EMPHYSEMA: VALVES, COILS, STEAM AND LUNG DENERVATION
F. HERTH
Thoraxklinik- University of Heidelberg, Pneumology and Critical Care Medicine, Heidelberg, Germany

Chronic obstructive pulmonary disease (COPD) is a progressive condition comprising a constellation of disorders from chronic bronchitis, airflow obstruction through to emphysema.

The global burden of COPD is estimated at more than 6% of the population. The standard of care is based on a combination of smoking cessation, immunization, pharmacological treatments and pulmonary rehabilitation. However, the more advanced stages of COPD are challenging to manage. In this situation, our current standards of care do not adequately control patient symptoms nor halt the progressive decline. For the emphysema phenotype, lung volume reduction surgery has shown a beneficial effect in selected patients but is counterbalanced by the morbidity experienced by some patients. Bronchoscopic volume reduction technologies have been developed to improve the clinical situation of emphysema patients. This presentation provides broad guidance regarding patient selection and the current position of the available techniques for patients with advanced emphysema.

Conflict of interest
Disclosure statement: Aboard activities for BTG, Broncus, Pulmonx, Olympus, Uptake

INTERVENTIONAL TECHNIQUES 2: UPDATE ON INTERVENTIONAL PULMONOLOGY FOR THE MANAGEMENT OF PULMONARY CONDITIONS
APS3R6-0816

CHALLENGE IN GINA GUIDELINE IMPLEMENTATION
S. HASHIMOTO
Japan

Bronchial asthma (asthma) is a common respiratory disease affecting 1-18% of the population in different countries and its prevalence is increasing in many countries. Although hospitalization and death from asthma have declined, asthma still is a serious problem on health care systems and loss of productivity in the workplace. It is quite important to have a common guideline for diagnosis and management of asthma to recognize global health problem, although the backgrounds of each country such as the medical environment, hygienic environment, education, etc. are different. The Global Initiative for Asthma (GINA) report (“Global Strategy for Asthma Management and Prevention”), has been updated annually since 2002. The GINA report has been updated in 2016 for providing recommendations based on current evidence for best practice in the management of asthma. In this symposium, I will present the latest information about GINA report in 2016 for better understanding asthma diagnosis and management.

ORAL PRESENTATION 1- ASTHMA: IMPROVING ASTHMA TREATMENT
APS3R6-0203

HOW EFFECTIVE ARE ORAL STEROIDS IN ASTHMA ACTION PLANS?
T.K. LIM, N. SAID, J. BEEVI, C.C. GAN, S.Y. LEE
National University Hospital, Department of Medicine, SINGAPORE, Singapore

Background and Aims: Self-administered asthma action plans (AAPs) are a key element in the maintenance of long term asthma control. We performed this study to evaluate the effectiveness of self-administered oral prednisolone (OP) in the management of acute asthma exacerbations (AAEs) with AAPs.

Methods: This is a before Vs after study of consecutive adult patients attending an asthma clinic all of whom had previously received training in AAPs. During the intervention period, we deliberately and actively promoted the prescription of “standby” OP by physicians and the use of OP by patients during their execution of AAPs during AAEs.

Results: We compared patient behavior and clinical outcomes in 94 AAEs before Vs 106 AAEs after the intervention. There was a significant increase in the use of OP from 30/94(32%) to 66/106(62%), p = 0.0002. By contrast, there was no significant change in the proportion of patients who needed emergency room visits and/or hospitalizations during AAEs: 26/94(28%) Vs 21/106(20%), p = 0.19. After our intervention, unscheduled doctor visits were still needed in 38/106 (36%) despite OP being self-administered in 30/38 (79%) of these failed AAPs. The duration of OP use was 5 or more days in 53/66(80%) of AAPs which received OP.

Conclusions: During AAEs, the self-administration of OP in AAPs was not very effective. However, the doses and duration of OP taken were usually adequate. To optimize the management of AAEs, further evaluation of preventable factors and case-specific interventions such as for poor baseline control, undisclosed triggers and delays in taking APP steps may be indicated.

IMPLEMENTATION OF GINA IN THAILAND
W. BOONSAWAT
Thailand

Implementation of GINA in Thailand: Asthma management guidelines were published in Thailand in 1994 and revised in 1997 following the publication of the GINA guidelines. However, asthma survey in Thailand found that asthma management in Thailand fell short of the goals determined for long-term asthma care indicated the failure of guidelines implementation.

The National Asthma Program was undertaken by The National Health Security Office during 2010 to 2012 to improve asthma management using the Easy Asthma Clinic Model. The program supported setting up the Easy Asthma Clinic in the hospitals throughout Thailand. The Easy Asthma clinic is the simplified specialized asthma clinic running by GP. In the clinic we simplified asthma guidelines and organized the system to facilitate the team work, emphasized the role of nurses and pharmacists to help doctors. We also developed on-line web database for registering and monitoring patients. The National Health Security Office also reimbursed for the use of inhaled corticosteroids.

There were 823 hospitals participated in this program. There were 44,124, 87,623, 106,693 patients with 133,012, 260,290, 350,834 visits attended the Easy Asthma Clinic in 2010, 2011 and 2012 respectively. Peak flow was measured in 87.76%, 88.62% and 91.34% in 2010, 2011 and 2012 respectively. Inhaled corticosteroids used increased to 79.43%, 86.51% and 86.78 in 2010, 2011 and 2012. Asthma Admissions decreased 17.8% from 67,813 visits in 2010 to 55,745 visits in 2012. The National Asthma Program in Thailand using the Easy Asthma Clinic Model improved asthma management and decreased asthma admissions. The successful of the program was due to setting up the Easy Asthma Clinic and the reimbursed for the use of inhaled corticosteroids policy.

Conflict of interest
Disclosure statement: I received lecture honorarium from Astra Zeneca, Boehringer Ingelheim, MSD, Novartis and Thai Otsuka.

I was also Advisory Board Member forAstra Zeneca (BUD/FOR), Novartis, Boehringer Ingelheim.

© 2016 Asian Pacific Society of Respirology
Respirology (2016) 21 (Suppl. 3), 3–213
EFFECTIVENESS AND SAFETY OF BRONCHIAL THERMOPLASTY IN JAPANESE PATIENTS WITH SEVERE UNCONTROLLED ASTHMA

M. IKURA, S. ISHI, S. IZUMI, M. HOJO, H. SUGIYAMA
National Center for Global Health and Medicine, Respiratory Medicine, Tokyo, Japan

Background and Aims: Bronchial thermoplasty (BT) is a bronchoscopic procedure that uses thermal energy to reduce airway smooth muscle and prevent chronic structural changes of asthmatic patients. BT was reported to improve asthma-related quality of life (QOL), suppress asthma exacerbation, and maintain pulmonary function for 5 years. BT treatment has been available in Japan since 2015. We aimed to clarify effectiveness and safety of BT treatment in Japanese severe asthmatic patients.

Methods: We prospectively included 11 uncontrolled severe asthma patients who underwent BT treatment at our institution. All patients completed 3 times of BT treatment. We analyzed asthma control, quality of life (QOL), pulmonary function, the fraction of exhaled nitric oxide (FeNO) levels, asthma exacerbation and adverse events in these patients.

Results: There were 11 severely asthmatic patients, with mean age of 53.8 years and disease duration of 26.1 years, on GINA treatment Step 5; exacerbation rate was 6.7 times/year. Average activation counts and time during BT treatment were 57.5 times (77.5 min) at right lower lobe, 54.9 times (73.1 min) at left lower lobe, 92.8 times (88.6 min) at bilateral upper lobes, respectively. Asthma-related QOL (AQLQ) improved from 4.9 to 5.9. Asthma control questionnaire (ACQ5) improved from 1.7 to 0.9. Forced exhaled volume at 1 second (FEV1) increased by 13.5%. Exacerbation decreased from 6.7 to 2.5 times/year. The change of FeNO levels was different in each patient. Transient reversible peribronchitis or atelectasis was observed in all of the patients. Pneumonia, asthma attack and hemoptysis were observed as minor severe adverse events requiring close attention.

Conclusions: BT improved asthma control, QOL, pulmonary function and exacerbation in severe Japanese asthmatic patients with few adverse events.

EFFECT OF COSTIMULATORY SIGNAL BLOCKADE ON STEROID RESISTANT ASTHMA

A. MORI, S. KOYAMA, M. YAMAGUCHI, A. OHTOMO-ABE, Y. KAMIDE, H. HAYASHI, K. WATAI, C. MITSUI, K. SEKuya, T. TSUBURAI, Y. FUKUTOMI, M. TANIGUCHI, T. OHTOMO, O. KAMINUMA
1National Hospital Organization - Sagamihara National Hospital, Clinical Research Center, Sagamihara, Japan, 2Tokyo University of Pharmacy and Life Science, Department of Pharmacotherapeutics, Tokyo, Japan, and 3University of Yamanashi, The Center for Life Science Research, Chuo, Japan

Background and Aims: To investigate the role of helper T (Th) cells in steroid resistant (SR) asthma, steroid sensitive (SS) and resistant (SR) Th clones were selected in vitro, and then adoptively transferred into unprimed mice. Effect of CTLA4-Ig was analyzed both in vitro and in vivo.

Methods: For in vitro evaluation, ovalbumin (OVA) reactive Th clones were cultured with antigen presenting cells and OVA in the presence of various concentrations of dexamethasone (DEX). Proliferative responses of Th clones were measured by 3H-thymidine incorporation. For in vivo assessments, unprimed BALB/c mice were transferred with Th clones, challenged with OVA, and administered with DEX subcutaneously. Bronchoalveolar lavage fluid (BALF) was obtained 48 hr after challenge, and the number of infiltrating cells was differentially counted. CTLA4-Ig was administered through nasal inhalation or venous injection.

Results: SS and SR clones were selected based on the effect of DEX on the proliferative responses of antigen-stimulated Th clones. Airway infiltration of eosinophils and lymphocytes of mice transferred with SS clones were effectively inhibited by the administration of DEX. In contrast, those of mice transferred with SR clones were not significantly inhibited by DEX. Administration of CTLA4-Ig significantly suppressed the proliferation of DEX-treated SR clones in vitro, and the eosinophil infiltration of SR asthma model transferred with SR clones in vivo.

Conclusions: Steroid sensitivity of Th clones assessed in vitro was consistent with that of adoptively transferred asthma model assessed in vivo. Costimulatory signal mediated through CD28 is crucial for the induction of steroid resistance both in vitro and in vivo.

PERSONALIZING ASTHMA TREATMENT BY ADDRESSING THE CO-MORBIDITIES : A MALAYSIAN SINGLE CENTRE PROSPECTIVE STUDY

N.Y. MOHD ESG, M.R. ISA, N. NORDIN, A.N. MUSA, M.A. MOHD ZIM, A.I. ISMAIL
Universiti Teknologi MARA UiTM, Internal Medicine, Sungai Buloh, Malaysia

Background and Aims: Optimal asthma control often failed, partly due to the untreated co-morbidities. However, the correlation between asthma control and the co-morbidities remains unexplored. We sought to evaluate the impact of asthma co-morbidities towards asthma control and their correlations, in order to effectively manage our asthma cases.

Methods: Single-centre, prospective analysis of the baseline and subsequent visits (after 6 months and 1 year) of patients who attended Universiti Teknologi MARA (UiTM) Selangor Respiratory clinic from 2010 till 2015. Besides clinical assessments, patients also filled up the Asthma Control Test (ACT) score form, and were given appropriate treatment. Patients' information and clinical data were obtained from UiTM Clinic online system and analysed via Statistical Package for the Social Sciences (SPSS) software.

Results: A total of 291 asthmatic patients (33.8% Male, 66.2% Female) with mean age of 54.58 years (SD: 41.01) were recruited. At baseline, the Asthma Control Test (ACT) mean score was 17.77 (SD: 5.26) with 55.2% uncontrolled (ACT score <20). Among the patients: 29.9% had Atopic Rhinitis (AR), 9.5% had Gastroesophageal Reflux Diseases (GERDs), 4.9% had Eczema, 10.9% had Obesity and 0.9% had Obstructive Sleep Apnoea (OSA). There were significant differences between baseline ACT score in asthmatic patients with and without AR (p = 0.033) and between those who were on Montelukast and who were not (p = 0.02). After 6 months treatment of asthma, AR and GERDs, the mean ACT score rose to 18.40 (SD: 5.30) (p = 0.075) with only 45.6% remained uncontrolled and it further rose to 18.69 (SD: 4.62) (p = 0.229) with only 48.4% remain uncontrolled after 1 year of treatment.

Conclusions: AR, Obesity and GERDs are common co-morbidities in asthma patients. Assessment of co-morbidities have to be incorporated in each clinic visit. Treating asthma co-morbidities lead to improved asthma control as manifested by improved ACT score. Personalizing asthma treatment by targeting the co-morbidities is paramount for optimized asthma care.
OUTCOME OF TAI CHI QIGONG EXERCISE-BASED PULMONARY REHABILITATION IN ASTHMA

S. KIAATBOONSRI, N. AMORNPUTTISATHAPORN, S. KHIAWAN, Y. KOOMWONG, S. PUALAI, K. PONGSUWAPARR, P. JANKUM, R. TONGPETCH, S. SUDARON PLAEMNGIAM, A. THEPRASIT
Division of Pulmonary and Critical Care Medicine, Department of Medicine- Ramathibodi Hospital- Mahidol University, Bangkok, Thailand

Background and Aims: Exercise training in the pulmonary rehabilitation program is an important adjunctive therapy in COPD. However, its effect when applied to chronic asthma has not been well explored. This observational study focuses on the impact of Tai Chi Qigong exercise-based pulmonary rehabilitation (TCQ-PR) on the disease course of chronic symptomatic asthma.

