically significant.

Conclusions: Based on the model-creating methods in the extant literature, the PF model created with bleomycin as the pathogenic factor could be deemed as successful. The three subtypes of LPA receptors 1, 2, 3 expressed a small amount in normal pulmonary tissue, and more in the PF process. The differences were statistically significant, indicated the pathways of the three receptors were involved in the emerging and developing of PF.

AP424

IPF OR NOT IS STILL IMPORTANT EVEN IN THE TERMINAL PHASE OF INTERSTITIAL PNEUMONIA

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Background: Although Idiopathic Pulmonary Fibrosis (IPF) is known with its short prognosis, only limited information exists about its terminal phase.

Aim: To see the difference in the terminal phase between the patients with IPF and other subtype of interstitial pneumonia.

Method: This is the retrospective cohort study. The patients with interstitial pneumonia (IP) who received our visiting physician service from 2012 to 2016 were enrolled. Patients were divided into two groups, IPF group and non-IPF group, by chest–CT appearance, serological test, and physical finding. Survival from the beginning of our physician visiting service to death, place of death, laboratory data and oxygen supply at the beginning of the service were compared between the groups.

Results: 4 patients with IPF and 11 patients with non-IPF were enrolled. We found significantly shorter survival in IPF-group (P<0.01). However, there were no difference between the groups in age, laboratory data, and oxygen supply.

Conclusion: In the terminal phase of IP, the diagnosis of IPF was still important for predicting prognosis of the patients with IP.

AP425

CHANGE IN COPD ASSESSMENT TEST SCORE IS SIGNIFICANTLY ASSOCIATED WITH CHANGE OF DISEASE STATUS IN IDIOPATHIC PULMONARY FIBROSIS IN ONE-YEAR FOLLOW-UP

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Background and Aim: COPD Assessment Test (CAT) is reported to have construct validity for measuring health status of patients with idiopathic pulmonary fibrosis (IPF) in a cross sectional study. However, it is unknown whether the change of CAT score captures longitudinal change in health status in IPF patients.

Methods: Using data of IPF patients from a cohort of ILD at our institution from June 2011 to February 2016, retrospective study was performed by examining Spearman coefficients between changes in CAT score and changes values of anchors (the mMRC dyspnoea score, distance walked during the 6-min walk test (6MWD), and FVC % pred) in one year. The ability to detect change was assessed using ANCOVA of changes in CAT score by changes in anchors at one year.

Results: A total of 150 IPF patients were included in the study. Characteristics of study subjects were age in 66.5 ± 7.5 y.o., 118 males (78.7%), FVC % pred in 84.3 ± 19.6%, DLco % predicted in 63.1 ± 20.9%, mMRC in 0.96 ± 0.85, 6MWD in 583 ± 131 m, min SpO2 immediately after 6MWT in 83.2 ± 10.6 %, and CAT in 12.4 ± 7.8. During follow up interval (366 ± 35days), a significant change was observed in FVC % pred (~3.8 ± 9.5 %), 6MWD (~29.9 ± 85.6 m), and CAT (2.2 ± 6.0). Changes in CAT score was significantly correlated with changes in values for each of the anchors. There was a trend for subjects with the greatest absolute deterioration from baseline in FVC % pred experienced the greatest deterioration from baseline in CAT score.

Conclusion: At one-year follow-up, change in CAT score is significantly associated with change in disease status in IPF patients.

AP426

This abstract has been withdrawn

AP427

A STUDY OF SURFUCTANT PROTIEN-D (SP-D) SERUM LEVEL IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background: Recent studies have clearly shown that Idiopathic pulmonary fibrosis (IPF) has a high mortality rate, and current therapies are only marginally effective. A serum biomarker that predicts clinical outcome would be useful to stage disease, indicate prognosis and the need for aggressive therapy, and help stratify patients for clinical trials. This study aimed to measure the level of surfactant protein D in serum of patients with idiopathic pulmonary fibrosis and its relation with clinical manifestation, also its role in predicting patient outcome.

Methods: This study included 35 IPF patients compared to 15 healthy non smokers volunteers. Serum level of surfactant protein D (SP-D) was measured in the serum of patients and control persons relating their levels with the measurements of arterial blood gases, ventilatory Functions (FVC% of predicted, FEV1% of predicted and FEV1/FVC% of actual), High Resolution Computed Tomography (HRCT) and with Arabic version of ST Gorge total score respiratory questionnaire.

Results: Serum level of SP-D were significantly increased in IPF patients as compared to control subjects also their levels were significantly increased in IPF smokers as compared to non smokers and ex smokers IPF patients. The mean values of (SGRQ-C) total score were found to be significantly higher in IPF patients as compared to control non smokers subjects. SP-D had statistically significant positive correlations with PaO2 but it had statistically significant positive correlations with FEV1/FVC% actual value, HRCT score and SGRQ total score. HRCT score had statistically significant positive correlations with FEV1/FVC% actual value, SGRQ total score and SP-D level.

Conclusions: SP-D level is higher in IPF patients also it increase in smoker IPF patients when compared to non smokers and ex-smokers IPF.
patients. SP-D had statistically significant negative correlations with PaO2 but it had statistically significant positive correlations with FEV1/FVC% actual value, HRCT score and SGRQ total score.

INTERSTITIAL PULMONARY DISEASES IN TURKEY

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Background and Aims: It was aimed to find out the arguments about prevalence of interstitial pulmonary fibrosis in Turkey.

Methods: The hospitalized patients in 249 hospitals with ICD10 code classification, J84 code as to data of TÜİK population of 2015, the prevalence calculations according to the age, gender and cities were made.

Results: The prevalence rate was reported as between 14.0 and 42.7 in hundred thousandth in vary studies. The population of Turkey in 2015 was 78.741.053, the expected number of IPF cases were between 11.024 and 33.623. In 2015, 396.393 patients with respiratory system disorders were treated as hospitalized 599.602 times. The average hospitalization time was 8.1 days. 261.83 times admission to the hospitals were done, and these admissions formed 4.6% of whole respiratory hospitalizations. Same men and women were hospitalized 1.5 times. The prevalence was 21.8 in 100.000. It was calculated 22 in men in 100.000 and in women 21.7 in 100.000.8.674 (50.5%) of them were men, 8.497 of them were women and the mean age was 64.8 years. In male patient it was found 63.9 years, and in women 65.7 years. The age standardized prevalence in 75-84 age group was found with 224.1 in 100.000 the highest. In men over 85 years of age group, it was calculated 271 in 100.000, and in women between 75-84 age group it was calculated as 200.6 in 100.000.1219 of hospitalized patients (6.7%) were died during the hospitalization time. 688 were men, 531 were women and the mean age was 71.4. Though it was average 8.6 days hospitalized patients with IPF, deaths from IPF average 13.8 days.

Conclusions: On the basis of inpatients, the prevalence of IPF in Turkey is found 22 in 100.000 with medium density. More detailed studies are required about this subject.

PIRFENIDONE INDUCED CUTANEous VASCULITIS

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Background and Aims: Currently Pirfenidone and Nintedanib are the drugs that have been approved by the US FDA for the treatment of mild to moderate idiopathic pulmonary fibrosis. The most usual dermal side effects of pirfenidone that were reported are photosensitivity reactions, rash, pruritis and dry skin. Ours is the first report that cutaneous vasculitis could be induced by the administration of pirfenidone.

Methods: A 58-year old male came with complaints of shortness of breath, dry cough for past 3 months. No history joint pain, Raynaud phenomenon. On physical examination, clubbing was present, fine end inspiratory crackles were heard in both lung bases. Chest X-ray showed bilateral diffuse reticular opacities. High resolution computed tomography scan thorax was done which showed subpleural reticular opacities with areas of honey combing and traction bronchiectasis predominantly in lower lobes. Patient was diagnosed to have IPF based on confident HRCT pattern. The patient was started on pirfenidone at the dose of 1200mg/day and other supportive measures. On next day, the patient developed erythematous elevated painful skin rashes all over the body with predominance over the trunk and forearms. The patient was advised to withhold pirfenidone and dermatologist opinion was sought immediately. The patient was admitted and pirfenidone was restarted under through observation at the lowest dose 200mg following which, he again developed similar rashes which were very painful.

Results: The skin biopsy was done after dermatologist opinion which showed evidence of cutaneous vasculitis.

Conclusions: Our case report on pirfenidone induced cutaneous vasculitis reveals that such adverse events are possible and there are no clear data on the prevalence of such pirfenidone induced cutaneous vasculitis due to lack of prospective studies.

AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS TREATED WITH SEQUENTIAL WHOLE LUNG LAVAGE AND GM-CSF FOLLOWED BY RITUXIMAB: A CASE REPORT AND REVIEW OF LITERATURE

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Background: Pulmonary alveolar proteinosis (PAP) is characterized by impairment of gas exchange secondary to intra-alveolar accumulation of phospholipoproteinaceous material rich in surfactant protein. The most common type of PAP in adult is autoimmune with presence of granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibodies. Standard of care consists of whole lung lavage (WLL) in patients with moderate to severe disease and alternative therapy is correction of GM-CSF deficiency with exogenous GM-CSF. Rituximab, an anti-CD20 monoclonal antibody, has shown promise in treating several autoimmune disorders.

Case Presentation: In this study, we reported a case of a 40 year old male diagnosed with PAP who developed severe hypoxaemic respiratory failure and was treated with WLL and GM-CSF. His condition relapsed three months after initial clinical remission and patient received consecutive WLL and patient received consecutive WLL and GM-CSF. Rituximab, an anti-CD20 monoclonal antibody, has shown promise in treating several autoimmune disorders.

Conclusion: Rituximab could be considered as an alternative therapy for PAP particularly in patients with refractory disease.

Conflict of interest: None declared.

Grant Support: None.

PERIPHERAL ALVEOLAR NITRIC OXIDE CONCENTRATION REFLECTS MACROPHAGE INFLAMMATION OF AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS (APAP)

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AP428

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AP431
Background and Aims: Nitric oxide (NO) is derived from the respiratory system and has a close relationship with the patho-etiology of respiratory diseases. However, the relationship between NO and the physiology of auto-immune pulmonary alveolar proteinosis (APAP) is not well understood. We therefore investigated whether the fraction of exhaled NO (F_{E_N2O}) and the peripheral alveolar NO concentration (C_{PNO}) are related to severity in APAP patients in this study.

Methods: Ten patients who were diagnosed according to the Japanese criteria of APAP were registered consecutively. The levels of F_{E_N2O}, including C_{PNO}, were measured using a chemiluminescence-based nitrogen oxide analyzer. The CT-score collection and molecular biological analysis were performed according to previous reports.

Results: After whole lung lavage (WLL), the values of C_{PNO} decreased, with improvements in the disease severity, serum markers (KL-6, LDH), diffusing capacity of the lung for carbon monoxide (DLCO) and imaging in APAP patients. Furthermore, we confirmed that C_{PNO} was produced by activated M1 type alveolar macrophages because high expression levels of the iNOS gene and proteins in these cells were observed in APAP patients.

Conclusions: Our results show that macrophage inflammation is essential for the patho-etiology of APAP, C_{PNO} reflects the severity of APAP and could be a non-invasive and useful marker for APAP.

Efficacy of whole lung lavage for patients with autoimmune pulmonary alveolar proteinosis

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Background and Aims: Pulmonary alveolar proteinosis (PAP) is a rare disease characterized by the intra-alveolar accumulation of surfactant lipids and protein. Autoimmune PAP (APAP) is defined by granulocyte/macrophage-colony stimulating factor (GM-CSF) autoantibody positive. Whole lung lavage (WLL) is the current standard therapy for APAP. There are a few reports about a large cohort of APAP patients treated with WLL. The aim of the study is to describe the clinical feature and prognosis of APAP patients treated with WLL.

Methods: We enrolled 21 APAP patients treated with WLL from consecutive 123 PAP patients prospectively registered in our institution from January 2001 to December 2016. We reviewed clinical records and evaluated clinical, pulmonary function, cell analysis of BALF, serum biomarkers including anti-GM-CSF autoantibody, efficacy and prognosis. Disease severity was evaluated by disease severity score (DSS). Efficacy was defined by improvement of DSS by 1 score and/or 10 Torr decrease in AaDO2. Progression of APAP was defined as additional treatment or admission after WLL.

Results: The median age was 52 years. Gender was Male/Female 14/7. Smoking history was 7 non-smokers and 14 smokers. Three patients had dust-exposure history. The median observation time from WLL was 3.5 years. The median AaDO2 and DSS were significantly improved between before and after WLL (AaDO2: 44.4 and 32.2, p<0.03, DSS: 3 and 2, p<0.009). WLL were effective in 16/21 (76%) patients. WLL was 3.5 years. The median AaDO2 and DSS were significantly more effective in Non-smokers (7/7, 100%) than Smokers (9/14, 64%)(p=0.03). The average progression free survival time was 1.9 year. The level of serum KL-6 tended to be higher in WLL-effective group. Serum anti-GM-CSF autoantibody levels, cell fractionation of BALF, and pulmonary function were not associated with efficacy and prognosis of WLL.