Methods: Chronic symptomatic asthmatics who attended our routine TCQ-PR service during 2010–2016 were recruited. Various clinical parameters from each individual before TCQ-PR were analyzed and compared with those obtained after TCQ-PR, within the same length of time-period (limited to ± 2 years).

Results: There were 93 patients in this study, age (mean ± SD) 57 ± 13 years, with 93.5% of them received inhaled-corticosteroid and long-acting β2 agonist combination as the main controller medication. All patients completed the 6-weeks daily-exercise program and have continued their home self-practices in most of the cases. In comparisons with the pre-TCQ-PR clinical parameters, post TCQ-PR parameters showed:

1. The improvement (mean ± SD) of force vital capacity (litter) (2.65 ± 0.75 vs 2.59 ± 0.77, p < 0.001), peak expiratory flow (litter/minute) (329.4 ± 110.4 vs 309.6 ± 111, p = 0.002), 6-minute walking distance (meter) (482.1 ± 76.9 vs 453 ± 77, p < 0.001), modified Medical Research Council dyspnea scale (0.69 ± 0.49 vs 1 ± 0.36, p < 0.001), Asthma Control Test (ACT) score (21.6 ± 3.34 vs 18.8 ± 5.26, p = 0.019) and Asthma Control Questionnaire (ACQ) (0.38 ± 3.3 vs 8.43 ± 4.95, p = 0.032) respectively.

2. The decrease (median [range]) of emergency room visit (0 [0]) vs 0 [12], p < 0.001), unscheduled- outpatient visit (0 [4] vs 1 [12], p < 0.001), uses of antibiotics (0 [4] vs 1 [12], p < 0.001) and uses of oral steroid (0 [5] vs 1 [12] p < 0.001) respectively.

3. The decrease of overall exacerbation (mean ± SD) by 59.8% (0.55 ± 0.22 vs 1.36 ± 0.65, p < 0.001, Hazard ratio 0.401, 95%CI = 0.631-0.998).

Conclusions: TCQ-PR is an effective adjunctive therapy for chronic symptomatic asthma leading to the improvement of lung functions and exercise capacity, a better disease control, a reduction of health-care utili-
ties and a marked reduction of asthma exacerbation.

REAL-LIFE EFFECTS OF SWITCHING LABA/ICS DRY POWDER INHALERS TO FORMOTEROL/FLUTICASONE IN KOREAN ASTHMA PATIENTS: THE TRANSFORM STUDY

D. PRICE,1 H.S. PARK,1 D. YOON,2 H.Y. LEE,1 S. WAN YAU MING3, J.F. VAN BOVEN4
1Ajou University School of Medicine, Department of Allergy and Clinical Immunology, Suwon, Republic of Korea, 2Ajou University School of Medicine, Department of Biomedical Informatics, Suwon, Republic of Korea, 3Observational and Pragmatic Research Institute, OPRI, Singapore, Singapore, and 4University of Groningen - University Medical Center Groningen, Department of General Practice, Groningen, Netherlands

Background and Aims: In Korea, the majority of asthma patients are prescribed dry powder inhalers (DPIs). Patients prescribed inhaled corticosteroid/long-acting beta agonists (ICS/LABA) may benefit from switching from a DPI to a pressurized Metered Dose Inhaler (pMDI), such as formoterol/fluticasone. The primary aim of this study was to evaluate the ‘switch success’ of changing asthma patients from ICS/LABA DPIs to formoterol/fluticasone pMDI in a real-world population in Korea. Secondly, we aim to determine if there are any differences in key clinical parameters (e.g. exacerbations, blood eosinophil counts) between patients who switch inhaler and those who continue on the same inhaler.

Methods: Historical cohort database study with baseline and outcome period designed to evaluate the proportion of asthma patients that continue to collect prescriptions of formoterol/fluticasone after initial prescription. Data source is the inhouse clinical asthma database of the Ajou University Hospital (Suwon, Korea). Switch success is considered as >70% of the population maintaining their treatment at least 6 months after the switch. The study is powered for the ‘switch success’ of asthma patients changing their therapy to and continuing on formoterol/fluticasone from existing ICS/LABA DPIs. Both patients switching to formoterol/fluticasone and those remaining on ICS/LABA DPIs will be fully characterised during baseline period. If sufficient numbers are available (sample size required: 163 per cohort), for all of additional outcomes, the outcome year will be compared to the baseline year within the switch cohort. The additional outcomes include: % non-exacerbating patients of ‘switch’ cohort at 1 year, compared to baseline, exacerbation rates, asthma con-
trol, reliever use, side effects and total ICS use.

Results: The protocol has been submitted to ENCePP. Study results (expected end 2016) will provide insights in the real-life effects of switching inhalers.

Conclusions: Outcomes of this study are expected to lead to hands-on recommendations for optimal, cost-effective, treatment options for asthma management.

A RETROSPECTIVE ANALYSIS OF FLEXIBLE BRONCHOSCOPY IN EVALUATION OF PULMONARY DISEASES IN CHILDREN WITH CONGENITAL CARDIOVASCULAR DISORDERS

T. CHEN, L. QIU, L. ZHONG, L. CHEN, H.M. LIU
West China Second University Hospital of Sichuan University, respiratory, Chengdu, China

Background and Aims: There are scarce data to show the role of flexi-
ble bronchoscopy (FB) in evaluating lung and airway diseases in children with congenital cardiovascular disorders in China. This study character-
ized the subjects with congenital cardiovascular disorders who underwent FB for pulmonary diseases, assessed the role of FB in guiding treatment and evaluated the safety of the procedures.

Methods: Retrospective analysis of 57 children with congenital cardio-
vascular disorders who underwent FB because of pulmonary diseases was performed. Demographics, bronchoscopic diagnoses, results of cellular analysis and microbiology of bronchoalveolar lavage fluid (BALF) were analyzed, side effects of FB were evaluated.

Results: 57 bronchoscopies were performed during the study period. Of these, 29 were male, 9 were intubated and mechanically ventilated, the mean age was 0.69 ± 1.27 years. The most common types of congenital cardiovascular disorders were atrial septal defect (42.2%), ventricular septal defect (19.3%) and patent ductus arteriosus (14.0%). 75.4% subjects had 2 or more bronchoscopic diagnoses besides infection. External compression of airways (33.3%), tracheobronchomalacia (28.1%), pharyngomalacia (21.1%) and airway narrowing (21.1%) were the most common airway abnormalities found by FB. The BALF cellular analysis revealed elevated total cell count and neutrophil percentage, 19.2% specimens had positive isolation of an etiological agent. The complications of FB were mild and transient.

Conclusions: FB is a safe and effective diagnosis and interventional tool in the management of children with cardiovascular disorders. FB could be considered as an initial tool in this special group of children.

© 2016 Asian Pacific Society of Respirology
Respirology (2016) 21 (Suppl. 3), 213
Respirology (2016) 21 (Suppl. 3), 3–213

**BRONCHOSCOPIC DIAGNOSIS AND TREATMENT OF PRIMARY TRACHEOBRONCHIAL AMYLOIDOSIS: A RETROSPECTIVE ANALYSIS FROM CHINA**

L. WANG, X. LU, C. QIONG, H. BIXIU, H. BAIMEI

Xiangya Hospital - Central South University, Department of Gerontology, Chang Sha, China

**Background and Aims:** Primary tracheobronchial amyloidosis (TBA) refers to a group of rare diseases which are caused by abnormal deposition of β-sheet amyloids in the tracheal and bronchial submu cosa. In China, only over 200 cases of TBA have been reported so far. The disease lacks typical clinical symptoms and imaging manifestations, misdiagnosis and missed diagnosis are high. In recent years, with the popularization of bronchoscopy, the number of TBA cases diagnosed by bronchoscopy has significantly increased than before. This paper aims to retrospectively analyze 2 cases of TBA patients in our hospital in recent years as well as 107 TBA patients reported from 1981 to 2015 in China, with the focus on explaining the value of bronchoscopy in the diagnosis and treatment of TBA.

**Methods:** Clinical data of 107 patients with TBA reported from 1981 to 2015 in China were retrospectively analyzed for clinical features, bronchoscopy manifestations, pathologies, treatments and outcomes.

**Results:** 105 of 107 TBA patients were pathologically confirmed by bronchoscopy. Main bronchoscopic manifestations of TBA were: single or multiple nodules and masses within tracheobronchial lumens; local or diffuse luminal stenosis and obstruction; luminal wall thickening and rigidity; rough or uneven inner luminal walls; congestion and edema of mucosa, which was friable and prone to bleeding upon touch; etc. 53 patients were treated with bronchoscopic interventions, including Nd:YAG laser, high-frequency electrotome cautery, freezing, resection, clamping, argon plasma coagulation (APC), microwaving, stent implantation, drug spraying and other treatments. 51 patients improved, 1 patient worsened, and 1 died.

**Conclusions:** Bronchoscopic biopsy is the primary means of diagnosing TBA. A variety of bronchoscopic interventions have good short-term effects on TBA. Bronchoscopy has important value in the diagnosis, severity assessment, treatment, efficacy evaluation and prognosis of TBA.

**Semi-Rigid Thoracoscopy: A Hybrid Knife with High-Pressure Water Jet for the Diagnosis of Pleural Effusions**

G. HOU, Y. YIN, R. EBERHARDT, X. WANG, Q. WANG, J. KANG, F. HERTH

1 The first hospital of China Medical University, Respiratory medicine, Shenyang, China, and 2 Thoraklinik University of Heidelberg, Pneumonology and Critical Care Medicine, Heidelberg, Germany

**Background and Aims:** Semi-rigid thoracoscopy is an important technique in the definitive diagnosis of pleural diseases with high diagnostic sensitivity and specificity. Obtaining adequate samples from thickened pleura is the most important limitation of semi-rigid thoracoscopy with standard flexible forceps (SFF) compared with rigid thoracoscopy, especially in patients with mesothelioma or benign fibrothorax. Developing a convenient, efficient and safe biopsy technique to obtain sufficient samples from such patients is a key topic in semi-rigid thoracoscopy. The hybrid knife (HK) is an innovative design fusing high-pressure water injection and a conventional diathermic knife that can allow for the safe resection of a larger lesion during gastrointestinal endoscopic dissection (ESD). Here, we investigated the feasibility of using a new pleural biopsy device in semi-rigid thoracoscopy when pleural lesions are difficult to biopsy by SFF.

**Methods:** We described three patients with unexplained pleural effusion who underwent semi-rigid thoracoscopy. The pleural lesions were difficult to be sampled by standard flexible forceps for the consistency and smooth surface of pleura. We used HK as an alternative, and investigated the efficacy and safety of the HK as a new pleural biopsy device in semi-rigid thoracoscopy.

**Results:** Three patients with exudate pleural effusion who were not diagnosed by analysis of pleural effusion, cytopathology and culture of pleural effusion underwent semi-rigid thoracoscopy. The biopsies were obtained successfully by HK, and diagnosis followed. One was the metastatic lung adenocarcinoma, the other two were tuberculosis pleurisy. The sizes of the biopsies collected by HK are larger than those collected by SFF. No complications were observed.

**Conclusions:** In conclusion, the use of an HK with a water jet is a potent feasible and convenient biopsy technique for semi-rigid thoracoscopy for the successful diagnosis of thickened pleural lesions. It is notably useful when fibrothorax and/or smooth, thickened lesions are encountered.
Background and Aims: To evaluate the effectiveness of sputum induction in nasotracheal aspiration.

Methods: - Prospective study.
- 100 cases were selected to satisfy with inclusion criteria.
- Inclusion criteria: all of pneumonia patients with bad response with initial antibiotic treatment.
- Exclusion criteria: patients with some underlying diseases:
  - haemoptysis of unknown origin
  - acute respiratory distress
  - unstable cardiovascular status, (arrhythmias, angina)
  - thoracic, abdominal or cerebral aeurysms
  - hypoxia (SaO2 less than 90% on room air)
  - lung function impairment (FEV1 less than 1.0 Litre)
  - asthma
  - pulmonary emboli
  - pneumothorax
  - fractured ribs or other chest trauma
  - recent eye surgery

Results: From December 2015 to March 2016, there were 100 pneumonia cases admitted to hospital in Children’s Hospital No.1, that were separated into two distinct groups: sputum induction by using nebulized hypertonic saline 3% and without intervention. The average age was 2.4 years with male and female proportion was 1.5/1. After using nebulized hypertonic saline, the results of lab tests showed the improvement of nasotracheal aspiration specimens quality: the Barlett’s score ≥ 3 (80% versus 40%, p < 0.001) the rate of columnar cell (84% versus 50%, p < 0.001), epithelial cell (90% versus 40%, p < 0.001, c2), positive and negative Gram bacteria stain (40% versus 5%, p = 0.002). In NTA results, the proportion of bacterial detection and antibiotic shown in microbiological tests (10 cases, 20% versus 2, p = 0.005): Klebsiella ESBL(+) 4%, Pseudomonas 4%, E.coli ESBL(+) 4%, E.coli ESBL(-) 2%, Acinetobacter 4%. Moreover, the rate of clinical improvement with nebulized hypertonic saline were detected. Along with, there were no cases with side-effects of using nebulized hypertonic saline in follow-up 3 months. After using nebulized hypertonic saline in pneumonia children with bad response with initial antibiotic treatment, nasotracheal aspiration lab tests improved significantly and also increased the rate of bacterial detection without side-effects.