Conclusions: WLL was effective (76%) in patients with APAP. Smoking history was associated with the efficacy of WLL.
extracts (PDE) antibodies in patients with chronic IP having a history of bird-exposure.

Methods: We studied 24 cases of chronic IP with a history of bird-exposure, from December 2015 to March 2017. We examined clinical characteristics of 22 cases retrospectively with the exception of 2 cases in which pathogenesis were identifiable (summer-type hypersensitivity pneumonitis and drug-induced pneumonia). We used interview questionnaires to identify bird-exposure history, immunoCAP (Phadia.com) to detect IgG antibodies against PDE, high-resolution computed tomography (HRCT) to evaluate chest images, and EZR as statistical software.

Results: The subjects’ median age was 74 in years, 13 cases were male (59%), 15 cases had smoking history (68.1%). 14 cases had direct exposure to birds, 8 cases had indirect exposure (36.3%). Anti PDE antibody (19.95±11.23 μg/ml) was significantly higher in the group of which white blood cell count in peripheral blood was over 10000/μl than in the sub 10000/μl group. HRCT showed a) subpleural shadow in 11 cases (50%), b) GGO in 11 cases (50%), c) granular shadow in 13 cases (59%), d) interlobar nodule in 18 cases (81.8%) and e) honeycomb in 5 cases (22.7%). There might be a weak correlation between the level of anti-PDE antibodies and existence of a) sub pleural shadow on HRCT, but not significant.

Conclusion: Serum level of anti-PDE showed correlation with some clinical characteristics in IP patients with bird exposure.

AP435

HYPERSENSITIVITY PNEUMONITIS – A CASE SERIES

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Chronic hypersensitivity pneumonitis (HP) is caused by repetitive inhalation of antigenic antigens. We report four cases of chronic HP.

Case 1: 50-year-old lady had progressive breathlessness with cough for 4 months and significant exposure to mercury and acids. Examination revealed bibasal fine crepitations. CT Thorax showed features of NSIP. BAL cytology showed mixed inflammatory cells with increased eosinophils. Lung biopsy showed mixed histological pattern of NSIP. She improved clinically once started on oral and inhaled corticosteroids with azathioprine.

Case 2: 58-year-old man with asthma presented with cough for 3 years and significant exposure to carbon, fiberglass, glue and paint thinner. Examination revealed fine left basal crepitations. HRCT showed features of possible UIP or NSIP fibrotic type pattern. Lung biopsy showed mixed histological pattern of NSIP with no casing granuloma. Plethysmography showed air-trapping. Symptoms resolved after starting on inhaled LABICS only.

Case 3: 70-year-old lady diabetic presented with cough for 6 months with significant exposure to detergents. Examination revealed finger clubbing and bilateral lower zone fine crepitations. CT Thorax was suggestive of chronic HP and plethysmography confirmed restrictive lung disease. She improved on oral prednisolone and azathioprine.

Case 4: 44-year-old man with underlying CTEPH presented with breathlessness for 6 months and significant chlorine exposure. He was hypoxic and had fine bibasal crepitations. HRCT Thorax was suggestive of chronic HP and he was started on LTOT and oral prednisolone but only responded well initially but became resistant after.

These highlights that diagnosis of chronic HP requires thorough history, CT imaging with or without lung biopsy. Patients with chronic HP often responds to steroids (case 1 and 3) but can be resistant (case 4) or has some other diagnosis causing their symptoms (case 2).
with average of 40%. The high resolution computed tomography (HRCT) changes revealed 1 case with subacute hypersensitivity pneumonitis and the rest with indefinite usual interstitial pneumonia pattern with mosaic attenuation. Only 2 cases underwent biopsy which histologically showed multinucleated giant cells and granuloma consistent with hypersensitivity pneumonitis. All cases received steroid treatment with 2 patients on steroid sparing agent (Azathioprine).

**Conclusion:** A thorough history taking on environment and occupation is crucial to identify the possible exposure and specific changes on HRCT in order to establish the diagnosis of hypersensitivity pneumonitis. A lung biopsy may be helpful in making diagnosis especially when the case is in doubt or non-steroid responder. Another additional test that might be useful will be serum precipitants and bronchial alveolar lavage.

**Background and Aim:** Interstitial lung disease (ILD) is a common pulmonary manifestation of systemic sclerosis (SSc). It is unknown whether radiographic fibrosis score predicts mortality in SSc-ILD. We retrospectively analysed patients with SSc-ILD to evaluate whether radiographic fibrosis score was a useful predictor of mortality.

**Methods:** We identified SSc-ILD patients evaluated at Kurashiki Central Hospital (Japan) from 2006 to 2016, and radiographic fibrosis scores based on the extent of reticulation and honeycombing on high-resolution computed tomography (HRCT) scanning were calculated by manually tracing around each fibrotic area. Independent predictors of overall survival were determined using the Cox proportional hazards model.

**Results:** The study included 48 patients, of which 19 had usual interstitial pneumonia on HRCT. The median follow-up period was 56.6 months, and over the follow-up period 15 patients died. Five-year survival was 72.4%. In the multivariate analysis, radiographic fibrosis score, age, being male, and forced vital capacity were independently associated with an increased risk of death, while HRCT pattern was not.

**Conclusion:** A high radiographic fibrosis score was a poor prognostic factor in SSc-ILD. More widespread fibrosis was associated with an increased risk of death, independent of HRCT pattern.

**Radiographic Fibrosis Score Predicts Survival in Systemic Sclerosis-Associated Interstitial Lung Disease**

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Echocardiogram revealed primary tricuspid valve prolapse with mild pulmonary hypertension but without atrium dilatation. She had profound desaturation to 71% on 6 minute walking test (distance=375 meters). CT Thorax showed widespread heterogenous lung attenuation with hypodense areas suggestive of bronchiolitis obliterans. Spirometry showed obstructive pattern without significant reversibility (FEV₁ of 0.95L (31%), FVC 1.48L (42%), ratio 0.65) and full lung function test showed significant air trapping (RV=313%) with reduced DLCO (61%). Her connective tissue disease screens were all negative. She was started on oral prednisolone and responded well.

This case highlights that an interesting case of idiopathic bronchiolitis obliterans initially misdiagnosed as asthma.

AP441
AN EXTREMELY RARE CASE IN WHICH THE PATIENT WAS DIAGNOSED WITH IDIOPATHIC DENDRIFORM PULMONARY OSSIFICATION
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Background and Aim: Diffuse pulmonary ossification (DPO) is a rare disease in which diffuse ectopic bone fragments develop in the lung tissue. The disease is typically asymptomatic and anomalies often cannot be identified on plain chest radiographs. Most reported cases to date have been discovered in autopsies. We report an extremely rare case in which the patient was diagnosed with idiopathic dendriform pulmonary ossification during their lifetime.

Methods: Case: The patient was a 46-year-old Japanese man with no medical history and no history of smoking. He was an office worker and had no history of exposure to dust or other substances. Several years earlier, an abnormal shadow had been noted in his chest in a health checkup, but was not investigated further. More recently, the patient had sought a consultation for coughing and difficulty breathing during times of exertion. Computed tomography revealed non-specific reticular shadows in the centers of the bilateral lower lobes. The patient subsequently underwent thoracoscopic surgical lung biopsy. A pathological examination revealed multiple sites of ossification in the peripheral lung area with fatty marrow inside the bone fragments. The patient was diagnosed with dendriform pulmonary ossification.

Results: Discussion: The patient in the present case was in good health and had no underlying disease that could have been the cause of DPO. Moreover, his only subjective symptoms were respiratory symptoms. Because the secondary cause could not be pathologically identified, the patient was diagnosed with idiopathic dendriform pulmonary ossification. No treatment exists for this disease and much remains unknown about the prognosis even though only a small number of patients have been diagnosed while alive. However, according to a 2007 report by Ahar et al., the long-term prognosis of idiopathic dendriform pulmonary ossification is at least not poor. The progress of the present patient will therefore need to be monitored carefully in the future.

AP442
CLINICAL FEATURES AND PROGNOSIS OF MULTICENTRIC CASTLEMAN’S DISEASE
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Background and Aims: Multicentric Castleman’s disease (MCD) is an uncommon lymphoproliferative disorder with systemic manifestation, and the clinical presentation and the clinical course in MCD are variable. Therefore, we aim to clarify clinical features and prognosis of MCD.

Methods: We reviewed the clinical, radiologic and histopathologic features of consecutive twelve cases of MCD in our institution between 1967 and 2016.

Results: There were seven males and five females. The median age at diagnosis was 46 years old (range: 25-70 years). Laboratory findings at diagnosis revealed polyclonal hyperimmunoglobulinemia in all cases, and elevation of serum IL-6 levels in 10 cases. Flow-volume curve at diagnosis showed normal (n=9), obstructive (n=1), and mixed (n=1) patterns. Chest CT showed centrilobular nodules and ground glass opacities in both lungs of all cases, and thin-walled cysts in two cases. All cases were plasma cell variants of MCD by histopathologic examination of specimens of lymph node biopsy (n=10) and surgical lung biopsy (n=2). In addition, surgical lung biopsy specimens of five cases showed hyalinizing granuloma. Eight cases had received treatment (prednisolone only; 3, prednisolone plus tocilizumab; 4, prednisolone plus mizoribine or methotrexate; 1), and four cases had been observed with no treatment. The median observation period was 96 months (range: 7-285 months). At the last follow up, one case died with progressive airflow obstruction complicated with recurrent pneumonia and enlargement of bulla despite treatment, and other cases are alive. All cases were negative for HIV antibody and HHV-8.

Conclusions: Their prognosis was relatively good whether with treatment or not, except for one case. Progression of airflow obstruction may suggest poor prognosis of MCD.

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Environmental & Occupational Health and Epidemiology

AP443
STRATEGIC TRENDS OF DEVELOPMENT AND INDICATORS OF EFFICIENCY OF PULMONARY CARE TO THE POPULATION (REGIONAL ASPECT)
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Background and Aim: Far Eastern Center of Physiology and Pathology of Respiration developed the regional program “Strategy of monitoring, prevention and control over chronic respiratory diseases” to fulfill basic conceptions of the WHO aimed at the improvement of quality and efficiency of preventive services in the sphere of population respiratory health protection. This program and the plan of activities realize the conception of GARD on the territory of the Amur Region of Russia. We aimed to analyse of clinical and social-economic efficiency of the program in the regional healthcare.
Methods: Based on the materials of the state statistical monitoring (Rosstat), the analysis of indicators of medical and socio-economic effectiveness of health care for the population (indicators of morbidity, disability and mortality of the population due to respiratory diseases and their dynamics) in the Amur region was carried out.

Results: Using the corresponding criteria the efficiency of management bodies and health care institutions, scientific and education institutions on the territory of the Amur region through the activities aimed at the improvement of efficiency of pulmonary care to the population was demonstrated. From 2006 till 2013 the disability caused by respiratory diseases decreased 8.1 times, the level of infant mortality was 2.5 times lower, the values of the population mortality from chronic respiratory diseases being 2.1 times lower than those at the federal level in general (2013) became 1.8 times lower. The level of mortality from pneumonia in the children’s group at present is 3 times lower than this level in Russia and 5.8 times lower than the same parameters in the Far-Eastern Federal District.

Conclusion: Organization-methodological provision of the system of medical care to pulmonologic patients with the use of information and education resources and methods of special purpose program planning is an important factor and the main condition of improving its efficiency.

GENDER AND AGE GRADIENTS OF THE POPULATION RATE OF DEATH CAUSED BY RESPIRATORY DISEASES ON THE TERRITORY OF THE FAR-EASTERN REGION OF RUSSIA

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Background and Aim: Respiratory diseases are one of the causes of untimely death in the Far-Eastern region of Russia: their specific weight in the structure of death causes is 4.5% (2015). We aimed to study dynamics and regional features of mortality caused by respiratory diseases in different age and gender groups of population on the territory of the Far East of Russia.

Methods: Federal Service of State Statistics data of the statistical monitoring of respiratory diseases on the territory of Russia for 1990-2015 were used. The analysis of dynamic rows of the mortality due to respiratory diseases in different gender and age groups was conducted. Spearman’s range correlation, intensive and extensive indices of death rate were used for statistical analysis.

Results: Intensive index of death rate caused by respiratory diseases are from 27.9 per 100 000 people in Sakha Republic (Yakutia) till 83.4 in Sakhalin region. The index is 2 times higher among men than women (people getting older, the difference becoming bigger, r=0.78). The highest mortalities due to respiratory diseases exceeding the federal level by 43.5% are observed in the group of people younger than the working age (6.2 and 3.5 per 100000 of the corresponding age, respectively). Statistical analysis of dynamics rows for 25 years shows that on the territory of Russia there is a stable tendency of decreasing rate of death caused by respiratory diseases except the age of 15-29 and 30-44 years old, in which the trend of death rates has a tendency to grow (Tav.=1.34 and +2.65%, respectively).