Conclusions: After using nebulized hypertonic saline in pneumonia children with bad response with initial antibiotic treatment, nasotracheal aspiration lab tests improved significantly and also increased the rate of bacterial detection without side-effects.
Background and Aims: To assess the effects of \( \beta \)-Elemene on the fibrosis and proliferation of airway granulation tissues by exploring its regulatory effect on the proliferation and biological activity of human pulmonary microvascular endothelial cells (HPMEC) and human airway fibroblasts (HAFB) as well as to elucidate its possible mechanism.

Methods: Primary HAFB culture was established using the conventional "tissue adherent method" and confirmed by pathology and immunocytochemical analyses. The HAFB were randomly divided into co-cultured group which were cultured in conditioned media and control group which were cultured in basic medium for 72 hours. The HPMEC were randomly divided into \( \beta \)-Elemene-treated group which were treated with varying concentrations of \( \beta \)-Elemene (30 to 210 \( \mu \)g/mL) and control group which were cultured with \( \beta \)-Elemene-free medium for 72 hours. The proliferation of HPMEC and HAFB in each period of 24 hours were determined by MTT assay. HPMEC were cultured in media containing 60, 150 and 180 \( \mu \)g/mL of \( \beta \)-Elemene for 72 hours, the expressions of VEGF-A, TGF-\( \beta \)-1 and PTX-3 were determined by Western blot analysis.

Results: Low concentrations of \( \beta \)-Elemene (<120 \( \mu \)g/mL) promoted the proliferation of HPMEC but high concentrations of \( \beta \)-Elemene (>120 \( \mu \)g/mL) inhibited (P < 0.05). Low-concentration \( \beta \)-Elemene (60 \( \mu \)g/mL) increased the expressions of VEGF-A and TGF-\( \beta \)-1 but high concentrations of \( \beta \)-Elemene (150 and 180 \( \mu \)g/mL) decreased (P < 0.05). The expression of PTX-3 was increased with the increasing concentrations of \( \beta \)-Elemene. HPMEC promoted HAFB proliferation, which was accentuated by low-concentration \( \beta \)-Elemene (60 \( \mu \)g/mL) but attenuated by high concentrations of \( \beta \)-Elemene (150 and 180 \( \mu \)g/mL).

Conclusions: The mechanism by which \( \beta \)-Elemene regulates the proliferation and fibrosis of airway granulation tissue could be due to the following: ①Regulating the proliferation and expressions of VEGF-A and TGF-\( \beta \)-1 in HPMEC; ②Regulating the proliferation of HAFB induced by HPMEC; ③\( \beta \)-Elemene promotes the expression of PTX-3 suggesting that \( \beta \)-Elemene could cause inflammatory injury to HPMEC.
Background and Aims: Specific microRNAs are proposed to be key epigenetic factors responsible for structural and functional abnormalities of asthmatic epithelial cells. We hypothesise that the level of microRNAs regulating proliferation (e.g. miR-17-92 cluster), differentiation (e.g. miR-22 and -132) or polarity (e.g. miR-132) are differentially expressed in asthmatic epithelium and play essential roles in epithelial cell abnormalities that characterize asthma. Further, we suggest that expression of these microRNAs is further dysregulated by influenza A virus (H1N1); an important pathogen responsible for enormous morbidity and mortality in annual epidemics. Our aims are to determine the level of these microRNAs in primary bronchial epithelial cells (pBEC) of asthmatics and non-asthmatics a) at rest, and b) following H1N1 infection. 

Methods: pBEC from severe asthmatic and non-asthmatic subjects were obtained from bronchial brushings and cultured under submerged or air liquid interface (ALI) conditions. Cells were incubated with H1N1 (MOI 5) or UV-inactivated-H1N1. microRNAs were isolated using RNAeasy mini kit and subjected to Taqman miRNA assays to assess expression of each microRNAs. Expression levels were quantified using the 2−ΔΔCt method. 

Results: In submerged culture, basal expression of miR-17-5p was significantly lower in asthmatic cells and infection with H1N1 had no effect on expression of any of these microRNAs over time (0,6,24h). In differentiated ALI culture, we saw no difference in basal expression of any of candidate microRNAs. The expression of miR-22 increased significantly in a time dependent manner (6,8,24h) in ALI cells from non-asthmatics, whereas infection had no effect on miR-22 in cells from asthmatics.

Conclusions: Some miRNAs are expressed abnormally in epithelial cells from severe asthmatics. The increase in miR-22 expression after H1N1 infection in non-asthmatic differentiated cells maybe a self-defence mechanism to avoid tissue remodeling which maybe subdue in asthmatic cells.

Acknowledgements: ECR grant-UoN and McDonald Jones Homes-HMRI to FM; NHMRC project grant # 1064405 to DK.

EXOGENOUS ADDED COPPER RESCUES ENDOTOXIN-INDUCED ACTUTE LUNG INJURY

J.R. PARK, H. LEE, S.R. YANG
School of Medicine - Kangwon National University, Department of Thoracic and Cardiovascular Surgery, Chunchon city, Republic of Korea

Background and Aims: Acute lung injury is characterized by acute inflammation and disruption of the alveolar-capillary membranes leading to alveolar flooding with protein-rich edema fluid. The tripeptide-copper complex glycyl-histidyl-lysine (Cu) (GHK-Cu) is a compound with safe use in wound healing and anti-aging skin care. Although GHK-Cu exhibits anti-oxidant, anti-inflammatory and tissue regenerative, and wound healing actions, its roles in acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) are unknown.

Methods: Therefore, we examined the effects of GHK-Cu in lipopolysaccharide (LPS)-induced RAW 264.7 macrophages in vitro and ALI in mice in vivo. 

Results: GHK-Cu mitigated reactive oxygen species (ROS) production, improved superoxide dismutase (SOD) activity, and decreased TNF-α and IL-6 production in LPS-induced RAW 264.7 macrophages. Moreover, we demonstrated that GHK-Cu exerts an anti-inflammatory effect via the suppression of NF-κB activation and p38 MAPK signaling. We also evaluated the effects of GHK-Cu on LPS-induced ALI in mice. GHK-Cu pretreatment resulted in a significant reduction in LPS-induced lung tissue damage. In addition, GHK-Cu significantly increased SOC activity and total GSH levels and downregulated TNF-α and IL-6 production in LPS-induced ALI in mice.

Conclusions: Collectively, these findings demonstrate that GHK-Cu possesses a protective effect in LPS-induced ALI by inhibiting excessive inflammatory responses; accordingly it may represent a novel approach for ALI/ARDS treatment. 

Acknowledgements: This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. NRF-2014R1A2A2A01003737).
Background and Aims: Chronic obstructive pulmonary disease (COPD), including emphysema and chronic bronchitis, is a progressive disease with high incidence and one of the leading causes of mortality and morbidity worldwide. Fuß (x1, 6-fucosyltransferase) has been implicated in the development of emphysema in Fuß-null mice. The disadvantages of Fuß knockout mice model are multiple organ dysfunctions and the high mortality rate soon after birth. Given the inherent limitations using animal model, our aim is to develop the Fuß gene knockdown in lung stem cells (LSCs) and establish 3D organotypic model of alveolar sacs to mimic the COPD-like changes.

Methods: We have first deciphered the glycoprotein expression pattern in lung cells by glycoproteomic strategy and identified surface markers for isolation of LSCs, which has the ability not only for self-renewal and differentiation, but also for in vivo engraftment and repair of lung tissues (Nature Nanotech 8:682 2013). Recently, we found that Fuß (x1, 6-fucosyltransferase) activity in the isolated LSCs was approximately 14 fold greater than that in the differentiating type II and I alveolar cells. We have thus developed organotypic cultures for lung alveologenesis using isolated LSCs to recapitulate formation of 3D alveolar sacs in COPD.

Results: So far, we have established a unique LSC-derived 3D organotypic tissue model which mimicked the structural alterations reminiscent of changes in COPD. In addition, an unexpected finding of the involvement of Fuß in type 2 epithelial-mesenchymal transition (EMT) in culture by which epithelial LSCs were converted to fibroblastic phenotypes upon differentiation was also found.

Conclusions: In order to elucidate molecular processes involved with the decrease of core-fucosylation in COPD, we have developed organotypic cultures for lung alveologenesis using isolated LSCs. In addition, we have studied the pathogenesis of small airway fibrotic changes and provide a model to study their correlations with pulmonary disorders.

SPNS2 in the Airway Epithelial Cells and Alveolar Macrophages Contributes Differently into Cigarette-Induced Deregulated S1P Signaling: A Translation to the Mechanism of COPD

H. TRAN, H. RHY, M. WEEN, G. HODGE, J. BARNAWI, P. REYNOLDS, S. PITSON, L.K. DAVIES, R. HABERBERGER, S. HODGE

Royal Adelaide Hospital, Thoracic Medicine, Adelaide, Australia, and Flinders University, Centre for Neuroscience-Anatomy and Histology, Adelaide, Australia

Background and Aims: We have previously established in COPD patients’ alveolar macrophages a link between impaired clearance of apoptotic cells and deregulated S1P signaling. SPNS2 is the S1P transporter allowing for S1P autocrine and paracrine effects. We hypothesize that airway epithelia, by a deficient export of S1P via SPNS2, may also contribute into deregulated S1P signaling in alveolar macrophages of COPD patients and cigarette smokers.

Methods: Human primary alveolar macrophages and bronchial epithelial cells, paraffin sections of human and mouse lung tissue, and cell lines of bronchial epithelium (HBE) and macrophages (THP-1-derived) were analyzed. Cell cultures were exposed for 24 h to 10% cigarette smoke extracts, or vehicle control. Mice were chronically (24 weeks) exposed to cigarette smoke by a remarkable SPNS2 down-regulation, in both the in vivo model (~ 60%, p < 0.001, n = 6 animals per group) and cell cultures of HBE (~ 70%, p < 0.001 in 3 experiments).

Results: Primary bronchial epithelial cells expressed bright SPNS2 in cilia; in HBE SPNS2 localized to plasma membrane, cytoplasm, and the nucleus. In primary alveolar macrophages and THP-1 macrophages SPNS2 was found in cytoplasm and nucleus but not membrane. A biparite Nuclear Localization Signal was predicted at the position aa282 of the human SPNS2 sequence. Exposure to cigarette smoke extract resulted in significant increase of SPNS2 protein in primary alveolar macrophages (+25% to 4 folds, 4 donors, p < 0.05) and THP-1 macrophages (+80%, p < 0.05, 3 experiments). In contrast, the epithelial cell type responded to cigarette smoke by a remarkable SPNS2 down-regulation, in both the in vivo model (~ 60%, p < 0.001, n = 6 animals per group) and cell cultures of HBE (~ 70%, p < 0.001 in 3 experiments).

Conclusions: New therapeutic designs targeting the effective effectorcysis in macrophages of COPD patients/cigarette smokers will have to consider different contribution of epithelial cells and macrophages into the mechanism of S1P signaling and cross-cell type interaction in this aspect.
Background and Aims: Muscle wasting is one of extrapulmonary manifestations that occur in 20-40% of patients with COPD. Muscle wasting can occur as a result of an imbalance of protein synthesis and degradation, where it is thought to be a consequence of chronic inflammation that occurs. One of the factor that affect muscle wasting is nutritional factor. The purpose of this study is to prove that nutrition therapy can improve inflammation (measured by levels of leptin, adiponectin) further improve muscle wasting and improve the quality of life of patients COPD with muscle wasting.

Methods: The clinical study design is pre and post auto control quasi experiment. Patients with COPD with comorbid muscle wasting. The experiment was conducted in Pulmonary Outpatient Clinic Dr. Saiful Anwar Hospital and Physiology Laboratory of Medical Faculty Brawijaya University January 2015-December 2015. COPD was diagnosed based on 2014 GOLD criteria. Muscle wasting was diagnosed through examination of the BIA. Levels of blood leptin and adiponectin was measured using ELISA method, and quality of life was assessed using CAT score. We measured BIA, BIA, Leptin, Adiponectin and CAT in 32 COPD patients with muscle wasting, before and after 12 weeks supplementation of Ophioccephalus striatus striatus extract 3x1000mg/day.

Results: There were significant increased of BMI (p = 0.046), no significant increase of FFMI (p = 0.056), a significant decrease in leptin levels (p = 0.000) and a significant increase in adiponectin levels (p = 0.048) and improvement of quality of life (score CAT) (p = 0.002) after administration of Ophioccephalus striatus extract for 12 weeks.

Conclusions: Supplementation of Ophioccephalus striatus extract for 12 weeks can improve BMI, decrease level of leptin, increase level of adiponectin resulting in improvement of quality of life in stable COPD patients with muscle wasting. Keywords: COPD, muscle wasting, Ophioccephalus striatus striatus extract, leptin, adiponectin, CAT.