Conclusion: Mortality from respiratory diseases in the Russian Far East has gender and age differences: the high level of death rate in the infant age and in older than the working age, domination in the death rate among men and direct proportional dependence of mortality on age.

SOCIAL-ECONOMIC BURDEN OF RESPIRATORY DISEASES

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Background and Aim: Respiratory diseases present a very important problem for the economy of the country as their treatment becomes a severe economic burden both for patients and for national systems of healthcare. The aim was to study the level and structure of social-economic burden to the Amur region (Russia) under respiratory pathology.

Methods: The methods of social-economic analysis at the assessment of morbidity, disability and mortality caused by respiratory diseases on the territory of the Amur region were used.

Results: Indirect losses make the biggest specific weight in the structure of economic burden (67.2%). The burden from underproduction of the domestic regional product (DRP) depends mainly on the morbidity and mortality of the working-age population. The losses from untimely death are much bigger than from disability and temporary disability. The average number of the years people couldn’t live because of the death caused by respiratory diseases is 9.6 years for men and 9.4 years for women in the city area, and 10.1 and 12.8 years in the rural area, respectively. The average age of people died from respiratory diseases is 50.1 for men, 44.4 years for women. Total indirect losses from respiratory diseases are 646.3 billions of rubles (2000), which corresponded to the losses in the national economy at the level of 0.39% of DRP (Amur region).

Conclusion: Intensive growth of underproduction of the DRP as a result of morbidity and mortality caused by respiratory diseases is found. The decrease in the level of morbidity and mortality caused by respiratory diseases demands from the government to conduct effective policy in the sphere of healthcare, which is possible on the basis of the knowledge about current state of epidemiologic situation, the dimensions of the social-economic burden from the morbidity because of respiratory diseases and its prediction value in the future.

PREVALENCE OF CHRONIC COUGH AND RURAL-URBAN DIFFERENCES IN RISK FACTORS ASSOCIATED WITH CHRONIC COUGH IN INDIA

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Background and Aims: Chronic cough is an important indicator of chronic respiratory morbidity. Our aim was to assess the prevalence of chronic cough and rural-urban differences in associated risk factors in India.

Methods: We conducted a population based cross-sectional survey, as a part of large community intervention study entitled UDAY, among 12243 participants aged ≥30 years residing in rural and urban areas of North (Haryana) and South (Andhra Pradesh) India. Participants were selected using a multi-stage cluster random sampling. Data were obtained using an interviewer administered questionnaire and

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anthropometry. Chronic cough was defined as cough and chronic mucous production on most days or nights of the week for at least three consecutive months during the past one year that was not due to a common cold. We calculated the age-standardized prevalence of chronic cough and measured its association with common risk factors by logistic regression.

**Results:** The mean age of participants was 46.8 (SD: 12.5 years) and 54% were women. Age-standardized prevalence of chronic cough was 6.5% (95% CI: 6.0 to 7.1), rural 9.4% (95% CI: 8.6 to 10.2) and urban 3.7% (95% CI: 3.1 to 4.4). Self-reported asthma and history of tuberculosis during past five years were associated with an increased risk of chronic cough in both rural [Asthma- Adjusted Odds Ratio (AOR): 3.05, 95% CI: 1.90-4.92], Tuberculosis- AOR: 16.67, 95% CI: 8.58-33.14] and urban areas [Asthma- AOR: 6.24, 95% CI: 3.75-10.39], Tuberculosis- AOR: 8.25, 95% CI: 3.77-18.06]. Increasing age was associated with increased risk and increasing years of education was associated with decreased risk of chronic cough in rural areas. Smoking was associated with increased risk of chronic cough in urban areas (AOR: 1.75, 95% CI: 1.17-2.61).

**Conclusions:** There is a high burden of chronic cough especially in rural India, which necessitates evaluation for its prevention and management.

**AP447**

**CORRELATION BETWEEN NITRIC OXIDE (NO) SPUTUM LEVEL AND LUNG FUNCTION OF INDOOR PARKING ATTENDANT**

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**Background and Aim:** Indoor air pollution causes inflammation of the respiratory tract. This will increase the level of NO sputum and change lung function of parking attendants. The aim of this study is to determine correlation between NO sputum level and lung function of indoor parking attendants.

**Methods:** The research was conducted in Samudra Department store, Tasikmalaya, West Java, Indonesia. This research involved 40 subjects, 20 indoor parking attendants as the exposed group and 20 administrative officers as a control group. NO levels sputum and lung function were examined in both groups. Measurement of NO sputum used Griess method and lung function were evaluated using Spirometry (brand Fukuda).

**Results:** The mean level of NO sputum in the exposed group was 6778.452. The mean sputum level of NO in the control group was 5.432%, while in control group FVC = 129.30/15.998, FEV1 / FVC = 75.15 ± 5.432%, while in control group FVC = 129.30 ± 11.961%, FEV1 = 118, 35 ± 12.844%, FEV1 / FVC = 83.45 ± 6.253. Lung function test results in both groups showed significant difference in FEV1 and % FEV1/FVC (p <0.05), but not in FVC (p >0.05). Pearson correlation test showed a strong positive correlation between the NO sputum level and lung function of indoor parking attendant (r = 0.461; p <0.041).

**Conclusion:** There is a correlation between NO sputum level and lung function of indoor parking attendant (r = 0.461; p <0.05).

**Keywords:** Indoor parking attendants, Nitric Oxide (NO), lung function

**AP448**

**INVESTIGATE THE EFFECT OF SMOKING CESSATION DEBATE BY PUBLIC BROADCAST TELEVISION AND OTHER TOBACCO INFORMATION RECOGNITION STATUS IN JAPAN**

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**Background and Aim:** Currently ongoing, the momentum for promoting smoking cessation is rising in Japan. The Ministry of Health, Labour and Welfare research group summarized estimates that the number of people who died due to passive smoking will amount to about 15,000/year in Japan on the No-World-Tobacco Day 2016. In addition, The Ministry of Health, Labour and Welfare has compiled a report on the health effects of smoking “tobacco white paper” on the 31/Aug 2016. Nevertheless, knowledge about tobacco is still very low in Japanese citizens. On the other hand, false tobacco information is prevalent and they are opposed to smoking. Therefore, we evaluated the effect and reaction of the smoking cessation debate (famous caster and comedian, quit-smoking research leader, viewer participation type Q & A style)program in public television broadcasting and other knowledge of tobacco information from TV.

**Methods:** Subjects (n=20) in a survey conducted in who admitted to the general medical examination venue, the day after the public broadcasting smoking cessation debate program (other Japanese broadcasting TV have commercials include tobacco industry). We performed a face-to-face question interview with hand out materials on quit smoking materials and the advice.

**Results:** Characteristics of subjects(n=20) were male/M/female/F (%)=55.0/45.0(n=11/9), 44.6±12.8 yrs(±SD)Range 21-63], respectively. Surprisingly, only one (0.2%; 56yrs-female) saw the program. The recognition rate of the risk of lung cancer 1.3 times higher among Japanese exposed to secondhand smoke was only 5.0%(M/F%; 0.0/11.1) (n=0/1). One pack(20 pieces) is nearly 3.5US$ in Japan, almost all subjects answered nearly 10US$, tell them 30US$/pack in Australia, very amazing reaction.

**Conclusion:** Still in Japan, smoking scenes are broadcast (especially in private broadcasting) with TV commercials and TV dramas, but unfortunately in this survey, despite the relatively popular public television broadcasting, watching rate was low. We suspected that this cause was influenced by the low degree of interest in other cigarettes of the subject and the poor announcement of this TV program. We should do more actions for quit smoking campaign and educate.

**AP449**

**ASSOCIATION OF HOUSEHOLD TOBACCO EXPOSURE IN HONG KONG YOUNG CHILDREN WITH LOWER FAMILY SOCIOECONOMIC STATUS AND MEDICAL SERVICE UTILISATION**

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**Background and Aim:** Household tobacco exposure in young children causes significant disease and economic burden. This study aimed to examine the prevalence and to explore the associations between household tobacco exposure and family socioeconomic status, recent respiratory symptoms and medical service utilizations in Hong Kong young children.
Methods: Analysis was performed on data obtained from a community-based cross-sectional pneumatic carriage surveillance study of healthy children aged under 2 years across 4 main regions of Hong Kong. Information on demographics, household tobacco exposure, family socioeconomic status, children’s recent respiratory symptoms and medical service utilisation was obtained by parent-reported questionnaires.

Results: 1541 subjects (mean age: 11.2 months, male: 50.7%) recruited from June 2013 to June 2014 were included in the analysis. The prevalence of household tobacco exposure was 31.5%, prevalence of prenatal and postnatal maternal smoking was 1.6% and 3.5% respectively. After adjustment for potential confounding factors, low household income (AOR=1.38, 95% CI: 1.08-1.76), overcrowding of household living area (AOR=3.13, 95% CI: 2.00-4.89), residing in Kowloon (AOR=1.55, 95% CI: 1.11-2.15) and New Territories West (AOR=1.65, 95% CI: 1.18-2.32) were independently and significantly associated with household tobacco exposure. Practice of breastfeeding was significantly associated with lower odds of having household tobacco exposure (AOR=0.65, 95% CI: 0.50-0.84). Prenatal maternal smoking exposure (AOR=2.30, 95% CI: 1.09-4.85) was significantly associated with doctor consultation in recent 3 months; postnatal maternal smoking exposure (AOR=2.70, 95% CI: 1.16-6.27) was significantly associated with hospitalisation in recent 3 months. However, household tobacco exposure was not significantly associated with recent respiratory symptoms in our cohort.

Conclusion: As home is the most significant source of environmental tobacco exposure for young children, efforts for reducing such exposure are essential especially in socially deprived population.

AP450
COMPARISON STUDY BETWEEN FACULTY AND COLLEGE STUDENTS ABOUT THE SITUATION OF TOBACCO IN OUR JAPANESE SMOKE FREE NON-MEDICAL CAMPUS

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Background and Aim: Smoke-Free-Campus (SFC) has not been fulfilled in Japan. Especially, quit smoking education is low level and smoking ratio is still high. Therefore, we investigated a comparative study on intergenerational tobacco interest and quit smoking situation in Non-Medical-SFC.

Methods: Questionnaire for all Students[Group A(B)] and Employees; faculty/staff[Group B(AB)] was performed[AB(n)].

Results: Characteristics of subjects(n=641132) were Male/Female (%)=53.4/46.6/60.6/39.4%:20.4:1.6;SD: [Range]:19-29] 44.6:11.6/23-72], respectively. Smoking prevalence(%) was Current: 8.2/Ex:5.6/Never:86.7/83.25.0/66.7. The starting smoking age was 17.9±3.2 [5-21] 19.1±3.1/16-32]. The reason of opportunity to start were almost equally, Out of interest/Incidentally/Stress/Neighbouring smoke(%):50.0/43.2/34.1/29.5/62.6/23.1/14.2/19.5/25.0 were accounted for a large number (*multiple answers act.). Only A was affected by TV and movies. Whereas, reasons for quit smoking were similar in both groups, For themselves health/For neighbour’s/Incidentally/Recommended. Approximately equal, regardless of age, their consciousness of health to their own and others was high. In this connection our campus was affected the great earthquake disaster area, after re-smoking rate was raised in both group. Unfortunately, the above was also cause of opportunity(%) to start(5.2/2.3). In contrast, we observed differences in hope of smoking cessation and how to collect tobacco information.

Conclusion: The result was considered to relate that anyone be able to easily purchased in Japan (e.g. convenience store, supermarket without presence ID), moreover daily TV commercials of the tobacco industry. Additionally, the raising of re-smoking after the great disaster, above result was presumed that tobacco industry distribute tobacco under the name of disaster relief is one of the cause of resumed based on situation reports of other disaster districts. There were no apparent relationship age differences from knowledge on tobacco regardless of generation, smoking was observed from adolescence. In recent everyone can easily purchase nicotine-free e-cigarettes (some adult smokers use for quit smoking), so we need countermeasure to prevent future smoking habits.

AP451
FEATURES AND PROBLEMS OF SMOKING CESSATION IN JAPANESE SMOKERS WITH HIV INFECTION COMPARED TO THOSE WITH NON-HIV DISEASES

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Background and Aims: Smoking is associated with the pathogenesis of diseases including cancer and cardiovascular and respiratory disease. Smokers with psychological disorders often have difficulty quitting smoking compared with smokers with other chronic diseases. With the widespread use of antidepressives, smoking cessation is considered to be a chronic disease, and HIV-infected smokers are less successful at their attempt to quit. We compared factors affecting smoking cessation in smokers with HIV infection and those with psychological disorders or other diseases.

Methods: Subjects were 146 smokers attending Jichi Medical University Hospital Smoking Cessation Clinic between April 2011 and March 2016. Subjects were divided into 4 groups: 25 with no underlying disease (“None”), 20 with psychological disorders (“Psy”), 7 with HIV infection (“HIV”), and 94 with underlying disease other than psychological disorders or HIV infection (“Other”). We administered smoking cessation therapy comprising smoking cessation intervention with medication and nurse counseling during visits over 52 weeks. Smoking characteristics, cigarette dependence, and 12- and 52-week smoking abstinence rates were examined.

Results: Median age (years): “None”: 43; “Psy”: 40; “HIV”: 52, “Other”: 63. Male/female ratio: “None”: 21:4; “Psy”: 11:9; “HIV”: 7:0; “Other”: 67:27. No intergroup difference was observed in Brinkman index or Tobacco Dependence Screen score. Most subjects received varenicline, but 7 of 20 subjects in the “Psy” group received nicotine patch. The “Psy” group had the highest 12-week program dropout rate (“None”: 12.0%; “Psy”: 45.0%; “HIV”: 14.3%; “Other”, 10.6%) and the lowest 12-week abstinence rate (88.0%, 35.0%, 85.7%, 73.4%, respectively). The 52-week abstinence rates (68.0%; 25.0%; 82.6%; 58.5%, respectively) were lower in the “Psy” and “HIV” groups.

Conclusions: HIV-infected smokers are likely to achieve successful short-term smoking abstinence but have high risk of re-smoking. Continued interventions for smoking cessation after initial short-term therapy should be considered in this population.
THE EFFECT OF EDUCATION ON SMOKING-RELATED KNOWLEDGE AND ATTITUDE AMONG ADMINISTRATION STAFF IN UNIVERSITAS INDONESIA

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Background and Aim: Indonesia is among five countries with highest smoking prevalence in the world. Indonesia, high smoking prevalence was found in employee occupation group and working age group. 81.3% of smokers already know the negative effects of smoking, but the amount of smokers still increases every year. Therefore, this research is designed to thoroughly assess the knowledge and attitude of smokers amongst the group mentioned above.

Methods: This experimental research is conducted from June until July 2016. The subjects, Universitas Indonesia’s staff who actively smoked over the past one year, were chosen by purposive sampling method from a health screening on 220 staffs. The subjects then gathered on a different day to be given an education by smoking cessation expert. The knowledge and attitude scores were measured before and after education by giving pre-test and post-test using validated questionnaires developed for this research. The descriptive analysis of this study used SPSS version 20, descriptive and inferential (Wilcoxon, chi-square, Fischer) statistic tests were performed.

Results: There is no drop-out subjects as all the subjects who had required the research condition and confirmed to attend education (n=17) participate from beginning until the end. Mean of the knowledge score increases significantly by education with pre-test score 18.41 (±4.72) and post-test score 27.0 (±6.66) = p<0.001. Mean of attitude score also increases significantly with pre-test score 80.18 (±9.49), and 84.65 (±7.47) = p=0.044. There is no correlation found between sociodemographic factors and the increase of smoking-related knowledge and attitude among the subjects.

Conclusion: Education increases knowledge and attitude of smokers significantly. Therefore, frequent and holistic education can provide good support and assistance for smokers wishing to quit.

EXHALED CARBON MONOXIDE SURVEY IN INDONESIAN ADULT POPULATION

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Background and Aim: Environmental tobacco smoke (ETS) and air pollutions are major environmental health problems in Indonesia. The exposure to these environmental agents increased the level of exhaled carbon monoxide (CO) at certain baseline. This study was performed to determine the baseline of exhaled CO between groups of smoker and non-smoker derived from the population of Jakarta, Indonesia.

Methods: This study was a cross sectional surveillance study involving healthy subjects of Persahabatan General Hospital, Jakarta, Indonesia in 2014. Exhaled CO levels were obtained and compared between population groups of smoker and non-smoker.

Result: Four hundred and thirty subjects, 113 are males and 317 are females, are grouped into smokers (45/430, 10.5%) and non-smokers (385/430, 89.5%). The mean age is 44.7 years old (range: 17-78 years old). The mean exhaled CO level is 4.9 ppm. The mean exhaled CO level among smoker group is significantly higher than among non-smoker group (5.0 vs 10.0 ppm, p=0.000). Smoking status is found to be the only independent factor influencing the exhaled CO level.

Conclusion: The difference of exhaled CO levels measured between smokers and non-smokers would provide insightful information of baseline for future study of environmental health problems...
Background and Aim: Forest fire is not only a serious problem in Indonesia but also seriously affects life and health at the regions in South-east Asia countries. Reduced air quality due to forest fires could exaggerate respiratory illness. At the end of 2015 forest fire had been affected the area of RimboPanjang, Riau. The aim of this study is to evaluate the pulmonary function test using spirometry of residents affected by forest fire smoke.

Methods: This is a cross sectional study involving resident in forest fire area. The pulmonary function test samples within the criteria, which have the age between 15-60 years old, did not smoke a cigarette in the last 12-24 hours and has domiciled in the village of RimboPanjang, Kampar, on January 2016. The study group consists of 97 people, with 28 of them (28.87%) smoke cigarettes and 69 of them (71.13%) did not. Statistical analysis was performed with the Mann-Whitney test.

Results: Spirometry results showed that 61 (62.89%) had normal lung function, 29 (29.90%) experienced mild restriction, 3 (3.09%) experienced moderate restriction, 1 (1.03%) experienced heavy restriction and 2 (2.06%) experienced mild obstruction and 1 (1.03) experienced moderate restriction and obstruction.

Conclusion: The results of spirometry showed that 36 of subjects had abnormal lung function. Since this is a cross sectional studies, further lung function analysis will be needed to seek relation of forest fire and lung function decline.

SERUM BENZOPYRENE LEVEL IN FIREFIGHTERS AFTER FORESTFIRE IN RIAU PROVINCE-INDONESIA

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Background and Aim: Forest fire in Sumatera-Indonesia in 2014 was responsible to health problems in region. In 2014, World Resources Institute (WRI) found 3,101 fire’s spots in Sumatera Island dan about 87% was found in Riau. The smoke which was produced from the forest fire contained carcinogenic compound such as Benzo[a]pyrene (BAP) with the main metabolite was Benzo[a]pyrene 7,8-diol 9,10-epociside (BPDE) that could damage the DNA. The aim of this study is to know the level of BPDE’s serum in The Firefighters of Pekanbaru City who had been contaminated after the forest fires in Riau Province.

Methods: Blood test was done to the samples whom qualified which aged between 18-60 years old with total sample was 50 firefighters in 2015, six months after forest fire had occured. The level of BPDE’s serum was read by ELISA’s reader 650. Statistical analysis was performed with univariate.

Results: The test was done to 50 firefighters with the average age was 33.36 years and median was 34.5 years (between 24-45 yearsold). Most gender was Male (96 %). The mean level of Benzo[a]pyrene within the respondents’ blood was 16.45 ng/mL with deviation standart about 6.79 ng/mL. The median was 14.89ng/mL. The lowest level of Benzo[a]pyrene within the respondents’ blood was 1.93 ng/mL and the highest was 50.51 ng/mL.

Conclusion: In this study, the mean level of Benzo[a]pyrene was16.45 ng/mL.

Keywords: Benzo[a]pyrene, carcinogenic, forest fire.

LUNG FUNCTION OF TAXI WORKERS EXPOSED TO THE 2015 FOREST HAZE IN PEKANBARU, RIAU, INDONESIA

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Background and Aim: Indonesia suffered from an environmental disaster caused by forest fires between August and October 2015, of which Riau, Sumatera was amongst the affected area. The study observed the impact of forest haze caused by the fire to the health and lung function of taxi workers in Pekanbaru, Riau, Sumatera.

Methods: This cross-sectional retrospective study involved 178 taxi drivers from a company in the study location during the 2015 forest haze. Data were obtained from respiratory questionnaires and lung spirometry tests. Data included for statistical analysis were respiratory symptoms, exhaled CO levels, exhaled HbCO levels, and lung function variables. In addition, Indonesia Health Department Research Center reported the value Air Pollution Index (API) range from 110 to 778 ppmv during the event.

Results: Forty six participants, 3 (6.52%) females and 43 (93.48%) males, were included in the analysis. Thirty three (71.74%) subjects showed respiratory symptoms, 27 (58.7%) subjects showed non-respiratory symptoms, and 4 (8.69%) showed respiratory and non-respiratory symptoms. Exhaled gas levels were shown to be elevated: mean exhaled CO level revealed to be 37.17±17.90 ppm and mean exhaled HbCO level revealed to be 6.59±2.9%. Lung function test revealed 30 (65.20%) subjects showed normal function, 13 (28.6%) subjects showed restrictive value, and 3 (6.52%) subjects showed obstructive value.

Conclusion: This study showed the detection of respiratory and non-respiratory symptoms and the elevation of exhaled CO and HbCO levels during the forest haze event.

Keywords: forest haze, lung function, exhaled CO, HbCO

HOW DOES BENIGN ASPEROSPLEURAL EFFUSION PROGRESS?

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Background and Aims: Benign asbestos pleural effusion (BAPE) is a pleuritis caused by asbestos exposure. While BAPE is thought to be the antecedent pathology of diffuse pleural thickening (DPT), little is known of its outcomes. Our aim is to clarify the progress in the imaging and clinical features of cases with BAPE.

Methods: We investigated the symptoms and the characteristics of pleural effusion and followed the images of the chest in 20 cases that were diagnosed with BAPE at our hospital.

Results: All twenty cases were men and the mean age at onset was 70.6 years. Eleven patients visited the clinic for subjective symptoms, and pleural effusion was detected at the medical check-up in nine cases. The

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type of asbestos exposure history was occupational in 17 cases, environmental in two cases, and unknown in one case. The mean latency time from the first exposure was 46.2 years. Pleural effusion was found more frequently on the right side. It was bloody and lymphocyte predominant. The mean total protein, adenosine deaminase and hyaluronic acid concentration test results were 4.1 g/dL, 24.2 IU/L and 33,608 ng/mL respectively. The mean observation period of the cases was 43.4 months. Followed CT images revealed residual pleural effusion, pleural plaques, DPT, rounded atelectasis, lung fibrosis, apical pleural thickening (apical cap) and fibrous strands (Crow’s feet) in 12 (60%), 17 (85%), 13 (65%), 12 (60%), six (30%), seven (35%) and 16 cases (80%), respectively. In four of the seven cases of apical cap, progression of the apical cap and accompanying pulmonary fibrosis was seen, as well as shrinking of the lungs and impaired pulmonary function.

Conclusions: Residual pleural effusion tended to be long-term and over half of the cases exhibited DPT. As apical cap and pulmonary fibrosis progressed to cause respiratory failure in some cases, this condition requires careful follow-up.

AP459
MINERALOGICAL ANALYSIS OF BRONCHOALVEOLAR LAVAGE (BAL) IN PULMONARY SILICOSIDEROSIS WITH RECURRENT PNEUMOTHORAX AND DEFAULT CASE OF TUBERCULOSIS: A CASE REPORT
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Background and Aims: Silicosis is a fibrotic lung disease attributable to the inhalation of crystalline silica. Pleural involvement in silicosis is rare and secondary spontaneous pneumothorax (SSP) is the only recognized pleural complication. Siderosis is caused by the inhalation of dust/fumes containing iron particles and usually benign.

Results: A 24-year-old male was admitted to hospital with shortness of breath and chest pain. In the last two years, he had a history of 1 year working in a warehouse; processing rusty iron/metal by sandpaper and a history of working in a cement factory for 6 months; processing the packing of cement into sacks, both without wearing any respiratory protection devices. Thoracal CT scan with contrast showed multiple infiltrates, fibrosis, centrilobular-paraseptal emphysema in both lungs and left pneumothorax. The patient was diagnosed as pulmonary silicosis and it was confirmed using mineralogical analysis of bronchoalveolar lavage (BAL) which showed positive results for silica (< 0.023 mg/L) and iron (0.760 mg/L) with Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES) method. The patient was also diagnosed as default case of tuberculosis (TB) with detected rifampicin sensitive MTb in sputum Xpert®MtB/Rif result and positive MtB DNA band in PCR-TB of the BAL. We managed the patient with oxygen supplementation, antituberculosis drugs and chest tube placement. After pleurodesis and the removal of the left chest tube, the patient had a right pneumothorax and another chest tube was placed. We removed the right chest tube after clinical and radiological improvements. The patient was discharged with continued antituberculosis and long term oxygen therapy.

Conclusions: Based on our findings, mineralogical analysis of BAL confirmed the diagnosis of pulmonary silicosis and it was confirmed using mineralogical analysis of bronchoalveolar lavage (BAL) which showed positive results for silica (< 0.023 mg/L) and iron (0.760 mg/L) with Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES) method. We diagnosed the patient as pulmonary silicosis and it was confirmed using mineralogical analysis of bronchoalveolar lavage (BAL) which showed positive results for silica (< 0.023 mg/L) and iron (0.760 mg/L) with Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES) method.