**LEVELS OF HDAC2 AND SGRQ-C IN C AND D POPULATION COPD PATIENTS WITH INHALED ICS/LABA AND HISTORY OF SMOKING**

S.H. RAHYU, T. ASTUTI, U. AGUS SETYAWAN
Universitas Brawijaya/Saiful Anwar Hospital, Pulmonology and Respiratory Medical Program, Malang, Indonesia

Background and Aims: In chronic obstructive pulmonary disease (COPD) especially in smoker patients there is a reduction in Histone Deacetylase 2 (HDAC2) activity and expression which is caused by oxidative stress. It is linked with corticosteroids resistance. GOLD recommendation therapy for C and D population COPD is combination of long-acting beta-2 agonist and corticosteroids (LABACS). There is no studies that associate levels of HDAC2 serum in patients with smoking history and efficacy of such therapy. We aimed to determine levels of HDAC2 serum in COPD patients with history of smoking and its relationship with the quality of life of these patients.

Methods: Cross sectional analytic study. 36 C and D population COPD patients in Saiful Anwar General Hospital Malang Indonesia were grouped into LABACS and no-LABACS. HDAC2 serum expression was assessed using Elisa and Quality of life was assessed using St George’s Respiratory Questionnaire (SGRQ-C).

Results: There was no significant difference in HDAC2 serum between these groups (p = 0.628). There was no significant difference in total score of SGRQ-C too (p = 0.476). There was a weak correlation between the levels of HDAC2 serum and total SGRQ-C score (r = 0.227, p = 0.183), but not significant.

Conclusions: There was no significant difference in HDAC2 serum expression and SGRQ-C score in LABACS and no-LABACS group in C and D population COPD patients. There was no significant correlation between HDAC2 serum expression and SGRQ-C score.

Keywords: COPD, HDAC2, LABACS, SGRQ-C

**EFFECT OF OPHIOCEPHALUS STRIATUS EXTRACT ON LEPTIN, ADIPONECTIN LEVEL AND CAT SCORE (COPD ASSESSMENT TEST) IN STABLE COPD PATIENT WITH MUSCLE WASTING**

K. WIDIASARI, S. DJAJALAKSANA, H. AL RASYID
Universitas Brawijaya/Saiful Anwar Hospital, Pulmonology and Respiratory Medicine, Malang, Indonesia, and Universitas Brawijaya/Saiful Anwar Hospital, Public Health Department, Malang, Indonesia

Background and Aims: Muscle wasting is one of extrapulmonary manifestations that occur in 20-40% of patients with COPD. Muscle wasting can occur as a result of an imbalance of protein synthesis and degradation, where it is thought to be a consequence of chronic inflammation that occurs. One of the factor that affect muscle wasting is nutritional factor. The purpose of this study is to prove that nutrition therapy can improve inflammation (measured by levels of leptin, adiponectin) further improve muscle wasting and improve the quality of life of patients COPD with muscle wasting.

Methods: The clinical study design is pre and post auto control quasi experiment. Patients with COPD with comorbid muscle wasting. The experiment was conducted in Pulmonary Outpatient Clinic Dr. Saiful Anwar Hospital and Physiology Laboratory of Medical Faculty Brawijaya University January 2015-December 2015. COPD was diagnosed based on 2014 GOLD criteria. Muscle wasting was diagnosed through examination of the BIA. Levels of blood leptin and adiponectin was measured using ELISA method, and quality of life was assessed using CAT score. We measured BIA, BIA, Leptin, Adiponectin and CAT in 32 COPD patients with muscle wasting, before and after 12 weeks supplementation of Ophioccephalus striatus striatus extract 3x1000mg/day.

Results: There were significant increased of BMI (p = 0.046), no significant increase of FFMI (p = 0.056), a significant decrease in leptin levels (p = 0.000) and a significant increase in adiponectin levels (p = 0.048) and improvement of quality of life (score CAT) (p = 0.002) after administration of Ophioccephalus striatus extract for 12 weeks.

Conclusions: Supplementation of Ophioccephalus striatus extract for 12 weeks can improve BMI, decrease level of leptin, increase level of adiponectin resulting in improvement of quality of life in stable COPD patients with muscle wasting. Keywords: COPD, muscle wasting, Ophioccephalus striatus striatus extract, leptin, adiponectin, CAT.

**BUFFEY YISHEN GRANULE DOWN-REGULATES NUCLEAR FACTOR-κB SIGNALING IN CIGARETTE-SMOKE EXTRACT INDUCED HUMAN PULMONARY FIBROBLAST CELLS**

Y. LI, Z. WU, J. MAO, J. LI, Q. BIAN, Y. TIAN, S. LI, Y. XIE, J. LI
1The first affiliated hospital of Henan University of TCM, Institute for Respiratory Diseases, Zhengzhou, China, 2Henan University of Traditional Chinese Medicine, Collaborative Innovation Center for Respiratory Disease Diagnosis and Treatment & Chinese Medicine Development of Henan Province, Zhengzhou, China, and 3The first affiliated hospital of Henan University of TCM, Department of Respiratory, Zhengzhou, China

Background and Aims: Inflammation happened in fibroblast cells plays a critical role in airway remodeling in chronic obstructive pulmonary disease (COPD). Bufei Yishen granule, a compounded Chinese medicinal prescription confirmed to elicit a variety of biological and clinical effects via anti-inflammatory-like property in previous studies. Whether the anti-inflammatory mechanism works in pulmonary fibroblasts is still unknown. We hypothesized that the potential protective role of Bufei Yishen granule in cigarette-smoke extract (CSE) induced human pulmonary fibroblast cells, MRC-5 cell line, and the underlying mechanism of nuclear factor (NF)-κB suppression.

Methods: Normal cultured and NF-κB small interfering RNA (siRNA) pre-treated MRC-5 cells were treated with normal serum, CSE, Bufei Yishen and aminophylline serum, respectively, for 24 h. Interleukin (IL)-1β, transforming growth factor (TGF)-β1 and tumor necrosis factor (TNF)-α in supernatant and gene and protein expressions of NF-κB and IκBα in cells were determined by quantitative polymerase chain reaction and western blotting.

Results: Bufei Yishen and aminophylline serum did not affect the cells with or without NF-κB siRNA pretreatment. All above observed markers were significantly elevated by CSE in cells with and without NF-κB siRNA pretreatment, and were depressed in Bufei Yishen and aminophylline serum treated cells, especially in NF-κB siRNA pretreated cells.

© 2016 Asian Pacific Society of Respirology Respiratory Medicine, Malang, Indonesia, and

APSR6-0210

APSR6-0210

APSR6-0245

APSR6-0245
PULMONARY INTERSTITIAL EMPHYSEMA CAUSES AIR LEAKS IN THE CASES OF INTERSTITIAL PNEUMONIA

Y. TACHIBANA,1 S. TSUJINO,1 M. HASHISAKO,1 Y. KONDOH,2 K. KATAOKA,2 N. HAMADA,2 T. HASHIGUCHI,1 K. ICHIKADO,2 T. KISHABA,6 S. SATO,7 Y. IMAOKA,1 R. GROEN,1 H. TANIGUCHI2, J. FUKUOKA1

1Nagasaki Educational and Diagnostic Center of Pathol. NEDCP, Pathol., Nagasaki, Japan, 2Tosei General Hosp., Resp. Med. & Allergy, Aichi, Japan, 3Kyushu Univ., Resp. Inst. for Diseases of the Chest-Graduate Sch. of Med. Sci., Fukuoka, Japan, 4Kurume Univ. Sch. of Med., Pathol., Fukuoka, Japan, 5Saiseikai Kumamoto Hosp., Respiratory Med., Kumamoto, Japan, 6Okinawa Chubu Hosp., Resp. Med., Okinawa, Japan, and 7Nagasaki Univ., Cntr. of Clin. research, Nagasaki, Japan

Background and Aims: Pulmonary interstitial emphysema (PIE) is a rare abnormal condition where air dissects through the adjacent interstitial tissues and forms cystic spaces. Cystic walls are characterized by absence of epithelium, and often coated by histiocytes and giant cells. PIE is well described in premature infants with respiratory distress syndrome, and in adults who use a ventilator. However, PIE can be seen in various interstitial pneumonia (IP) as well. Clinicopathological importance and variation of them are uncertain. We analyzed the clinical meaning of PIE in IP cases.

Methods: IP cases with PIE (IP-PIE) and 15 cases with idiopathic pulmonary fibrosis (IPF) without PIE were collected from 1218 outside consultation cases. Clinical radiological and pathological (CRP) diagnosis along with gender, age, smoking history, respiratory function test, presence of air leaks, and follow-up status of both IP-PIE and control cases were obtained. Wilcoxon rank sum test and Fisher’s exact test were performed to examine association between PIE and clinicopathological factors. Survival analysis was performed using Log-rank test, and Kaplan Meier curve was plotted.

Results: IP-PIE had a male predominance (11:6), a median age of 67 (ranged 46–75). The ratio of smoker and non-smoker was 10:7. The major histological pattern was usual interstitial pneumonia (UIP, 10, 58.8%). CRP diagnoses of 17 cases were 4 IPF, 4 hypersensitivity pneumonia and 4 idiopathic Pleuroparenchymal Fibroelastosis. During the follow-up, 11/17 of IP-PIE experienced air leaks (8/11 pneumothorax and 3/11 subcutaneous/mediastinal emphysema). These numbers were significantly higher to IPF (3/15, p = 0.02). The odds ratio was 7.33. We documented a trend of worse prognosis for patients with IP-PIE however, the difference did not reach statistical significance, probably due to the small number of cases (p = 0.28).

Conclusions: This result suggests that PIE in IP is a risk indicator of future air leaks, especially pneumothorax.
OBSERVATION OF THREE-DIMENSIONAL STRUCTURE REVEALS HYPOTHETICAL PATHOGENESIS OF PULMONARY EMPHYSEMA

A. YOSHIKAWA,1 S. SATO,2 T. TANAKA,1 H. MIKIKO,1 Y. KASHIMA,3 T. TSUCHIYA,4 N. YAMASAKI,4 T. NAGAYASU4, J. FUKUOKA1

1 Nagasaki University Hospital, Nagasaki Educational and Diagnostic Center of Pathology NEDCP, Nagasaki, Japan, 2 Nagasaki University Hospital, Clinical Research Center, Nagasaki, Japan, 3 Nagasaki University Graduate School of Biomedical Sciences, Department of Pathology, Nagasaki, Japan, and 4 Nagasaki University Graduate School of Biomedical Sciences, Department of Translational Medical Sciences, Nagasaki, Japan

Background and Aims: We newly developed a method to observe three-dimensional (3D) structure from paraffin embedded tissue. The method was applied to unveil the pathogenesis of pulmonary emphysema.

Methods: We reviewed tissues from 25 cases with/without emphysema and applied 3D observation method to the paraffin blocks. Based on the 3D characteristics of alveolar structure (Figure 1AB), we considered one face of alveolar polyhedron as a structural unit of gas-exchange and called it a framework unit (FU, Figure 1C). We categorized FUs based on their morphological characteristics and counted their number to evaluate destructive changes in alveoli. We also evaluated the number and the area of pores of Kohn in FUs (Figure 1D). We performed linear regression analysis to estimate the effect of these data on pulmonary function tests.

Results: In multivariable regression analysis, a decrease in the number of FUs without an alveolar wall had a significant effect on a decrease in diffusing capacity of the lung for carbon monoxide (DLCO, Table 1) and DLCO per unit alveolar volume (DLCO/VA, Table 2), and an increase in the area of pores of Kohn had a significant effect on an increase in residual volume (RV, Table 3).

Table 1. Reversible and multivariable regression analysis on DLCO

| Variables | DLCO 6% | DLCO 15% | DLCO 30% |
|-----------|---------|----------|----------|
| FEV1  | 0.49 | 0.65 | 0.73 |
| BMI     | -0.32 | -0.40 | -0.47 |
| Age     | -0.21 | -0.28 | -0.33 |

Table 2. Reversible and multivariable regression analysis on DLCOVA

| Variables | DLCOVA 6% | DLCOVA 15% | DLCOVA 30% |
|-----------|-----------|------------|------------|
| FEV1  | 0.49 | 0.65 | 0.73 |
| BMI     | -0.32 | -0.40 | -0.47 |
| Age     | -0.21 | -0.28 | -0.33 |

Table 3. Reversible and multivariable regression analysis on RV

| Variables | RV 6% | RV 15% | RV 30% |
|-----------|-------|-------|-------|
| FEV1  | 0.29 | 0.43 | 0.52 |
| BMI     | -0.23 | -0.29 | -0.35 |
| Age     | -0.15 | -0.20 | -0.25 |

Conclusions: A breakdown in lung framework and an increase in pores of Kohn are associated with a decrease in DLCO, DLCOVA, and RV. According to our results, morphological progression of pulmonary emphysema is hypothesized as follows. Alveoli in the normal state (Figure 2A-A') start to show an increase the number and size of pores of Kohn (Figure 2B-B'). The framework structure and alveoli merge and break down because of mechanical stress and/or inflammation (Figure 2C-C'). Finally, remodeling of acini results in enlarged air spaces of emphysema (Figure 2D-D').

CLINICAL FEATURES OF ANEMIC COPD

J.H. PARK,1 Y.M. OH,2 J.S. LEE,2 K.H. YOO,3 J.H. LEE,4 S. SHEEN,1 E.K. KIM4, S.D. LEE2

1 Ajou University School of Medicine, Department of pulmonary and critical care medicine, Suwon, Republic of Korea, 2 Asan Medical Center- University of Ulsan College of Medicine, Department of Pulmonary and Critical Care Medicine, Seoul, Republic of Korea, 3 Department of Internal Medicine-, Konkuk University School of Medicine, Seoul, Republic of Korea, and 4 CHA Bundang Medical Center- CHA University, Department of Internal Medicine, Seongnam, Republic of Korea

Background and Aims: Anemia is an important prognostic factor and one of the major co-morbidities in COPD. Therefore, this study was performed to evaluate the clinical features of anemic COPD and investigate factors linked with serum hemoglobin level in COPD.

Methods: We analyzed 407 COPD patients of Korean Obstructive Lung Disease (KOLD) cohort enrolled from 16 hospitals in Korea. Anemia was defined by serum hemoglobin: < 12 g/dL for women and < 13 g/dL for men.

Results: Anemic COPD had older age, lower BMI, lower cholesterol level, lower serum albumin level, and shorter walk distance in six minute walk test, compared to non-anemic COPD, (p < 0.05). However, there was no difference in pulmonary function tests and radiologic findings between two groups. The survival period of non-anemic COPD (mean survival = 8.96 ± 0.16 years) was longer than anemic COPD (6.75 ± 0.78 years, p = 0.002). By multivariate linear regression analysis, older age (p < 0.001), lower FEV1 (p = 0.023), lower BMI (p = 0.018), and lower serum albumin level (OR = p < 0.001) were independent factors associated with serum hemoglobin level.

Conclusions: Older age, lower serum albumin level, lower FEV1 and lower BMI were independent factors associated with serum hemoglobin level in COPD. The survival period of anemic COPD was shorter.
Comparision of Presenting Clinical Symptoms and Outcomes of Ischemic Heart Disease Patients Admitted to Coronary Care Unit with and Without Chronic Obstructive Pulmonary Disease

S. ASHRAF, A. ASHRAF, M. ZAMAN

Khyber Medical College & Teaching Hospital, Pulmonology, Peshawar, Pakistan; Khyber Teaching Hospital, Cardiology, Peshawar, Pakistan; and Khyber teaching Hospital, Pulmonology, Peshawar, Pakistan

Background and Aims: Ischemic heart disease (IHD) and Chronic Obstructive Pulmonary Disease (COPD) may co exist as they share common risk factors. Such patients admitted to coronary care unit may have different presenting symptom and outcomes as compared to non-COPD patients.

Objective: To compare presenting clinical symptoms and in hospital outcomes of Ischemic heart disease patients admitted to CCU with and without COPD.

Methods: This was a prospective cohort study among IHD disease patients admitted to CCU with COPD (gp 1) and without COPD (gp 2). Presenting clinical symptoms and in hospital outcomes were documented on a structured proforma.

Results: All IHD patients, with 57 COPD and 69 without COPD, who fulfilled the inclusion criteria were recruited in the study after informed consent. Mean age of the study population was 57.9 ± 12 years, with 63.6 ± 10 in gp 1 vs 54 ± 11 yrs in gp 2 (p < 0.05). Male to female ratio in 2 groups were 39/18 Vs 35/54. Chest pain, breathlessness, palpitations and cough were present in 83.77, 30 and 63 % in COPD gp vs 65 % smokers as compared to 81.44, 26 and 22 % with only 29% smokers respectively in non COPD gp. Only breathlessness and cough were statistically significant different presenting symptom in the two groups. Length of hospital stay was 6.4 ± 1day vs 4.6 ± 1.2 days in the two groups with p < 0.05. There was no statistically significant difference in the 2 groups in terms of death, arrhythmia or cardiogenic shock.

Conclusions: Ischemic heart disease patients with COPD most likely present with breathlessness and cough with longer duration of hospital stay as compared to non COPD IHD patients.

Factors Affecting Mortality in Acute Exacerbations of Chronic Obstructive Pulmonary Disease

M. MADAN, S.K. CHHABRA

Vallabhbhai Patel Chest Institute, Department of Pulmonary Medicine, New Delhi, India

Background and Aims: Acute exacerbations of COPD (AECOPD) are major events in the natural course of COPD because of mortality risk besides accelerating the decline in lung function and worsening the quality of life. Factors that have been shown to be associated with mortality risk in acute exacerbation of COPD include higher age, male sex, acidaemia and lower BMI. The present study was carried out to indentify additional or hitherto unreported risk factors for mortality.

Methods: In a prospective and observational study in a tertiary care hospital, consecutive patients admitted to the wards/intensive care unit with a diagnosis of AECOPD over a period of one year were included. Diagnosis was established as recommended by the GOLD guidelines. Standard protocol of management was followed including chest radiographs, arterial blood gas analysis, blood and sputum investigations. Noninvasive or invasive ventilatory support was given as indicated.

Results: There were 145 episodes in 101 patients (86 males) In our study. Overall mortality was 8.2%. Noninvasive support was required in 66 episodes, with further invasive support required in 16 patients. All the patients who had mortality required mechanical ventilatory support. Factors found to be significantly associated with higher mortality were acidosis, hypercapnia, higher potassium and higher blood glucose on presentation, isolation of pathogens in respiratory specimens, need for change of antibiotics and prior FEV1.

Conclusions: Knowledge of factors associated with increased mortality in AECOPD is important as this can be utilized in management decisions and may improve outcomes.

The Utility of GOLD’s COPD Screening Questionnaire in the Community

Q. VU TRAN THIEN, L. THI TUYET LAN

University of Medicine and Pharmacy– Ho Chi Minh City, Physiology, Ho Chi Minh City, Vietnam

Background and Aims: The prevalence of COPD is increasing worldwide, but most of COPD patients have been diagnosed at advanced stages. Spirometric results are gold standard to diagnose COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Therefore, early diagnosis of COPD in the community is facing a challenge because it requires a lot of human and economic resources. GOLD guidelines also recommend to use a questionnaire of five questions for screening COPD. This study was conducted to validate the utility of GOLD’s COPD screening questionnaire in the community.

Methods: This is a cross-sectional study. 767 subjects were randomly sampled from 10 districts of Ho Chi Minh City, Vietnam. All the subjects were interviewed using questionnaires with 14 types of ques-tions among COPD patients in Persahabatan Hospital Jakarta.

Results: Of 767 subjects, 408 (53.2%) were male. The average age was 54.28 ± 17.48; the average body mass index was 23.0 ± 3.7 kg/m². 281 (36.6%) subjects were current or ex-smoker; 199 (25.9%) had ever exposure to occupational dust. 69 (9.0%) subjects were diagnosed with COPD. Out of 69 COPD patients, 48% were in group A, 22% in group B, 14% in group C, and 16% in group D according to GOLD classification. Compared to the gold standard of COPD diagnosing, the utility of the GOLD’s COPD screening questionnaire was as follows: the area under the curve (AUC) was 0.8146; at the optimal cut-off value of 3 points, the sensitivity was 68.12% and the specificity was 80.66%.

Conclusions: The GOLD’s COPD screening questionnaire may be useful for screening COPD in the community.

Smoking Behaviours and it’s Characteristics among COPD Patients in Persahabatan Hospital Jakarta

W. PANDU ARIAWAN, F. YUNUS

University of Indonesia, Pulmonology and Respiratory Medicine, East Jakarta, Indonesia

Background and Aims: In Indonesia, the COPD prevalence is 3.7% per mile in subjects with age ≥30 years old, especially in male. Smoking behaviours among people aged ≥15 years is 36.3%, 64.9% male, and the average number of cigarettes smoked was about 12.3. The purpose of this study was to determine the smoking behaviours and it’s characteristics among COPD patients in Persahabatan Hospital Jakarta.

Methods: We conduct an administered questionnaire based study with 43 male subjects, 13.9% age <60 years old and 86.1% age ≥60 years old. All subjects were interviewed using questionnaires with 14 types of questions.

Results: From all subjects, 4 (9.3%) had never smoked, 69.2% subjects started smoking at age 10–20 years old, 76.9% subjects started smoking because of their friends. The longest period of smoking is 20–30 years, 51.3% subjects with severe Brinkmann Index score. Clove cigarettes is the most type used by the subject (66.6%). There are 1–3 smokers in one family, both subjects as a family member (72.1%) or head of household (90.5%). Most of the subjects were diagnosed COPD at the age ≥40 years old (97.7%) with group D as the largest (69.7%). 92.8% subjects are ex-smokers, most stop smoking at age ≥40 years old (84.6%). Reasons to quit most was due to illness (87.1%) by the effort to quit smoking 1–3 times. Cancer is the most widely known impact of smoking (26.5%). Most subjects said images on cigarette packs does not give effect to smoking cessation (55.8%).

Conclusions: Most of our subjects have history of early smoking and quit smoking at a later age, severe Brinkmann Index score and most of the subjects were diagnosed COPD at the age ≥40 years old with group D as the largest. Smoking behaviours and it’s characteristics might have strong influence on the severity of disease.
ORAL PRESENTATION 6 - RESPIRATORY INFECTIONS (NON-TUBERCULOUS) + BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES: TOPICS IN LUNG INFECTION 1

APSR6-0033

ETIOLOGICAL ANALYSIS AND EPIDEMIOLOGICAL COMPARISON AMONG ADULT CAP AND NHCAP PATIENTS IN OKINAWA, JAPAN

G. PARROTT,1 D. NEBEYA,1 T. KINJO,1 S. HAFANAGA,1 F. HIGA,2 T. MASAO,1 J. FUJITA1
1University of the Ryukyus, Department of Infectious Diseases- Respiratory and Digestive Medicine- Graduate School of Medicine, Nishihara, Japan, and 2National Hospital Organisation Okinawa National Hospital, Chief of Respiratory Department, Ginowan, Japan

Background and Aims: Etiological epidemiology and diagnosis are important issues in community acquired- (CAP) and nursing and healthcare-associated- (NHCAP) pneumonia. Despite the availability of effective therapies, significant morbidity and mortality ensues. This study provides a current understanding of the pathogens, risk factors, patient outcomes, and treatment techniques encountered in the Japanese prefecture of Okinawa.

Methods: We retrospectively analyzed the bacterial etiology of 200 pneumonia patients at the University of Ryukyu Hospital. According to Japanese Respiratory Society (JRS) guidelines, patients were categorized into CAP (n = 97) or NHCP (n = 103). Diagnoses were made using clinical tests including, Gram stain, bacterial culture as well as serum and urinary tests.

Results: Pathogens were detected in 71% of patients, and identified as the source of infection in 52% (104/200). The majority of patients suffered from Streptococcus pneumoniae (32/200), Haemophilus influenzae (22/200), and Moraxella catarrhalis (16/200). Twenty-two patients were infected with two or more pathogens. All cases of atypical pneumonia (n = 6) were found in CAP patients. Linear regression determined the severity of pneumonia was associated with age (p < 0.001), length of stay (p = 0.002) and male sex (p < 0.001), and preexisting conditions such as chronic heart failure (p < 0.001), COPD (p = 0.030) and lung cancer (p = 0.006). Use of systemic steroids, chemotheraphy and antibiotics 6 weeks prior to pneumonia diagnosis, had no effect on severity of pneumonia. CAP patients were admitted more frequently during the winter months, while NHCP patients were more frequently admitted during all other seasons. No seasonal patterns were distinguished for individual pathogens.

Conclusions: The pathogens affecting CAP and NHCP patients were not significantly different. However, a basic understanding of pathogens commonly found within the community can provide accurate diagnostics and therapeutic solutions for physicians.

THE EVALUATION OF COAGULATION PARAMETERS FOR ASSESSING SEVERITY OF COMMUNITY-ACQUIRED PNEUMONIA

Y. ZHAO, W. CHONG
The first hospital of China Medical University, Emergency, Shenyang, China

Background and Aims: Community Acquired Pneumonia (CAP) is a common infection in patients visiting the Emergency Department (ED). Emergency physicians are continually searching for convenient tools to aid them in clinical decisions. Traditional diagnostic models and biomarkers are often clinically limited and inconvenient. Coagulation disorders are usually present in severe pneumonia. The relationship between coagulation parameters of patients with CAP upon their arrival at ED was evaluated in this study.

Methods: A total of 97 ED patients with CAP were recruited in this retrospective study. Patients were divided into high/medium risk group (Meds score ≥8) and low risk group (Meds score <8), as well as hospital survivor group and non-survivor group. Serum samples conducted upon the patients’ arrival at ED were compared respectively. The significant factors were put into the logistic regression model to determine the independent risk factors for the high/medium risk group and the hospital non-survivor group. Moreover, receiver operating characteristic (ROC) curves were drawn to assess the predictive value of these factors.

Results: Compared with the low risk group, the high/medium risk group had a significantly higher value on mortality, age, TBIL, Cr, BUN, BNP, PT, APTT, D-D, INR and lower PLT. Based on the aforementioned univariate analysis, the multivariate analysis demonstrated that age, PLT, BUN, D-D and INR were the independent risk factors. The area under the ROC curve for D-D × INR, D-D, INR and age and BUN was 0.692, 0.686, 0.619, 0.611 and 0.602 respectively. Similarly, when compared with the hospital survivor group, non-survivor group had a significantly higher value on Cr, PT, INR and D-D. The multivariate analysis showed that D-D and INR were the independent risk factors. The areas under the ROC curve for D-D × INR, INR and D-D were all >0.7.

Conclusions: D-D and INR are reliable and convenient coagulation parameters for assessing the severity of CAP in ED.