AP460
IS THE COMPUTER TOMOGRAPHY USEFUL FOR DIFFERENTIAL DIAGNOSIS OF SUSPICIOUS PNEUMOCONIOSIS?
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Background and Aim: Pneumoconiosis is diagnosed with simple chest X-ray by ILO classification. However, the accuracy or validity of chest PA reading is different from the readers due to their different experience. In a clinical view, the suspicious pneumoconiosis by chest PA may be diagnosed with different diseases. Therefore, we evaluated the previously exposed workers with chest computer tomography (CT) to evaluate the mimicking lesion for suspicious pneumoconiosis.

Methods: A total of 414 patients who took both chest PA and chest CT simultaneously were enrolled in/outpatient at the Department of Occupational and Environmental Medicine of Seoul St. Mary’s Hospital between Jan 1st, 2013 and May 25th, 2015. A total of 354 patients were eligible in the present study. Those with a suspicious pneumoconiosis was defined as who have ever diagnosed as suspicious pneumoconiosis in the screening program for dust exposed workers in Korea. Their age, sex, smoking history, job history, social history, radiologic findings were assessed. A multiple logistic regression analysis were performed for estimating the odds ratio for a suspicious pneumoconiosis. All analyses were performed by using Statistical Analysis System (SAS) version 9.4 (SAS Institute, Cary, NC, USA).

Results: A total of 140 (39.4%) had a history of diagnosis as suspicious pneumoconiosis. After an adjustment of the age, sex, smoking history, job history, social history, radiologic findings were assessed. A multiple logistic regression analysis were performed for estimating the odds ratio for a suspicious pneumoconiosis. All analyses were performed by using Statistical Analysis System (SAS) version 9.4 (SAS Institute, Cary, NC, USA).

Conclusions: Of 81.5% of those who diagnosed with suspicious pneumoconiosis by chest PA were classified as misdiagnosed suspicious pneumoconiosis in the present study. Therefore, chest CT is useful to differential diagnose the suspicious pneumoconiosis.

AP461
THE ASSOCIATED FACTORS WITH NONTUBERCULOUS MYCOBACTERIA INFECTION AMONG PREVIOUS DUST EXPOSED WORKERS
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Background and Aim: The detection and prevalence of Nontuberculous Mycobacteria (NTM) are increasing in Korea. A patient with silicosis or Coal Workers’ Pneumoconiosis (CWP) is classified into a potential high risk group for NTM infection. The purpose of the present study is to estimate the associated factors with NTM infection among previous dust exposed workers.

Methods: A total of 1,438 patients with previous dust exposure history who took a Acid-Fast Bacilli (AFB) culture in/outpatient at the Department of Occupational and Environmental Medicine of Seoul St. Mary’s Hospital between May 1st, 2011 and February 28th, 2016.
Silicosis from Engineered Stone Products: The Return of Occupational Lung Disease - First Case Series in Australia

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Introduction: Silicosis is a broad category of disease entities characterized by a non-neoplastic reaction of the lung parenchyma to inhaled aerosolized silica. It is typically from work related exposure and results in conditions ranging from acute pneumonitis to asthma/chronic obstructive pulmonary disease, interstitial fibrosis and malignancy. Engineered stone products are a relatively recent invention in 1987 of a quartz polymer resin compound, and are commonly used in kitchen bench tops because of its wear-resistance. Pulmonary complications of exposure to these products are beginning to emerge.

Aim/Methods: To report cases of engineered stone silicosis who presented to our respiratory clinics 2016-2017. All presented with cough and had imaging abnormalities. They underwent pulmonary function testing and high resolution computed tomography (HRCT).

Results: Four cases are described. All are males over the age of 50 years. Cases 1 & 2 demonstrated preserved lung function with features of upper lobe predominant interstitial changes and lymphadenopathy on HRCT. Cases 3 and 4 demonstrated a restrictive ventilatory defect with impaired gas transfer and evidence of progressive massive fibrosis on HRCT. Both have respiratory failure with significant hypoxia. One is currently listed for and awaiting a lung transplant.

Discussion: Our case series is the first in Australia to describe occupational lung disease as a result of exposure to engineered stone product dust. As there is no treatment for these conditions, our cases reinforce the importance of adequate safety measures for workers exposed to occupational dusts. The importance of educating employers and workers, as well as the value in regular health surveillance is raised. As new materials are created and workers are exposed to new dusts, adequate protection must be taken until complications can be excluded.

The Relationship Between PAHs Exposure and INHALED ALLERGIC DISEASES

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Background and Aims: To determine whether environmental factors, such as smoking, crowding, and inhaling large amounts of exhaust gas can lead to the deposition of polycyclic aromatic hydrocarbons (PAHs) in human body, increase oxidative stress, and then affect airway allergic diseases.

Methods: 131 subjects were recruited in The First Affiliated Hospital of Guangzhou Medical University, including 61 children and 70 adults. All the subjects had been asked to compete a questionnaire containing the core content of the symptoms of ISAAC questionnaire and the related issues of environmental exposure including living or staying in a crowded environment, cigarette smoke exposure and inhaling large amounts of exhaust gas. Levels of malondialdehyde (MDA) as a biomarker of...
A STUDY PROTOCOL FOR ASSESSING NURSES KNOWLEDGE OF THE FIVE MOMENTS FOR HAND HYGIENE (5MHH) PROGRAM

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Background and Aim: Influenza poses is a significant burden on patients and health care facilities. An Australian study found influenza causes 18,000 admissions to hospitals per year. During hospitalisation a key evidenced based intervention in preventing further influenza transmission and infection of healthcare workers is hand hygiene. This protocol outlines a study that aims to determine Australian Registered Nurses (RNs) level of knowledge of the "five moments for hand hygiene" within acute hospital settings.

Methods: A prospective cross sectional research design study of RNs within a Local Health District (LHD) will be employed. The validated WHO Hand Hygiene knowledge questionnaire will form the basis of the cross sectional survey. A sample size of 354 has been estimated and surveys will be disseminated to all ward areas across 6 hospitals within a LHD.

Results: Levels of 5MHH knowledge will be determined and stratified by area of practice and nurse qualification level. Specifically individual knowledge gaps pertaining to the 5MHH elements (1) before touching a patient, (2) before a procedure, (3) after a procedure or body fluid exposure, (4) after touching a patient, (5) after touching a patient's surroundings, will be identified.

Conclusion: This study will be the first to establish the 5MHH knowledge of Australian registered nurses. Identification of significant gaps in knowledge will assist in forming relevant and targeted 5MHH educational strategies to improve hand hygiene and reduce the transmission of respiratory infections.

DISSEMINATED PENICILLIOSIS (NON-P. MARNEFFEi) IN AN IMMUNO-COMPETENT INDIVIDUAL IN MALAYSIA

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Penicilliosis caused by Penicillium marneffei is the third most common opportunistic infection in HIV patients in South-east Asia. Both immunocompetent and immunocompromised individuals can be infected. It is rare to find systemic infections in non-HIV individuals. Penicillium infection caused by species other than P. marneffei is uncommon. Possible routes of transmission are through inhalation, ingestion or skin contact.

A 45-year-old male with background history of poorly controlled diabetes and nephrotic syndrome presented with weight loss, intermittent fever and dyspnoea. He had recurrent right-sided lung empyema, found on computed tomography (CT) scans 4 months earlier. He also had recurrent episodes of absence spells and hypoxia. Widespread fungal-like lesions were noted on his body. He enjoyed fishing and worked as a janitor at a microbiology laboratory.

Bedside ultrasound revealed a right-sided consolidation with bilateral effusion, which was transudative. Bronchoscopy revealed areas of inflamed mucosa in the right middle lobe. Broncho-alveolar lavage and
pleural fluid revealed pericellium species. No malignancy was detected and the fluids were both lymphocytic predominant. Cerebral CT and MRI scans revealed cerebral atrophy and multi-focal infarcts. Electroencephalogram (EEG) was normal. Lumbar puncture showed high protein, with zero white cell count and no organisms. For the penicillosis, intravenous liposomal amphotericin B was given with partial response, following failure of therapy with oral itraconazole. He received high dose anti-seizure medication. He had a prolonged hospital stay complicated by multi-organ dysfunction and died 8 weeks later.

In retrospect, intravenous amphotericin B may have resulted in better outcome with earlier diagnosis. Survival rates of 59% have been quoted (Supparatpinyo 1994). We believe this is the first reported case of disseminated penicillosis in an immuno-competent patient in Malaysia.

MULTIPLE PULMONARY NODULES IN AN IMMUNOCOMPETENT INDIGENOUS MALE
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Introduction: Cryptococcus is a yeast-like fungus known to cause disease in humans.

Case Report: A previously well indigenous male ranger in his early 30s from a rural community in tropical Australia was admitted to hospital with a 2-week history of pleuritic chest pain, fevers, chills and cough. Several days prior to symptom development he had been involved in leaf blowing at the ranger camp, with many dead eucalyptus trees in the surrounding area. Physical examination was unremarkable. CXR and CT chest revealed numerous (>50) bilateral lung nodules ranging in size from a few millimetres to several centimetres in diameter. HIV, HTLV-1 and cryptococcosis was more common in the immunocompromised but can also occur in immunocompetent individuals. In Australia, C. gattii has been particularly associated with eucalyptus trees and cryptococcosis disproportionately affects Aboriginal people. The 3 main chest radiographic patterns in immunocompromised patients include solitary or multiple lung masses (usually large), air space consolidation or reticulonodular interstitial changes. C. gattii is considerably more likely than C. neoformans to lead to large masses (cryptococcomas) in the lungs and/or brain. Radiological presentation with numerous lung nodules such as in the aforementioned patient is rare. Treatment involves antifungal therapy and consideration of surgical resection in selected patients.

Discussion: Innoculation of C. gattii is usually via inhalation and pulmonary involvement is the most common presentation. Haematogenous spread can then occur to the central nervous system, and less commonly to other sites. Cryptococcosis is more common in the immunocompromised but can also occur in immunocompetent individuals. In Australia, C. gattii has been particularly associated with eucalyptus trees and cryptococcosis disproportionately affects Aboriginal people. The 3 main chest radiographic patterns in immunocompromised patients include solitary or multiple lung masses (usually large), air space consolidation or reticulonodular interstitial changes. C. gattii is considerably more likely than C. neoformans to lead to large masses (cryptococcomas) in the lungs and/or brain. Radiological presentation with numerous lung nodules such as in the aforementioned patient is rare. Treatment involves antifungal therapy and consideration of surgical resection in selected patients.
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Background and Aims: Pulmonary Nocardiosis is a rare bacterial infection seen commonly in immunocompromised patients. Lack of suspicion and non specific clinico-radiological features leads to delay in diagnosis and misdiagnosis of this condition, which could lead to fatal outcome.

Methods (Case Report): 63 years old gentleman, newly diagnosed diabetes mellitus (HBA1C-8.8), hypertensive presented with cough and breathlessness for 1 week duration. On examination GCS was 15/15, RR-26/min, HR-120/min, BP-160/80 mmHg, Spo2-92% at room air and chest auscultation revealed bilateral crackles. Evaluation revealed hypoxic respiratory failure, neutrophilic leukocytosis & CT thorax showed multiple consolidation in both lung fields. Patient was started on IV support and Cefaperazone + Sulbaactum. Patient was subjected for bronchoscopy to rule out fungal pneumonia, which revealed thick muco purulent secretions in both bronchial tree. BAL- gram stain revealed many thin acid fast bacilli species, immediately patient was started on Inj.Ceftriaxone + Inj.Amikacin + T.Cotrimoxazole. BAL- culture showed scanty growth of burkholderia species, hence menopenam was added. After 2 weeks of IV antibiotics, discharged with Tab cotrimoxazole. Patient symptomatically improved, showed good radiological resolution after one month of treatment. Tab cotrimoxazole was continued for 6 months. Nocardiosis is caused by aerobic gram positive filamentous bacteria, which commonly affects lung. It can also affect CNS, skin and sometimes present as disseminated disease. Clinico-radiological features are usually non specific. Isolation and identification of organism from the clinical specimen establishes the diagnosis. Cotrimoxazole is the drug of choice. Other alternatives are amikacin, ceftriaxone, imipenam, linezolid. Treatment duration is usually 6 months to 1 year.

Results and Discussion: Chest x ray showing B/L alveolar opacities consolidation CT showing B/L upper lobe

Conclusions: Pulmonary nocardiosis is commonly under reported or misdiagnosed. The disease should be always considered in the differential diagnosis of pneumonia in immuno compromised host. Early recognition and appropriate treatment is the key for successful outcome.

SUCCESSFULLY TREATED CASE OF PULMONARY NOCARDIOSIS AND BURKHOLDERIA INFECTION IN A ELDERLY MAN WITH DIABETES MELLITUS

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Background and Aims: The most common causes of pleural effusion in children is Streptococcus pneumonia but in developing country Staphylococcus aureus is the most common and 50% of this infection can be parapneumonic effusion and empyema. Myroides species are commonly found in soil and water and not considered pathogenic. Clinical infection with this bacteria is rare and usually difficult to treat due to its resistance to many antibiotics but usually respond to meropenem.

Methods:

Results: We report a 12 years old immunocompetent boy, presented with persistent cough since 3 months, difficult to breath and got worsen with daily activity and low grade fever. There were no common systemic symptoms of tuberculosis infection such as night sweat, loss appetite and weight loss. There was a decrease in lung sound but no wheezing or rales in the right hemithorax. CXR showed suspected loculated pleural effusion and thorax USG confirmed a loculated pleural effusion in the right hemithorax. USG guided pleural puncture was difficult to perform. Patient was given ceftalosporin and amikacin but no clinical response within 7 days and Thorax CT scan was performed. Chest CT showed multiloculated pleural effusion with thickening and fibrotic parietal-visceral pleura. Video Assisted Thoracic Surgery (VATS) was decided in this case and its pleural fibrotic area were released. The result from culture of pleural fluid was myroides species. After VATS the patient underwent pulmonary rehabilitation with breathing exercise, chest fisotherapy and incentive spirometry.

Conclusions: We conclude that myroides species was very rare species caused parapneumonic effusion and pleural thickening. From the literature myroides responds with meropenem and our patient responds to the meropenem as well.

FIBROTIC PARAPNEUMONIC EFFUSION CAUSED BY MYROIDES SPECIES IN IMMUNOCOMPETENT CHILD

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Background and Aims: Pulmonary nocardiosis is commonly under reported or misdiagnosed. The disease should be always considered in the differential diagnosis of pneumonia in immuno compromised host. Early recognition and appropriate treatment is the key for successful outcome.

Conclusions: Pulmonary nocardiosis is commonly under reported or misdiagnosed. The disease should be always considered in the differential diagnosis of pneumonia in immuno compromised host. Early recognition and appropriate treatment is the key for successful outcome.

DISEASE SPECTRUM AND MANAGEMENT OF CHILDREN ADMITTED WITH ACUTE RESPIRATORY INFECTION IN VIET NAM

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Background: Acute respiratory infection (ARI) is the most common reason for admission to paediatric wards in Viet Nam, being responsible for 39.9% of hospital admissions and 7.9% of hospital deaths in southern Viet Nam. However, few studies have explored the ARI disease spectrum observed in central Viet Nam or differences between primary (district), secondary (provincial) and tertiary (national) level hospitals.

Aims: To assess the acute respiratory infection (ARI) disease spectrum, duration of hospitalisation and outcome in children hospitalised with an ARI in Viet Nam.

Methods: We conducted a retrospective descriptive study of ARI admissions to primary (Hoa Vanh District Hospital), secondary (Da Nang Hospital for Women and Children) and tertiary (National Hospital of Paediatrics in Ha Noi) level hospitals in Viet Nam over a 12-month period (01/09/2015 to 31/08/2016).

Results: ARIIs accounted for 27.9% (37,436 / 134,061) of all paediatric admissions; nearly half (47.6%) of all children admitted to Hoa Vang District Hospital. Most (64.6%) children hospitalised with an ARI were <2 years of age. Influenza/pneumonia accounted for 69.4% of admissions; tuberculosis for only 0.3%. Overall 284 (0.8%) children died; most deaths (269/284; 94.7%) occurred at the tertiary referral hospital. The average duration of hospitalization was 7.6 days (median 7 days). The average direct hospitalization cost per ARI admission was 157,563 JPY in Da Nang Provincial Hospital. In total, 62.6% of admissions were covered by health insurance.

Conclusions: ARI is a major cause of paediatric hospitalization in Viet Nam, characterized by prolonged hospitalization for relatively mild disease. There is huge potential to reduce unnecessary hospital admission and cost.

Acknowledgements: Data departments at all participating hospitals. Dr Maryam Montazerolghaem at the Sydney Informatics Hub, the University of Sydney for data analysis. Dr Tran Thi Hoang, vice director of Da Nang Hospital for Women and Children for data collection and ethical process.

Background and Aim: Group A streptococcus (GAS) is known as a pathogenic bacterium for community infection. However, GAS is also known to cause a severe disease such as streptococcal toxic shock syndrome (STSS).

Methods: We retrospectively collected adult patients (>18 years old) who were treated as infectious diseases caused by GAS, from April 2014 to March 2017. A total of 65 cases (33 men and 32 women) were diagnosed with infectious diseases caused by GAS and enrolled in this study. The median age was 43 years. We grouped them into the following three groups. Group A were diagnosed as STSS by the Japanese diagnostic criteria of STSS, Group B were diagnosed as invasive GAS infection (excluding Group A). Group C were neither Group A nor Group B.

Results: Infection sources of Group A were 2 cases of necrotizing fasciitis, 1 case of pressure ulcer and 1 case of pneumonia. Infection sources of Group B were 1 case of necrotizing fasciitis, 3 cases of pleuritis, 1 case of pneumonia, and 2 cases of arthritis. Respiratory infections caused by GAS tended to become severe.

Conclusion: Respiratory infections caused by GAS are not common. However, among GAS infections, not only necrotizing fasciitis but also respiratory infections become severe.
Aims: To describe the bacteriology and antibiotic resistance pattern of patients with pneumonia hospitalized in a respiratory center.

Methods: Retrospective descriptive study of patients with pneumonia hospitalized in Respiratory Center of Bach Mai hospital in Ha Noi, Vietnam, from January 2015 to December 2015. Our study included 357 patients divided into 3 groups: 1st group including 225 CAP patients and 2nd group including 53 HAP patients, 3rd group including 79 HCAP patients.

Results: Among total 357 patients, only 19.6% patients had documented bacteriological results, 91.4% of those was caused by 1 single bacterium and 84.4% of them were Gram-negative bacteria. The most common bacteria isolated in CAP patients were P. aeruginosa 20.5%, K. pneumonia 17.9%, S. pneumonia 10.25%, in HCAP patients were P. aeruginosa (37.5%), A. baumannii 31.3% and in HAP patients were A. baumannii 50.0%, K. pneumonia 13.6%, S.aureus 13.6%. The proportion of bacteria exhibiting resistance to multiple drugs in CAP patients was 27.8%, in HCAP patients was 53.8% and in HAP patients was 77.3%.

Conclusions: The bacteriological characteristic of pneumonia is changing over time, with a higher level of multi-drug resistant bacteria.

PATHOGENIC BACTERIA ISOLATED FROM SPUTUM SAMPLES AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERN IN ADULT PATIENTS TREATED AT CENTRAL CHEST CLINIC, SRI LANKA

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Background and Aim: A descriptive cross sectional study carried out at Central Chest Clinic (CCC) to identify currently circulating respiratory pathogens and their antibiotic sensitivity pattern(ABST) to enable in deciding on appropriate empirical antibiotics and to contribute to the antimicrobial resistance surveillance in Sri Lanka.

Methods: All reports on sputum culture and ABST of patients over the age of 18 years with presumptive lower respiratory tract infections attending CCC, which was generated by the microbiology laboratory at Medical Research Institute for a one year period in 2015 were analyzed.

Results: Out of the 1372 sputum cultures analysed, 404(29.4%) samples have yielded a growth of pathogenic bacterial organisms. Coliforms (43.6%) and Pseudomonas spp. (29%) were the commonest isolates followed by Moraxella, Haemophilus and Pneumococci respectively. Majority of reports (58%) were from patients diagnosed with chronic lung diseases. Out of 176 coliforms isolated 43% were probable pathogens among total 357 patients, only 19.6% patients had documented bacteriological results, 91.4% of those was caused by 1 single bacterium and 84.4% of them were Gram-negative bacteria. The most common bacteria isolated in CAP patients were P. aeruginosa 20.5%, K. pneumonia 17.9%, S. pneumonia 10.25%, in HCAP patients were P. aeruginosa (37.5%), A. baumannii 31.3% and in HAP patients were A. baumannii 50.0%, K. pneumonia 13.6%, S.aureus 13.6%. The proportion of bacteria exhibiting resistance to multiple drugs in CAP patients was 27.8%, in HCAP patients was 53.8% and in HAP patients was 77.3%.

Conclusions: The bacteriological characteristic of pneumonia is changing over time, with a higher level of multi-drug resistant bacteria.

RISK FACTORS AND OUTCOMES OF HOSPITAL ACQUIRED PNEUMONIA CAUSED BY MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA

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Background and Aim: This study aimed at evaluating the risk factors and outcomes associated with hospital acquired pneumonia (HAP) caused by multidrug-resistant (MDR) pseudomonas aeruginosa (PA).

Methods: Data were collected related to all episodes of HAP caused by PA infection that occurred in the third affiliated hospital of Sun Yat-sen University between January of 2013 and December of 2016. Information prior to the date of PA infection was collected. In addition, age, gender, white blood cell count(WBC), neutrophil count(Neu), lymphocyte count(LYM), monocyte count(Mono), neutrophil to lymphocyte count ratio (NLR) and hemoglobin(HGB) in peripheral blood, effect of antibiotic treatment and the 30-day mortality were recorded.

PRESSIVE FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS IN HEMODIALYSIS PATIENTS WITH PNEUMONIA: A MULTICENTER STUDY

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Background and Aims: In patients with hemodialysis-associated pneumonia (HDAP), information on both microbiologic features and antimicrobial strategies is limited. The aim of this study is to investigate predictive factors of infection with multidrug-resistant (MDR) pathogens in HDAP patients.

Methods: This was a multicenter, retrospective, and observational study. We analyzed the associations between risk factors of HDAP and infection with MDR pathogens and created a decision support tool to predict infection with MDR pathogens.

Results: The median age of the enrolled patients was 71. MDR pathogens were identified in 24 (22.8%) out of a total of 105 HDAP patients and in 7 (11.4%) of 61 pure HDAP patients without other components of healthcare-associated pneumonia. The most common MDR pathogens were methicillin-resistant Staphylococcus aureus (10 patients, 9.5%). Logistic regression showed two variables were independently associated with the isolation of MDR pathogens: prior hospitalization (odds ratio [OR]: 3.109, 95% confidence interval [CI]: 1.043 – 9.272) and PSI score (OR: 1.021, 95% CI: 1.001 – 1.042). The optimal cut-off value for PSI score using ROC curve analysis was 147. As the risk determined by the two-factor prediction tool increased, the prevalence of infection with MDR pathogens in each group also increased (P < 0.001 for trend). The area under the curve of the prediction tool was 0.764 (95% CI: 0.652 - 0.875).

Conclusions: We demonstrated that prior hospitalization and PSI > 147 are risk factors of infection with MDR pathogens in HDAP patients. This simple proposed tool would facilitate more accurate identification of MDR pathogens in these patients.
Results: 157 patients with PA-HAP were included, of which 69 patients were caused by MDR-PA. The first logistic regression analysis identified the independent risk factors of MDR-PA HAP included prior endotracheal intubation, prior mechanical ventilation, prior ICU stay in previous 90 days, initial inappropriate antibiotic therapy (IAT), treatment department changed in previous 30 days, low HGB level, low NLR. In the second multivariable analysis, there were differences between MDR-PA and non-MDR-PA on the following variables: treatment department changed in previous 30 days (P = 0.00, OR 1.86, 95%CI 0.702-4.768), IAT (P = 0.00, OR 1.10, 95%CI 0.844-2.244) and low NLR (P = 0.02, OR 0.91, 95%CI 0.843-0.985). The outcome showed that the effect of antibiotic treatment was significantly different (P = 0.00, OR 4.26, 95%CI 2.14-8.48), even two groups were given a targeted therapy based on in vitro susceptibility tests (P<0.001, OR 2.009, 95%CI 1.241-3.254).

Conclusion: NLR declined, treatment department changed in previous 30 days and IAT were significantly associated with HAP caused by MDR-PA. The antibiotic treatment had better effect on non-MDR-PA group than MDR-PA group based on in vitro susceptibility tests.

IMPACT OF NATIONAL GUIDELINES-ADHERENCE ON EMPIRIC ANTIBIOTIC THERAPY ON MORTALITY AMONG PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA IN PERSAHABATAN HOSPITAL JAKARTA, INDONESIA

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Background and Aim: Community Acquired Pneumonia (CAP) remains to be one of the highest mortality diseases worldwide. In order to decrease mortality rate of this disease, Indonesian Society of Respiriology have developed a recommendation for empiric antibiotic guidelines for patients with community-acquired pneumonia. The aim of this study is to determine the impact of national guidelines-adherence on empiric antibiotic therapy on mortality among patients with community acquired pneumonia.

Methods: This is a cohort retrospective study among patients with community-acquired pneumonia admitted to Persahabatan Hospital Jakarta during July 2014 until July 2016.