LONG-TERM PREDICTORS OF DEATH FROM PNEUMONIA IN A GENERAL JAPANESE POPULATION: NIPPON DATA80

M. NGUYEN,1 H. ARIMA,2 K. MIURA,1 Y. NAKANO,3 A. KADOTA,1 A. FUJIIYOSHI,4 S. TANAKA,5 N. TAKASHIMA,6 T. HAYAKAWA,6 Y. KITA,7 T. OKAMURA,8 R.D. ABBOTT,1 A. OKAYAMA9, H. UEISHIMA1
1Shiga University of Medical Science, Center for Epidemiological Research in Asia, Shiga, Japan, 2Fukuoka University, Department of Preventive Medicine and Public Health- Faculty of Medicine, Fukuoka, Japan, 3Shiga University of Medical Science, Division of Respiratory Medicine- Department of Internal Medicine, Shiga, Japan, 4Shiga University of Medical Science, Department of Medical Statistics, Shiga, Japan, 5Fukushima Medical University, Department of Hygiene and Preventive Medicine- School of Medicine, Fukushima, Japan, 6Tsuruga Nursing University, Department of Nursing Science, Fukui, Japan, 7Keio University, Department of Preventive Medicine and Public Health- School of Medicine, Tokyo, Japan, and 8Research Institute of Strategy for Prevention, Research Center for Lifestyle-Related Diseases, Tokyo, Japan

Background and Aims: Pneumonia is a major cause of morbidity and mortality among adults. This study aims to investigate predictors of long-term mortality from pneumonia in a longitudinal study of a representative sample from the general Japanese population.

Methods: Data are from the National Intergrated Project for Prospective Observation of Noncommunicable Disease and its Trend in the Aged 1980-2009 (NIPPON DATAB0). The sample includes 9,462 participants aged ≥30 years from randomly selected areas in Japan. Subjects were followed for up to 29 years. Risk factors investigated were age, sex, body mass index, systolic blood pressure, diabetes, serum albumin, total cholesterol, smoking, drinking, and history of stroke. Effects of risk factors on death from pneumonia were estimated using Cox’s proportional hazards regression models.

Results: During the 29-year period of follow-up, 326 deaths from pneumonia were observed (1.43 per 1,000 person-years of follow-up). There were significant associations of age, sex, diabetes, serum albumin, and smoking status with pneumonia death. Associations remained significant after adjustment for other risk factors. The multivariable-adjusted hazard ratio (HR) for pneumonia death per 10-year increase in age was 5.07 (95% CI 4.42 to 5.83). For serum albumin, a 1 standard deviation increase [3 g/L] was associated with an HR of 0.76 (95% CI 0.66 to 0.86). When compared with the hospital survivors, the HR was 1.38 [95% CI 1.01 to 1.88].

Conclusions: In this long-term prospective study of a general Japanese population sample, age, male sex, diabetes, serum albumin, and current smoker were associated with an increased risk of death due to pneumonia.
ASSOCIATED FACTORS INFLUENCING THE MORTALITY OF INFLUENZA AMONG REFERRED PATIENTS

T. SEWATANOON, A. JUTIVIBOONSUJK
Maharat Nakhonratchasima, Internal Medicine, Nakhonratchasima, Thailand

Background and Aims: Mortality rate in referred patients from primary healthcare to tertiary healthcare due to influenza in our region is high. Factors such as co-morbidities, age or delayed treatment with antiviral relate with mortality. To identify factors which influence the mortality are able to improve referral system and treatment of influenza.

Methods: A descriptive cross-sectional study was conducted among patients with confirmed influenza whom referred to Maharat Nakhonratchasima hospital between October 2014 and March 2015. Demographic, clinical, laboratory, radiological findings, treatment and outcome were collected from medical records. Associated factors influencing the mortality of influenza were assessed by using the Fisher exact test and multiple logistic regression analysis.

Results: There were 52 patients enrolled to the study and 21 (40.4%) of them were dead. There was no significant difference in sex, age and co-morbidities. Duration of treatment in primary healthcare was not different but onset of symptoms until referral in mortality group was longer than survival group (5.2 ± 2.7 vs 3.1 ± 2.5, p = 0.004). All of patients in mortality group were intubated, while 58.1% of patients in other group were intubated. In tertiary healthcare, incidence of HAP or VAP, hypotension within 24 hour and acute kidney injury also increased in mortality group. Multi-variate analysis showed that delayed or do not start treatment with antiviral within 4 days (Adjusted Odds Ratio = 26.0, 95% CI: 2.1 to 319.2) and acute kidney injury after admission in tertiary healthcare (Adjusted Odds Ratio = 92.7, 95% CI: 7.0 to 1,223.4) significantly related to mortality.

Conclusions: Delayed or do not receive antiviral treatment within 4 days and acute kidney injury after admission in tertiary healthcare influenced the mortality of influenza among referred patients. Accordingly, early start antiviral in patients with influenza-like symptoms and prevention of acute kidney injury may help reduce the mortality of influenza.

INTRAPLEURAL STREPTOKINASE AS A BIBRONYCTIC IN PARAPNEUMONIC EFFUSIONS

N. MOHD JAFAFAR,1 K.N. MOHD HIRMIZ,2 L.D. ZAINUDIN,2 M.A. MOHD ZIM,2 A.I. ISMAIL2, M.F. ABDUL RANI1
1SELEYANG HOSPITAL, MEDICINE, SELANGOR, Malaysia, and 2Universiti Teknologi MARA, Respiratory Unit, Selangor, Malaysia

Background and Aims: Parapneumonic effusions are common, which if not treated properly can lead to serious morbidity and mortality. They can be influenced by treatment delay and delay in referral system to tertiary care. The aim of this study is to explore the relationship between the expression of human IFN-1 and respiratory tract pathogen macrolide resistance.

Methods: We report our experience in using intrapleural streptokinase for complicated parapneumonic effusions.

Results: Five patients with multi-loculated pleural effusion were selected. The presence of multi-loculated effusion was initially detected via bedside ultrasound, further confirmed via formal ultrasound, followed by insertion of a pigtail chest tube. Broad-spectrum antibiotics were started. The chest tubes were initially flushed with 20 ml of normal saline regularly (3–4 times/day) for a period of 3–5 days. The amount of pleural fluid drained after normal saline flushes were variable but generally less than 100 ml/day. The CXRs did not show significant improvement. Intra-pleural streptokinase was then instilled at the dosage of either 2.5 or 1.5 megau-nits. Chest tubes were then clamped for 3 hours. The amount of pleural fluid drained post streptokinase increased significantly to more than 200 ml/day on average.

Conclusions: Overall we conclude that in our limited experience of intra-pleural streptokinase use in multi-loculated effusion, we found that it was efficacious and is relatively safe.

TESTING OF MUTATION IN BORDETELLA PERTUSSIS TO EVALUATE RESISTANCE TO MACROLIDE IN OKINAWA, JAPAN

S. NAHIR, T. KINJO, G. PARROTT, D. NABEYA, J. FUJITA
Graduate School Of Medicine- University of the Ryukyus, Department of Infectious Diseases- Respiratory- and Digestive Medicine, Okinawa, Japan

Background and Aims: Resistant strains of B. pertussis to macrolide have been reported in several countries such as US, Taiwan, and China. Nowadays, it has become more prevalent in China. As China and Taiwan is closer to Okinawa, we intended to evaluate the macrolide resistant strain of Bordetella pertussis in Okinawa. Several studies have proven that macrolide resistance to B. pertussis strain is caused by transition mutation at position 2047 (A to G) of Sanger Center sequence of B. pertussis 23S rRNA gene (binding site of macrolide in bacteria). In this study, we aimed to identify mutational change at that position of B. pertussis isolates.

Methods: From 2012 to 2016, 7 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 targeted to 23S ribosomal RNA gene followed by sequencing of amplified product was performed in 5 samples showing 521 bp PCR product generated with primers 1970U and 2408L among 7 samples 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 x68323), no mutation at nucleotide base position 2047 (A to G) of the 23S ribosomal RNA gene was detected in any strains.

Conclusions: Although no evidence of mutation at A2047G position was found in the strains tested from Okinawa, monitoring of antimicrobial resistance is necessary to evaluate the individual treatment failure.

THE STUDY OF RELATIONSHIP BETWEEN THE EXPRESSION OF IFN-1 AND RESPIRATORY TRACT PATHOGEN

Z. LILI, L. SHUPING, H. XIAN
Hunan Provincial People’s Hospital, Pediatric center, changsha, China

Background and Aims: Respiratory tract infection is one of the serious diseases that threaten the health of children in the world. The virus is an important pathogen of respiratory infection, but lack of effective treatment. IFN-1 is proven to play a positive role in antiviral activity. This study to explore the relationship between the expression of human IFN-1 and respiratory tract pathogen and provide basic data and scientific basis for developing new treatments of children respiratory tract viral infection.

Methods: 1. The children nasopharyngeal swab were collected in The First People Hospital of Chenzhou from July 2013 to June 2014. The nasopharyngeal swabs samples were total 489, and health children nasopharyngeal swabs were 244.

2. The IFN-1 mRNA and GAPDH mRNA in samples were detected using Real-time PCR method. In the same time, these batch specimens were screened with common respiratory tract pathogen including 18 kinds of respiratory virus and 11 kinds of bacteria.

Results: 1. The expression level of IFN-1 mRNA in respiratory tract infections group was significantly higher than those in the control group, (t=2.276 P = 0.027).

2. The IFN-1 mRNA of cases who with RSV infection was significantly higher than control group(t = 2.25 P = 0.026). There were no difference between IFN-1 expression level and RSV copies(r = 0.12 P = 0.41).

3. There was significantly difference of IFN-1 mRNA level between the infection specimens with HRV infection (t = 2.8 P = 0.015). 

4. There was significantly difference of IFN-1 expression level between RSV infection specimens and HRV infection specimens(t = 2.19 P = 0.045).

5. Compared with the normal group, there was no difference of IFN-1 expression level in bacterial infection cases (t=0.17 P = 0.87).

Conclusions: 1. It was proved that IFN-1 was involved in the pathogenesis of respiratory infections.

2. RSV can induce the mRNA expression of IFN-1 and stronger than HRV.

3. Respiratory tract bacterial infection may have no obvious effect on mRNA expression of IFN-1.

Respirology (2016) 21 (Suppl. 3), 2–213 © 2016 Asian Pacific Society of Respirology
Background and Aims: Idiopathic pulmonary fibrosis (IPF) is the major and complicated respiratory disease, with multi-factors for clinical outcome; indicators, and pathology reported outcome (PRO) instrument is an important component of IPF clinical effect evaluation. However, IPF assessment tools lack of China’s cultural background and elements, especially lack of reflecting the advantages of the combination of disease and syndrome theory at present. This manuscript aims to put forward and construct the multidimensional conceptual framework for specific PRO.

Methods: According to the concept of quality of life, intensity of patient-reported outcome, characteristics of idiopathic pulmonary fibrosis, notion of holism and humanism and standard and method for scale development internationally, summarize and concise the traditional Chinese medicine concept of lung, especially ancient and modern literatures for IPF. Then propose theoretical model and the conceptual framework based on the combination of disease and syndrome theory, and next selecting and establishing the item bank.

Results: The multidimensional conceptual framework includes physiology domain, psychology domain, environment domain, society domain and satisfaction domain. The physiology domain has aspects: main symptoms, accompanied by other symptoms and its influencing factors; activity, the effects of illness on daily life, diet, sleep, urine and excrement, cold and disease prevention. Depression, anxiety, and mood swings are the aspects of psychology domain. The environment domain with eight aspects: season, day and night, geographic area, air pollution, physical and chemical pollution, indoor environment pollution, poor ventilation, and abnormal stimulus. Social relations, social support, disease burden, medical payments style and health education are the aspects of society domain. The satisfaction domain includes improvement satisfaction, disease understanding satisfaction and psychological improvement satisfaction, treatment convenient satisfaction and seek medical advice satisfaction.

Conclusions: The conceptual framework provide theoretical basis for the development of therapeutic evaluation tool for IPF-PROs.

A RARE CASE OF PULMONARY ALVEOLAR PROTEINOSIS

C. Bunpaul, V. Im, S. Chan

Background and Aims: Pulmonary alveolar proteinosis (PAP) is a rare lung disorder of unknown etiology characterized by alveolar filling with floccular material that stains positive using the periodic acid-Schiff (PAS) method and is derived from surfactant phospholipids and protein components. PAP was first described in 1958. Auto-immune PAP represents 90% of all PAP cases. Symptoms are not specific. The diagnosis of pulmonary alveolar proteinosis can be made with confidence on the basis of the appearance of the lung on the HRCT scan of the thorax in conjunction with an examination of lavage fluid obtained from segmental alveolar lavage.

Methods: We reported a rare case of Pulmonary Alveolar Proteinosis (PAP).

Results: A 17 year-old-girl has been admitted for progressive shortness of breath since many months. She has been treated with different kinds of antibiotics including anti-tuberculose drugs without any improvement. She has reported that her two sisters died of respiratory disease of unknown origin. CXR: diffuse interstitial patchy. Chest-Scan: smooth thickening of interlobular and intra-lobular septal lines, and ground glass opacities (crazy paving pattern).

We performed a fiberoptic bronchoscopy and obtain bronchoalveolar lavage (BAL) fluid with an opaque, milky appearance. Histology exam showed a presence of periodic acid-Schiff (PAS) staining of bronchoalveolar lavage (BAL) fluid. Bronchoalveolar (whole lung) lavage remains the treatment of choice.