Results: We included 107 patients that diagnosed with CAP during our study. The mean (±SD) age was 53.61 ± 16.8 years. The proportion of male and female were 70.1% and 29.9%. Adherence to national empiric antibiotic therapy guideline was 68.2%. National guideline-adherence on empiric antibiotic therapy was associated with a significant decrease of mortality rate among patients with OR 3.2 (CI 95%: 1.3-7.6).

Mortality rate of CAP patients also associated with Pneumonia Score Index (PSI). Patient with PSI class (IV/V) had higher mortality than patient with PSI class (II, III) with OR 3.5 (CI 95%: 1.4-8.6). Age, comorbid diseases, and time administration of antibiotics were not have significant impact on mortality patients in our study.

Conclusion: National guidelines-adherence on empiric antibiotic therapy have significant impact on mortality among patient with Community Acquired Pneumonia.

RESISTANCE TO MACROLIDES IN STREPTOCOCCUS PNEUMONIAE. HOW FAR WE CAME IN 50 YEARS?

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Introduction: Resistance to erythromycin in Streptococcus pneumoniae was first detected 50 years ago in 1967 in the United States and subsequently worldwide. The mechanism was rapidly identified as ribosomal
methylation. The development of antibiotic resistance among Streptococcus pneumoniae strains is causing significant health problems in developing countries. The aim of this study was to determine macrolide resistance pattern of Streptococcus pneumoniae strains isolated from lower respiratory tract specimens in one of the reference centers of our region.

Material and Methods: We investigated specimens of patients hospitalized with the diagnosis of lower respiratory tract (LRT) infection into Pulmonology Department Uludag University, the tertiary reference center of Marmara Region of Turkey, between January 2008-June 2015. Susceptibility to antibiotics of 75 pneumococcus strains recovered from sputum (38 isolates), bronchoalveolar lavage (20 isolates), bronchial lavage (15 isolates) and endotracheal aspirate (2 isolates) of patients with LRT infection were investigated by using E test, gradient diffusion method (Epiisolometer, and Phoenix 100 otomatic systems). MIC values were evaluated according to criteria of Clinical and Laboratory Standards Institute (M100-S24, 2014. CLSI, Wayne, PA).

Results: We found that 38 strains (58%) were susceptible to erythromycin, 3 strains (4.5%) indicated intermediate resistance and 24 strain (37 %) was resistant to erythromycin. We also demonstrated that three strains (6%) had intermediate resistance and none (0%) had complete resistance to penicillin, whereas 94% of strains were susceptible to penicillin. The 66 strains (94.3%) were susceptible to ceftriaxone, three (4.3%) indicated intermediate resistance and 1 strain (1.4 %) was resistant to ceftriaxone. The 62 strains (95%) were susceptible to levofloxacin whilst 3 strains (5%) indicated resistance to levofloxacin.

Conclusion: We observed that resistance rate to erythromycin in isolated Streptococcus pneumoniae strains of our region was high. The emergence of Streptococcus pneumoniae strains with resistance to widely used antibiotics in LRT infections needs permanent monitoring of antibiotic susceptibility patterns of clinical isolates.

AP483

LOW CD4 COUNT IN HIV SERONEGATIVE PATIENT CAUSED BY PNEUMONIA AND SEPSIS

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Background: Sepsis is a systemic inflammatory response syndrome due to infection. Infection triggers a complex and prolonged host response, in which both the innate and adaptive immune response are involved. Within the immune system, CD4 T cells are important players in the proper development of numerous cellular and humoral immune responses.

Case: This is a case of young patient 28 year-old female presented with dyspnea, cough and flu like syndrome. Chest x-ray showed bilateral infiltrates and blood gas analysis showed respiratory failure type 2. Screening test for HIV was negative. Patient was intubated and treated at intensive care unit, meropenem and levofloxacin was given. Chest x-ray evaluation showed lobar pneumonia. CD4 and CD8 count was low, with decreased CD4:CD8 ratio. Sputnum culture was negative for bacteria and no fungal infection. Antibiotics were changed to moxifloxacin and azithromycin. Chest x-rays showed improvement. CD4 count evaluation a week after patient discharged showed normal value.

Conclusion: Sepsis remains the primary cause of death from infection in hospital patients. Despite sufficient clinical evidence of CD4 T cell loss in septic patients of all ages, the impact of sepsis on CD4 T cell responses is not well understood. Proper antibiotic and hemodynamic stabilization are keys to treat sepsis.

Keywords: CD4, pneumonia, severe infection, sepsis
Methods: A descriptive study was done. 119 very elderly patients with CAP were included in the study and their data reviewed from the charts.

Results: A total of 371 out of 86,340 admissions, in UST Hospital in 2011 to 2014, were very elderly who had CAP as an initial diagnosis. The mean age of these patients were taken and the most common symptoms as well as the vital signs on initial presentation were also taken. The most common comorbid conditions, vital signs on presentation and empiric treatment as well as outcomes were recorded as percentage.

Conclusion: In this study, the very elderly group of patients manifested with the most common symptoms of pneumonia such as cough, dyspnea and fever. The mean age was 86 years old and most of the patients had cardiovascular diseases. Less than 10% required mechanical ventilatory support and 18.49% expired and the rest were discharged improved. 80.67% were treated with empiric combination therapy majority of which were 3rd generation cephalosphorin and macrolides, however there were no sufficient data regarding common etiologic organism due to lack of or incomplete sputum studies.

APL016

PREDICTING THE MORTALITY OF PNEUMONIA PATIENTS VISITING THE EMERGENCY DEPARTMENT THROUGH MACHINE LEARNING

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Background and Aims: Machine learning in the medical field is not yet widely used. The aim of this study is to compare the performance of pre-existing severity prediction models and Random forest(RF) based models for mortality prediction in pneumonia patients.

Methods: We retrospectively collected the data of patients who visited the emergency department of a tertiary training hospital in Seoul, Korea from January to March 2015. The pneumonia severity index(PSI) and SOFA score were calculated for both group and the AUC for mortality prediction was computed. For RF model, data were divided into a test set and a validation set by random split 100 times. The training set was learned in an RF model and the AUC was obtained from the validation set. The mean AUC was compared with the other two AUCs. RF model was built using python scikit-learn library 0.18 version.

Results: Of the 443 people, 395 were enrolled and 41 of them were died. The AUC values of PSI and SOFA scores were 0.799 (0.737 - 0.862) and 0.865 (0.811 - 0.918), respectively. The mean value of AUC obtained by RF method was 0.916 (0.909 - 0.923) and there were significant differences statistically (p < 0.001). The five major features used in the random tree model were vasoactive agent, platelet, lactate acid, GCS score, and albumin.

Conclusions: Classification through machine learning may help to predict the mortality of patients visiting the emergency department.

AP487

MICROBIOLOGICAL AND CLINICAL SIGNIFICANCE OF PRIOR HOSPITALIZATION IN PATIENTS ADMITTED WITH COMMUNITY-ONSET PNEUMONIA: A PROPENSITY SCORE MATCHING STUDY

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Background: Although prior hospitalization (PH) has been considered as a risk factor for infection with potentially drug-resistant (PDR) pathogens in patients with community-onset (CO) pneumonia, the evidence is limited. We aimed to elucidate the clinical impact of PH on these patients.

Methods: This retrospective observational cohort study with prospectively collected data was conducted at Jeju National University Hospital between January 2012 and December 2014. We classified the study patients into PH-associated pneumonia (PHAP) and community-acquired pneumonia (CAP) groups. Propensity scores were constructed to improve the balance of baseline characteristics between two groups, and the clinical outcomes were compared. We also conducted subgroup analyses based on prior antibiotic use, duration of PH, and time to re-admission.

Results: A total of 704 patients were identified; the PHAP group included 97 patients (13.7%). Patients with PHAP had more comorbidities than those with CAP. And the median CURB-65 and PSI scores were higher in patients with PHAP than in those with CAP. After matching according to propensity scores, the baseline characteristics of the PHAP group were balanced between the two groups.

Conclusions: Previous hospitalization was significantly associated with pneumonia in a community setting.
Background: Streptococcus pneumoniae is one of the primary causes of Community Acquired Pneumonia (CAP) worldwide. However, there is no such pooled analysis available for CAP patients in Indian population, so far.

**Aim:** This systematic review and meta-analysis was performed to evaluate the incidence of Streptococcus pneumoniae in Indian adult patients with CAP.

**Methods:** We performed systematic search of both indexed and non-indexed publications using PubMed, databases of National Institute of Science Communication and Information Resources (NISCAIR), Annotated Bibliography of Indian Medicine (ABIM), google scholar and hand search including cross references using key terms “community acquired pneumonia AND India”. Studies that included Indian patients aged above 12 years with confirmed diagnosis of CAP and published from 01/01/1990 to 08/01/2017 were eligible to be included in this review. The primary and secondary outcomes of this study were proportion of patients affected with Streptococcus pneumoniae and determination of the range of all etiological agents along with their incidence, respectively.

**Results:** Of the total 182 studies retrieved, 17 studies were included for the systematic review of all etiological organisms, and only 12 were included in the meta-analysis of S. pneumoniae. The pooled proportion of patients with Streptococcus pneumoniae infection was 19% (95% CI: 12-26%). I²=94.5% where I² represents heterogeneity). The range of proportion considering each study included in this meta-analysis was found to be 1.0%-56.7% with the highest incidence rate of 17.9%. Other major etiological agents are Mycobacterium pneumoniae [15.4% (1.1-35.4%)] and Klebsiella pneumoniae [10.5% (1.6-24.0%)].

**Conclusion:** Analysis found a high proportion of Streptococcus pneumoniae infection in adult Indian CAP patients. Also, its incidence rate was found to be highest as compared to other etiological agents. This data would help physicians tailor appropriate antibiotic therapy in patients with CAP. Strategies for prevention of pneumococcal pneumonia need appropriate address.

**Table 1. Proportion of Incidence of Streptococcus pneumoniae in CAP patients**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Study (Reference, Number)</th>
<th>Proportion of Incidence of Streptococcus pneumoniae</th>
<th>95% Confidence Interval</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acharya et al. J Clin Diagn Res., 2014</td>
<td>0.120</td>
<td>0.056-0.184</td>
<td>8.68</td>
</tr>
<tr>
<td>2</td>
<td>Bansal et al. Indian J Chest Dis Allied Sci., 2003</td>
<td>0.271</td>
<td>0.271-0.167</td>
<td>7.73</td>
</tr>
<tr>
<td>3</td>
<td>Dey et al. Natl Med J India., 1996</td>
<td>0.083</td>
<td>0.083-0.019</td>
<td>8.68</td>
</tr>
<tr>
<td>4</td>
<td>Dharmadhikari et al. Int J Pharm Bio Sci., 2013</td>
<td>0.183</td>
<td>0.183-0.108</td>
<td>8.46</td>
</tr>
<tr>
<td>5</td>
<td>Jain et al. IJSS., 2014</td>
<td>0.167</td>
<td>0.167-0.100</td>
<td>8.62</td>
</tr>
<tr>
<td>6</td>
<td>Kejriwal et al. IOSR-JDMS., 2015</td>
<td>0.567</td>
<td>0.567-0.441</td>
<td>7.16</td>
</tr>
<tr>
<td>7</td>
<td>Khadanga et al. J Global Infect Dis., 2014</td>
<td>0.147</td>
<td>0.147-0.114</td>
<td>9.18</td>
</tr>
<tr>
<td>8</td>
<td>Menon et al. J Family Med Prim Care., 2015</td>
<td>0.324</td>
<td>0.324-0.248</td>
<td>8.41</td>
</tr>
<tr>
<td>9</td>
<td>Mythri et al. IOSR-JDMS., 2013</td>
<td>0.100</td>
<td>0.100-0.041</td>
<td>8.78</td>
</tr>
<tr>
<td>10</td>
<td>Shah et al. Lung India., 2010</td>
<td>0.010</td>
<td>0.010-0.01</td>
<td>9.30</td>
</tr>
<tr>
<td>11</td>
<td>Shrikhande et al., JEMDS., 2015</td>
<td>0.220</td>
<td>0.220-0.105</td>
<td>7.45</td>
</tr>
<tr>
<td>12</td>
<td>Sreekanth and Reddy. COPD., 2015</td>
<td>0.200</td>
<td>0.200-0.089</td>
<td>7.55</td>
</tr>
</tbody>
</table>

*Binary Random-Effects Model was applied to get pooled proportion and 95% confidence interval [0.19; 95% CI 0.12-0.26; P<0.01]
Table 2. Incidence Range of Etiological Agents in Community Acquired Pneumonia in Indian Setting

<table>
<thead>
<tr>
<th>Micro-organisms Involved in Etiology of Community Acquired Pneumonia</th>
<th>Minimum Percentage of Incidence Range</th>
<th>Maximum Percentage of Incidence Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1.6</td>
<td>10.5</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>1.1</td>
<td>35.4</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>1.0</td>
<td>56.6</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0.83</td>
<td>11.6</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1.0</td>
<td>12.8</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>0.83</td>
<td>5.0</td>
</tr>
<tr>
<td>Enterobacter Spp.</td>
<td>0.83</td>
<td>4.0</td>
</tr>
<tr>
<td>E.Coli</td>
<td>0.83</td>
<td>8.5</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>2.5</td>
<td>23.8</td>
</tr>
</tbody>
</table>

**Paediatrics Lung Disease**

**AP489**

EFFECT OF IMMUNOGLOBULIN FOR CHILDHOOD SEVERE MYCOPLASM PNEUMONIA

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**Background and Aims:** To observe the clinical curative effect and safety of human immunoglobulin for intravenous injection in treating childhood severe mycoplasm pneumonia.