ORAL PRESENTATION 7 - CLINICAL ALLERGY AND IMMUNOLOGY + INTERSTITIAL LUNG DISEASE: INTERSTITIAL LUNG DISEASE REVISITED

PRELIMINARY CONSTRUCTION OF CONCEPTUAL FRAMEWORK FOR IDIOPATHIC PULMONARY FIBROSIS PATIENT REPORTED OUTCOME SCALE BASED ON THE COMBINATION OF DISEASE AND SYNDROME THEORY

Y. Xie, J. Wang, H. Zhao, H. Li, J. Li

The first affiliated hospital of Henan University of TCM, Department of Respiratory, Zhengzhou, China, and 2Henan University of Traditional Chinese Medicine, Collaborative Innovation Center for Respiratory Disease Diagnosis and Treatment & Chinese Medicine Development of Henan Province, Zhengzhou, China

Background and Aims: Idiopathic pulmonary fibrosis (IPF) is the major and complicated respiratory disease, with multi-factors for clinical outcome indicators, and pathology reported outcome (PRO) instrument is an important component of IPF clinical effect evaluation. However, IPF assessment tools lack of China’s cultural background and elements, especially lack of reflecting the advantages of the combination of disease and syndrome theory at present. This manuscript aims to put forward and construct the multidimensional conceptual framework for specific PRO.

Methods: According to the concept of quality of life, intensity of patient-reported outcome, characteristics of idiopathic pulmonary fibrosis, notion of holism and humanism and standard and method for scale development internationally, summarize and concise the traditional Chinese medicine concept of lung, especially ancient and modern literatures for IPF. Then propose theoretical model and the conceptual framework based on the combination of disease and syndrome theory, and next selecting and establishing the item bank.

Results: The multidimensional conceptual framework includes physiology domain, psychology domain, environment domain, society domain and satisfaction domain. The physiology domain has aspects: main symptoms, accompanied by other symptoms and its influencing factors; activity, the effects of illness on daily life, diet, sleep, urine and excrement, cold and disease prevention. Depression, anxiety, and mood swings are the aspects of psychology domain. The environment domain with eight aspects: season, day and night, geographic area, air pollution, physical and chemical pollution, indoor environment pollution, poor ventilation, and abnormal stimulus. Social relations, social support, disease burden, medical payments style and health education are the aspects of society domain. The satisfaction domain includes improvement satisfaction, disease understanding satisfaction and psychological improvement satisfaction, treatment convenient satisfaction and seek medical advice satisfaction.

Conclusions: The conceptual framework provide theoretical basis for the development of therapeutic evaluation tool for IPF-PROs.

IDIOPATHIC INTERSTITIAL PNEUMONIAS: THE ROLES OF SERIAL MULTIDISCIPLINARY DISCUSSIONS

Y. Indue, M. Kitachi, M. Akira, T. Johko, A. Hebisawa, I. Yamadori, T. Arai, C. Sugimoto, A. Matsumuro, J. Hirose, K. Tachibana, T. Kasai, W. Wallace, D. Hansell, W. Travis

1National Hospital Organization Kinki-Chuo Chest Medical Center, Clinical Research Center, Osaka, Japan, 2National Hospital Organization Minami Wakayama Medical Center, Pathology, Wakayama, Japan, 3Kinki Central Hospital, Radiology, Hyogo, Japan, 4National Hospital Organization Tokuo National Hospital, Pathology, Tokyo, Japan, 5Fukuyama Medical Association, Clinical Pathology Center, Hiroshima, Japan, 6David Geffen School of Medicine at UCLA, pathology, Los Angeles, USA, 7Royal Brompton Hospital, radiology, London, United Kingdom, and 8Memorial Sloan Kettering Cancer Center, Pathology, New York, USA

Background and Aims: Classification and diagnostic criteria of Idiopathic Interstitial Pneumonias (IIPs) was stated in 2002 by ATS/ERS. In 2013, the classification was updated and “Disease behavior” of IIPs was introduced. In addition, clinics; radiological and pathological diagnosis and the multidisciplinary discussion (MDD) has been emphasized for the diagnosis of IIPs. We have registered the biopsy proven IIPs and followed up 5 years. In this cohort, we performed MDD during the follow-upperiod. The aims of this study is to clarify the role of MDD and disease behavior.

Methods: Patients with IIPs from 33 Japanese hospitals were retrospectively registered and prospectively annually followed for 5 years. The clinical data, prognosis, high resolution CT, pathological slides were re-evaluated. The diagnosis of local hospital (Local diagnosis), was compared with the diagnosis of the MDD in 2012 and 2013 (MDD2012-2013). All cases were re-evaluated in 2014 and 2015 (MDD2014-2015) again. The diagnostic criteria was based on the criteria of ATS/ERS 2002, ATS/ERS/JURS/ALAT 2011, and ATS/ERS 2013.

Results: 181 cases with biopsy proven IIPs were registered. By the first MDD (MDD2012-2013), 5 cases were excluded from IIPs. The number of IIP, idiopathic non-specific interstitial pneumonia (NSIP), and unclassifiable IIP (UIIP) were changed from 70 (Local Diagnosis) to 77 (MDD), from 68 to 48, and from 27 to 40 respectively. By the second MDD (MDD2014-2015), additional 13 cases were excluded. The number of IPF, NSIP, and UIIP were changed from 77 to 78, from 48 to 48, and from 40 to 24 respectively. There was not significant difference between the survival of IPF, NSIP, and UIIP using the “Local diagnosis” by Kaplan-Meier analysis, but there was significant difference using “MDD2012-2013”, and “MDD2014-2015” (p < 0.05).

Conclusions: MDD is necessary for the better diagnosis of IIPs. Re-evaluation by serial MDD with more time axis information of disease behavior may serve the theoretical diagnosis.

© 2016 Asian Pacific Society of Respirology Respirology (2016) 21 (Suppl. 3), 3–213
PREDICTION OF THE EXACERBATION OF INTERSTITIAL PNEUMONITIS DURING CHEMORADIOTHERAPY BY PET-CT AT THE DIAGNOSIS OF LUNG CANCER

H. OHNISHI, M. TAKAOKA, S. AKITA, M. SAKAI, T. KUBOTA, A. YOKOYAMA
Kochi University- Kochi Medical School, Department of Hematology and Respiratory Medicine, Nankok, Japan

Background and Aims: The uptake of 18 F-fluorodeoxy glucose (FDG) to active inflammatory lung lesions on positron emission tomography-computed tomography (PET-CT) was reported in patients with radiation pneumonitis, drug-induced pneumonitis, and sarcoidosis. The aim of this study was to evaluate whether FDG uptake in lungs without cancerous lesions on PET-CT at the diagnosis of lung cancer predicts for the development of interstitial lung diseases (ILD) including drug-induced pneumonitis, radiation pneumonitis, and/or exacerbation of preexisting ILD during lung cancer treatment.

Methods: The PET-CT scan and medical records of 277 patients with primary lung cancer, who were diagnosed and treated with chemotherapy and/or radiation therapy at the Kochi University Hospital, was retrospectively analyzed.

Results: Thirty-five patients complicated with preexisting ILD. The development or exacerbation of ILD during lung cancer treatment was significantly higher in patients complicated with preexisting ILD than patients without ILD (20.0% vs 7.4%, p = 0.025). The exacerbation or development of ILD in patients received chemoradiation therapy (n = 59) was significantly higher in patients with obvious FDG uptake to preexisting ILD than patients without FDG uptake to preexisting ILD or patients without ILD (80%, 50%, 21.2%, respectively, p = 0.014). The incidence of ILD was not different among these 3 groups in patients received chemotherapy alone (n = 216) (0%, 9.1%, 3.7%, respectively, p = 0.437).

Conclusions: The FDG uptake to preexisting ILD on PET-CT at the diagnosis of lung cancer is associated with the exacerbation of ILD during chemoradiation therapy.

SURFACTANT PROTEIN-D LEVEL AS A PREDICTOR OF PROGNOSIS OF INTERSTITIAL LUNG DISEASE INDUCED BY ANTICANCER AGENTS IN ADVANCED LUNG CANCER

M. KATO, S. SASAKI, T. SHUKUYA, K. NAKAMURA, Y. SEKIMOTO, T. HIIRA, R. SHIBAYAMA, R. KOYAMA, N. SHIMADA, O. NAGASHIMA, F. TAKAHASHI, S. TOMINAGA, K. TAKAHASHI
1Juntendo University Graduate School of Medicine, Department of Respiratory Medicine, Bunkyo-ku, Japan, and 2Juntendo University Urayasu Hospital, Department of Respiratory Medicine, Urayasu, Japan

Background and Aims: Intersitial lung diseases induced by anticancer agents (ILD-AA) are known to be a rare adverse effect of anti-cancer therapy. However, predictive prognostic fibrotic biomarkers of ILD-AA have not been identified in patients with advanced lung cancer (ALC). Our aim is to analyze the association between serum fibrotic biomarkers, including KL-6 and surfactant protein D (SP-D), onset and types of ILD-AA by chest high resolution computed tomography (HRCT) findings in ALC patients.

Methods: KL-6 and SP-D were defined as follows: the values of KL-6 and SP-D level at the onset of ILD-AA - KL-6 and SP-D level prior to ILD-AA, respectively. Then, patient’s data, including ΔKL-6, ΔSP-D, ILD-AA patterns on chest HRCT, and outcome in ALC patients were retrospectively collected and were evaluated.

Results: Thirty-five patients diagnosed with ILD-AA at 2 hospitals from April 2011 to January 2016 were enrolled in this study. Of these patients, 13 died of ILD-AA. ΔSP-D in the deceased patients was significantly higher than that in the surviving patients (p < 0.001). However, ΔKL-6 was not significantly different between the two groups. Moreover, these patients were further classified into 4 categories based on chest HRCT findings: organized pneumonia (9 patients), diffuse alveolar damage (DAD) (15), chronic interstitial pneumonia (7), and hypersensitivity pneumonia (5). ΔSP-D was significantly higher in DAD than in other types (p < 0.001). Additionally, ΔKL-6 was not significantly different among the ILD-AA types. Multivariate analysis revealed that ΔSP-D was a significant prognostic risk factor of ILD-AA (p = 0.03).

Conclusions: These findings suggested that ΔSP-D was only significantly associated with ILD-AA outcome and HRCT findings. ΔSP-D might be a predictive prognostic biomarker of ILD-AA in ALC patients.

INTER-OBSERVER AGREEMENT OF USUAL INTERSTITIAL PNEUMONIA DIAGNOSIS CORRELATED WITH PATIENT OUTCOME

M. HASHISAKO, T. TANAKA, Y. TERAOKU, T. UEKUSA, R.D. ADCHAR, B.I. ASWAD, H.S. BAMELEH, V.L. CAPELOZZI, J.C. ENGLISH, A.T. FABRO, K. KATAOKA, T. HAYASHI, Y. KONDOH, H. TANIGUCHI, J. FUKUOKA
1Nagasaki University Hospital, Department of Pathology, Nagasaki, Japan, 2Kindai University Faculty of Medicine, Department of Pathology, Osaka, Japan, 3Nippon Medical School, Department of Analytic Human Pathology, Tokyo, Japan, 4Kanto Rosai Hospital, Department of Pathology, Kanagawa, Japan, 5National Jewish Health, Division of Pathology, Colorado, USA, 6Rhode Island Hospital and Warren Alpert School of Medicine at Brown University, Department of Pathology, Rhode Island, USA, 7King Abdullah Medical City, Department of Pathology and Laboratory Medicine, Riyadh, Kingdom of Saudi Arabia, 8University of São Paulo, Faculty of Medicine, São Paulo, Brazil, 9Vancouver General Hospital, Department of Pathology, British Columbia, Canada, 10University of São Paulo, Department of Pathology, São Paulo, Brazil, 11Tosei General Hospital, Department of Respiratory Medicine and Allergy, Aichi, Japan, and 12Nagasaki Prefecture Shimbara Hospital, Department of Pathology, Nagasaki, Japan

Background and Aims: The low reproducibility of histopathological diagnosis for IPF among pathologists has been reported as a matter of grave concern. Although the histopathological criteria for IPF were revised by the ATS/ERS/JRS/ALAT in 2011, the evidence of IPF diagnosis based on the guidelines needs further investigation. We examined whether the revised histopathological criteria for IPF improved inter-observer agreement among pathologists and predicted prognosis in patients with interstitial pneumonia (IP).

Methods: 20 consecutive surgical lung biopsy specimens from cases of IP were examined for histological patterns by 11 pathologists without knowledge of clinical and radiological data. Diagnosis was based on consensus guidelines of 2002 and 2011. Pathologists were grouped by cluster analysis, and inter-observer agreement and association to the patient prognosis were compared with the diagnoses for each cluster.

Results: The generalized k coefficient of diagnosis for all pathologists was 0.23. If the diagnoses were divided into 2 groups: UIP/probable UIP (UIP group) or possible/not UIP (non-UIP group) according to the 2011 guidelines, k improved to 0.37 (Table 1). The pathologists were subdivided into 2 clusters (Figure 1) in which 1 showed an association between UIP group diagnosis and patient prognosis (P < .01) (Figure 2).

Conclusions: Inter-observer agreement of pathological diagnosis for IP after 2011 guidelines is still low, however minor modification to simplify the classification into two groups, UIP and non-UIP may provide a preferable approach to standardize pathological diagnosis. The cluster analysis may suggest the direction of standardization for IPF diagnosis.