**Methods:** Eighty children with severe mycoplasm pneumonia in clinic and wards of this hospital from March 2015 to March 2016 were randomly divided into treatment group(n=40)and control group(n=40). All the patients were administered with erythromycin,azithromycin and symptomatic treatment for two weeks. The treatment group also received human immunoglobulin for intravenous injection 400 mg / (kg · d) for 5 days compared to the control group.

**Results:** The symptom-free period of fever,cough,wheeze and wet rales in the treatment group were \((3.1 \pm 1.4)\) d,\((5.2 \pm 1.3)\) d,\((5.5 \pm 1.1)\) d and\((4.6 \pm 1.2)\) d, respectively, and in the control group\((4.3 \pm 1.1)\) d,\((6.6 \pm 2.4)\) d,\((5.3 \pm 2.4)\) d and\((5.4 \pm 1.7)\) d, respectively. The difference between the two group was statistically significant( P <0.01).

**Conclusions:** Human immunoglobulin for intravenous injection has a greater efficacy and fewer side effects on children with mycoplasm pneumonia.

**AP490**

MOLECULAR EPIDEMIOLOGY OF SEVERE RESPIRATORY SYNCYTTIAL VIRUS (RSV) INFECTIONS IN CHILDREN UNDER 2 YEARS OF AGE IN AUSTRALIA

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**Background:** With a worldwide estimate of 34 million respiratory syncytial virus (RSV) infections per year in young children, RSV is a major cause of morbidity and mortality. Currently, there are no data on RSV genotypes circulating within Australia and specifically those responsible for the most severe infections.

**Aims:** This study aims to: (1) identify circulating RSV genotypes and (2) evaluate potential risk factors for severe RSV disease.

**Methods:** This is a prospective, cohort study in Australian children <2 years admitted to paediatric intensive care(PICU) or general paediatric ward at the Royal Children’s Hospital Melbourne with RSV lower respiratory tract infection . A sample of convenience of age-matched patients with non-severe RSV is being collected contemporaneously for comparison. Basic clinical and outcome data are being collected. Leftover nasopharyngeal or lower airway samples, obtained as part of routine clinical care, are collected and processed at a centralised research facility (Murdoch Children’s Research Institute) where G glycoprotein gene sequencing and phylogenetic analysis are being performed.

**Results:** Data collection is continuing through the current RSV season. To date, 35 patients have been included in this pilot study.
Preliminary data show a median age of 58 days (range 10-709d), approximately half are male (n=18,51%). In total 5(14%) were admitted to PICU. Children admitted to PICU are younger (median age=36d). Breastfeeding rates are similar between children admitted to PICU versus ward admissions (40% vs 41%, respectively). Overall, 31% of children were born via caesarean section, and were over-represented with respect to ward versus PICU admissions (33% vs 20%, respectively). Genotyping data are not yet available but will be included in a multi-variate analysis.

Conclusion: During the 2017 RSV season in Australia we will further examine the clinical risk factors associated with severe RSV disease and investigate whether specific RSV genotypes and molecular signatures are associated with severity outcomes.

AP491
AN UNUSUAL CAUSE OF CHRONIC COUGH IN CHILDREN
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Background and Aims: Achalasia is a rare motility disorder of the oesophagus which results from lack of enervation of the lower oesophageal sphincter muscles and leading to dilatation of proximal oesophagus. Patients with achalasia presents typically with dysphagia, vomiting of undigested food and failure to thrive. Cough can be present in achalasia patients due to aspiration of food or due to airway compression by the dilated oesophagus.

Methods: An 11 year old girl was presented with 12 months history of nocturnal cough and post-tussive emesis. Cough was predominant during night followed by vomiting of undigested food. She received several courses of antibiotics with no clinical improvement. She was also started on inhaled albuterol and budesonide medications with no response. A course of anti tubercular drugs was also empirically given with no significant improvement. On examination she was malnourished. Chest examination revealed bilateral occasional wheeze. Routine blood investigations were within normal limits, she underwent computed tomography (CT) of chest which demonstrated grossly dilated oesophagus with air fluid level from stagnated food material. The trachea was compressed by dilated oesophagus. A barium swallow study done later revealed dilated oesophagus with bird-beak like tampering of distal oesophagus consistent with achalasia cardia. This patient underwent esophagomyotomy following which symptoms of chronic cough disappeared.

Results: Oesophageal achalasia is a relatively rare problem in children. Achalasia is a primary oesophageal motility disorder caused by failure of the lower oesophageal sphincter to relax and an absence of oesophageal peristalsis leading to a functional obstruction at the gastro-oesophageal junction. Incidence of achalasia has been estimated as 1 in 10,000. Only 4-5% of patients with achalasia are symptomatic prior to 15 years of age.

Conclusions: Early diagnosis and surgical oesophagomyotomy leads to a successful outcome.

AP492
ASSOCIATION BETWEEN CHILDHOOD OBESITY AND ASTHMA: A CROSS-SECTIONAL STUDY AMONG SCHOOL CHILDREN IN BANGLADESH
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Background: Obesity and asthma are diseases of high prevalence in childhood with significant increase in the last two decades. Obesity has been identified as a major risk factor for higher prevalence of asthma in children.

Objective: To investigate the association between the prevalence of childhood asthma and obesity among school going children.

Methods: This cross-sectional study was conducted among 1630 school children of 8-11 years of age through cluster sampling. The International Study of Asthma and Allergies in Childhood (ISSAC) questionnaire was used to identify the children having asthma and it’s categorization. Body mass index (BMI) was calculated from the measured weight and height of the children as weight in kilogram (Kg) divided by square of height in meters (Kgm2). Centre for Disease Control (CDC) BMI-for-age growth charts were used. Over weight was defined as a BMI between the 85th and 94th centiles and obesity was defined as a BMI equal to or greater than 95th centile. The relationship between asthma and obesity and overweight were determined by using chi-square tests.

Results: The prevalence of ever wheezing, current wheezing, obesity and overweight was 20.42%, 6.9%, 17.2% and 13.4% respectively.

Conclusions: An association was found between childhood asthma and obesity and overweight status among school going children of both sex.

AP493
A RARE CASE OF ANTERIOR MEDIASTINAL AND RIGHT LATERAL NECK MASS: TUBERCULOSIS WITH HODGKIN’S LYMPHOMA
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Background and Aims: Tuberculosis presenting with Hodgkin’s Lymphoma is a rare presentation and provides a challenge to the clinician. This case is presented to help us widen our diagnosis as to the possible causes of a mass located on the anterior mediastinal and neck.

Results: We report a case of an eighteen year old female who had cough, weight loss, anterior mediastinal mass, and right lateral neck mass which was solid, immovable and occasionally painful. The lateral neck mass initially measured 5 x 5 cm in diameter and after two months was noted to be enlarged to 13cm x 10 cm (Figure 1). Antibiotic therapy was given but without improvement. Mantoux skin test was positive. Fine needle aspiration biopsy of the anterior mediastinal mass showed acute and chronic inflammation with occasional gram negative cocci and rare acid fast bacilli suggestive of tuberculosis. Medications for tuberculosis such as Isoniazid, Rifampicin, Pyrazinamide and Ethambutol were taken. However, there was a rapid enlargement of the right lateral neck and anterior mediastinal mass. Tumor markers such as lactate dehydrogenase, beta human chorionic gonadotrophin and alpha fetoprotein were within normal.

Further work up such as biopsy of the right lateral neck mass revealed Hodgkin’s Lymphoma. Sputum TB culture and gene xpert were negative.
Human Immunodeficiency screening showed negative result. She was advised chemotherapy along with the medications for tuberculosis.

Conclusions: Tuberculosis occurring in a patient with rapidly enlarging mass can deter the diagnosis of a malignancy if proper work up is not done. Mass located in the anterior mediastinal is usually diagnosed with a tumor, however a concomittant infection with Tuberculosis can be of a diagnostic dilemma to immediately manage an enlarging tumor. Therefore, further investigation has to be included so as not to delay appropriate treatment.

Methods: A 17 months girl child was presented with fever, weight loss, irritability and refusal to eat. Chest X-ray and ultrasonography was suggestive of left sided multiloculated parapneumonic effusion. Tube thoracostomy was done. Fluid analysis was suggestive of tubercular empyema. Tube thoracostomy was dry on day second, there was no clinical and radiological improvement seen. Video-Assisted Thorascopic Surgery was planned but parents did not give consent for the same. Intrapleural streptokinase instillation was given at 12 hours time interval as an alternative therapeutic option.

Results: The pleural fluid drainage after streptokinase instillation was significantly increased up to 300 ml. There was also significant expansion of lung both clinically and radiologically after third dose of intrapleural streptokinase. Patient was discharge on day six with prescribed anti tubercular regime.

Conclusion: Intrapleural streptokinase appears to be a useful strategy to reduce the need for surgery. There are no therapeutic advantages between VATS and fibrinolysis for the treatment of empyema; however intrapleural fibrinolysis has less morbidity and is more cost effective than Video-Assisted Thoracoscopic Surgery.

A 2 YEAR OLD MALE WITH PLEUROPULMONARY BLASTOMA TYPE II – A CASE REPORT

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Background and Aim: Pleuropulmonary Blastoma (PPB) is a very rare, highly aggressive malignant tumor that originates from either the lungs or pleura. It has poor prognosis and mainly occurs in children less than five or six years with three different subtypes: cystic [type I], combined cystic and solid [type II] and solid [type III]. We report a case of a 2 year old boy presenting with cough, fever and dyspnea, whose management was carried out successfully with surgical resection followed by neoadjuvant chemotherapy.

Results: The patient was initially managed as a case of pneumonia two months prior. TB work up was negative. Chest X-ray showed opacity filling the right hemithorax leading to mediastinal shift to the opposite side. Computed Tomography revealed large hypodense mass in the right hemithorax containing solid and cystic components. He was transferred in this institution intubated, chest examination showed asymmetric chest expansion, subcostal retractions and vesicular breath sounds over the left lung. Dulness on percussion, decreased vocal and tactile fremitus, and absent breath sounds on the right hemithorax. Alpha Feto protein, Urea and creatinine were normal. Serum lactate dehydrogenase was elevated. On 2D echocardiogram, the mass was compressing the right atrium, prompting emergency surgery. Excision with frozen section was done. Final tissue biopsy aided by immunohistochemistry staining revealed Pleuropulmonary Blastoma Type II. He was successfully extubated and discharged improved. He recently completed the first course of chemotherapy after discharge.

Conclusions: We report a case of a 2 year old male with PPB type II which is a rare aggressive tumor that usually occurs in young children. Clinicians should have a high index of suspicion for lung masses that present in pediatric age and should be managed with multimodal therapy despite the presence of poor prognostic factors, it may provide remission and a long-term disease-free period.
Background and Aims: Congenital Pulmonary Airway Malformation (CPAM) encompasses a spectrum of variably sized cysts with differing histology. Type 2 lesions constitute 15-30% cases. This type usually involves a single lobe and has the poorest prognosis due to the presence of other systemic anomalies. CPAM is an independent etiological factor for the development of pulmonary artery hypertension (PAH). Although the initial insult in PAH involves the pulmonary vasculature, survival of patients is closely related to right ventricular (RV) function. The aim of this case report is to provide options of management of CPAM based on symptomatology, lung involvement, and presence of associated problems.

Results: A 1-year old presented with recurrent pneumonia and signs of RV dysfunction. 2D-echo showed moderate pulmonary artery hypertension, valvular defects, and RV failure. Chest X-ray showed reticulonodular densities on both lungs with cystic lucencies. Chest CT-scan pointed to a CPAM type 2. Lung biopsy was consistent with CPAM type 2. Due to the extensive involvement of the cystic lesions and presence of concomitant problems, conservative medical management was done.

Conclusions: This is a case of type 2 CPAM involving several lobes on both lungs. Patient had complications of PAH and RV dysfunction. Patient was managed conservatively due to the adverse outcome of surgery in this patient.

Figure 1. Chest X-ray of the index case showing reticulonodular densities on both parahilar, right upper and both paracardiac areas with interspersed cystic lucencies.

Figure 2. Chest CT-scan showing ground glass and interstitial densities in both lungs with multiple vari-sized predominantly < 2cm thin walled, air and fluid filled cysts. The main pulmonary artery appears dilated for patient’s age measuring 1.6cm.
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