Acknowledgements: This study was partly funded by the study group on Diffuse Pulmonary Disorders, Scientific Research/Research on intractable diseases from the Ministry of Health, Labour and Welfare of Japan.
SHORT-TERM SAFETY OF NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

J. SAIJ,1 M. OKAMOTO,2 S. MATSUZAWA,3 B. OYAMA,2 R. ONOE,2 K. KARINUMA,2 S. AZAGAMI,4 H. MURAOKA,4 K. MORIKAWA,5 M. TAKEMURA,5 T. INOUE,5 H. KIDA,5 N. FURUYA,5 H. HANDA,5 H. NISHINE,5 A. ISHIDA,5 T. INOUE,5 T. MIYAZAWA,5 M. MINESHIITA2

1Kawasaki Municipal Tama Hospital, Division of Respiratory Disease-Department of Internal Medicine, Kawasaki, Japan, and 2St. Marianne University, Division of Respiratory Disease-Department of Internal Medicine, Kanagawa, Japan

Background and Aims: Nintedanib, an intracellular inhibitor of tyrosine kinases, was approved for the treatment of idiopathic pulmonary fibrosis (IPF). According to a previous report, nintedanib reduced the decline of FVC, which is consistent with a slowing of IPF progression. The rates of severe adverse events were 29.8-31.1% over a 52-week treatment period. The most frequent adverse event was diarrhea (61.5-63.2%) and 5% of patients discontinued therapy. The aim of this study is to evaluate the short-term safety of nintedanib in patients with IPF in Japan.

Methods: We investigated short-term adverse events of nintedanib, 150 mg twice daily, using the Common Terminology Criteria for Adverse Events (CTCAE) Ver. 4, in patients with IPF. Patients were enrolled consecutively at two institutions, and were observed over a 4-week period.

Results: Twenty patients were enrolled in this study. Six patients on home oxygen therapy, 6 patients had a history of acute exacerbations sequentially at two institutions, and were observed over a 4-week period.

Events (CTCAE) Ver. 4, in patients with IPF. Patients were enrolled consecutively at two institutions, and were observed over a 4-week period.

Conclusions: There was no incidence of acute exacerbation. There was no incidence of acute exacerbation.

THE CUT OFF VALUE OF SERUM KL-6 LEVEL FOR DISCRIMINATION OF AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS AND INTERSTITIAL PNEUMONIA

E. YAMAGUCHI, A. TAKAHASHI, N. YOKOE, K. KOSAKA, A. MATSUBARA, M. NISHIMURA, H. TANAKA, A. KUBO

Aichi Medical University School of Medicine, Internal Medicine - Division of Respiratory Medicine and Allergology, Nagakute, Japan

Background and Aims: Krebs von den Lungen-6 (KL-6) is sialylated carbohydrate and a typical serum marker of interstitial pneumonia (IP). Serum levels of KL-6 are also markedly increased in pulmonary alveolar proteinosis (PAP). Both diseases have similar radiologic features such as ground glass opacities and reticular patterns in CT images leading to occasional misdiagnosis of PAP as IPs. The diagnosis of PAP in adult patients is usually made by bronchoalveolar lavage (BAL) and verification of anti-GM-CSF autoantibody in serum. We attempted to determine the appropriate cut off value of KL-6 which can reliably suggest PAP more than IPs, thus indicating the necessity of BAL and measurement of autoantibodies.

Methods: Study subjects included 39 patients with autoimmune PAP (PAP) and 97 with miscellaneous types of interstitial pneumonia. Patients with PAP had milky-white BAL fluid and/or biopsy findings compatible PAP along with an increased level of autoantibody in serum. Patients with IPs had compatible CT findings according to ATS/ERS 2013 classification of IIPs. Coincidence of PAP in IP patients was excluded by BAL and/or transbronchial biopsy. Serum levels of KL-6 were measured by the Electro-chemiluminescence immunoassay. The difference in KL-6 levels were evaluated by the Mann–Whitney U test. Cut off values were determined using receiver operating characteristics curves and Youden index.

Results: Serum KL-6 levels in patients with APAP and IPs were 4850 (median) [range, 304–39740] U/mL and 791 [160–5542] U/mL, respectively. Patients with APAP had significantly higher serum KL-6 levels than those with IPs (1.2E–13). The cut off value useful for differential diagnosis of APAP from IPs was estimated to be 1850 U/mL of KL-6 level with 92% sensitivity and 84% specificity.

Conclusions: Patients with a serum KL-6 level more than 1850 U/mL should be scrutinized for the possibility of APAP, which may lead to avoidance of unnecessary administration of immunosuppressive agents such as corticosteroids.

ORAL PRESENTATION 8 - PEDIATRIC LUNG DISEASE + PULMONARY CIRCULATION: LUNG DISEASE IN CHILDREN

L. LIU, L. QIAN, Z. XIAOBO

Children’s Hospital of Fudan University, Department of Respiratory Medicine, Shanghai, China

Background and Aims: Infants hospitalized with viral lower respiratory tract infections are prone to subsequent wheezing and asthma. Asthma prevalence is considerably rising in Chinese children. However, there are few studies about clinical characteristics and lung function in infants with acute lower respiratory tract infections (ALRIs) induced wheezing in China.

Methods: A review of the medical records of infants under one year of age with ALRIs during one-year was conducted. The infants were classified into wheezing and non-wheezing groups. Subjects were followed up by questionnaires at 6 and 12 months after discharge. Measurements of lung function were performed during the initial hospital admission and at 6 months after discharge.

Results: A total of 1726 infants with ALRIs were admitted, and 471 (27.3%) had a wheezing episode. The majority (262/471, 55.6%) of infants with wheezing were reported having a family history of atopy. The total detection rate of viruses (73.7%) and respiratory syncytial virus (RSV, 68.6%) in wheezing group were higher than those of non-wheezing group (both p <0.001). The wheezing group had lower TiPTE/TE and VPTEF/VE compared to the non-wheezing group, especially for those under 6 months. After 6 months, the wheezing group still had normal lung function. Patients with wheezing were more likely to develop subsequent wheezing and atopic dermatitis during the following year (both p <0.05).

Conclusions: Wheezing in infants with ALRIs is related to the infection of viruses, especially to RSV. Hospitalization for wheezing ALRIs is associated with impaired lung function and a higher frequency of subsequent wheezing and atopic dermatitis.
A NOVEL SURFACANT PROTEIN C MUTATION RESULTING IN ABDERRANT PROTEIN PROCESSING AND ALTERED SUBCELLULAR LOCALIZATION CAUSES PEDIATRIC INTERSTITIAL LUNG DISEASE

L. LIU, D. HONG, Y. QI, H. WANG, J. LIU, L. QIAN
Children’s Hospital of Fudan University, respiration, Shanghai, China, and Children’s Hospital of Fudan University, molecular genetics laboratory, Shanghai, China

Background and Aims: Genetic defects of surfactant metabolism are known causes of pediatric lung disease. Mutations in the surfactant protein C gene (SFTPC) result in sporadic and familial interstitial lung disease (ILD). Identification of novel mutations in SFTPC as well as its related functional study are crucial in definite diagnosis of such ILD patients and development of future therapy. Our objective was to report a novel SFTPC mutation in a Chinese infant with ILD and evaluate the effect of this mutant on protein synthesis.

Methods: The patient presented chronic cough and dependence on supplemental oxygen from first month of life. Chest HRCT showed bilateral ground-glass opacity and interstitial changes. Genomic DNA was extracted from whole blood and candidate genes associated with ILD were sequenced by next-generation sequencing. The variant was validated by Sanger sequencing. Subclones of wild-type and mutant SFTPC were sequenced by next-generation sequencing. The variant was validated by Sanger sequencing. Subclones of wild-type and mutant SFTPC were generated and transiently transfected into A549 cells. In vitro expression of SP-C was evaluated by Western blotting. Ultrastructure of A549 cells was examined by transmission electron microscopy. Intracellular localization of mutant SP-C was analyzed by immunofluorescence.

Results: A novel heterozygous mutation SFTPC: c.337T > C, p.Y113H was identified in this ILD infant. The variant was not found in the 1000 genomes or ExAC and predicted to be harmful or disease-causing by MutationTaster, Ployphen2 and SIFT respectively. The amino acid was highly conserved across species. Neither of the parents carries this mutation. The amino acid was highly conserved across species.

Conclusions: We detected a novel mutation in SFTPC causing ILD in infancy. The Y113H mutation results in aberrant proSP-C processing and altered subcellular localization which ultimately leads to pulmonary dysfunction.

RESPIRATORY FEATURES OF CHILDREN WITH ANTINEUTROPHIL CYTOLAMIC ANTIBODY-ASSOCIATED VASCULITIS

X. ZHANG, C. ZHANG, W. LIBO
Children’s Hospital of Fudan University, Respiratory Department, Shanghai, China

Background and Aims: To analyze the clinical, laboratory and radiologic features of respiratory system among children with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: 12 children with AAV who were hospitalized from 2005 to 2016 in our hospital were retrospectively reviewed.

Results: Of the 12 children, 9 were girls and 3 were boys with a mean age of 10.35 years. 11 children were categorized as microscopic polyangiitis (MPA). The time to diagnosis varied from 1 to 48 months, mean time 8 months. Lung involvement was present in 10 cases at diagnosis, and respiratory signs in 2 cases during the follow-up of 1–62 months. Symptoms included nasal obstruction and discharge (n = 2); sore throat (n = 1); cough (n = 4); sputum (n = 4); hemoptysis (n = 4), including 1 case of MPA secondary to IVU; dyspnea (n = 4); chest pain (n = 2); wheezing (n = 1); fever (n = 10); dizziness (n = 5); anemia and renal involvement (n = 12). Of serum immunological markers, CANCA positive (n = 1); PR3 positive (n = 2); PANCA positive (n = 7); MPO positive (n = 11). Imaging manifestations were various: exudative patchy and mass (n = 8); ground-glass opacity (n = 4); follicular shadow (n = 1); fine particles (n = 1); fine grid opacities (n = 2); cystic lucency shadow (n = 3); nodules (n = 2). Pulmonary function tests may have a reduced small airway function, restricted lesions and mixed lesions, et al.

Conclusions: The clinical manifestations were varied and lack of specificity. More attention should be paid to AAV among school age girls with anemia or pulmonary diseases, and proposed early examination of ANCA and urine routine, renal function. Children with hyperthyroidism should be alert to AAV.

SUDDEN ONSET OF TACHYPNEA IN A NEWBORN: A THERAPEUTIC DILEMMA

W. ENRIQUEZ
Cebu City, Philippines

Background and Aims: Persistent Pulmonary Hypertension of the Newborn (PPHN) is a syndrome of failed circulatory adaptation secondary to delayed relaxation of the pulmonary vasculature associated with diverse clinical pulmonary pathology seen in 1/500-1,500 live births. We report herein our experience in managing PPHN without advanced technologies such as Extracorporeal Cutaneous Membrane Oxygenation and Nitric Oxide.

Results: We present a case of BGB, delivered term via primary caesarean section secondary to placenta previa totalis, to a 27 year old, G1P1 mother with an APGAR score 9, 9, ballards Score 39 weeks, birthweight 3,200 grams, appropriate for gestational age. She was observed to be tachypneic during the initial hours of life with noted desaturatation. Monitoring was done, but tachypnea persisted. Oxygen inhalation was given and work up was done. Chest radiograph revealed Pneumonia and Pneumothorax with ABG showing respiratory acidosis. Antibiotics and nitrogen washout were instituted. Despite these, tachypnea persisted. Repeat chest radiograph revealed clearing of Pneumonia and disappearance of Pneumothorax, however, repeat ABG showed persistent respiratory acidosis. 2D echocardiography was then done, revealing pulmonary arterial pressure of 80mmhg confirming PPHN. The cornerstone management which includes oxygenation, vasodilatation, and alkalination, were instituted.

Endotracheal intubation with sedation using Midazolam and Fentanyl was done. Milrinone (nondiactor), iloprost (prostacyclin analog), Milizalomal (Benzoazepine), Magnesium Sulfate (pulmonary vasodilator), Sildenafil (phosphodiesterase inhibitor) were given, as well as Sodium Bicarbonate, Dobutamine (intrave), and Surfactant (phospholipidprotein). After 1–2 days, significant improvement was noted, and downward spiral decline of PPHN was defied and the patient survived.

Conclusions: Despite unavailability of advanced technology, the “odds” of PPHN can be turned over through prompt recognition, collaboration of various subspecialties with a hint of resourcefulness.
PULMONARY ARTERIAL HYPERTENSION IS ASSOCIATED WITH REDUCED VASCULOGENESIS BUT NOT REMODELLING OR INCREASED VASCULAR REACTIVITY IN A MOUSE MODEL OF BRONCHOPULMONARY DYSPLASIA

J.E. BOURKE, E. LAMANNA, C. BUL, S.G. ROYCE, J. PEARSON, M. KROON, M. NOLD, C. NOLD
Monash University, Biomedicine Discovery Institute- Department of Pharmacology, Clayton, Australia, and Australian National University, Ritchie Centre, Clayton, Australia, and National Cerebral and Cardiovascular Center Research, Department of Cardiac Physiology, Osaka, Japan

Background and Aims: Previous research suggests that reduced vasculogenesis is a key factor in the development of pulmonary arterial hypertension (PAH) in patients with bronchopulmonary dysplasia (BPD). To date, the role of remodelling in BPD-related PAH has been less well-defined. We hypothesised that PAH would develop in mice exposed to perinatal hyperoxia and that this would lead to altered structure and contractile responses of the pulmonary vasculature, consistent with PAH. Methods: Pregnant C57BL/6J dams received 150 μg/kg LPS i.p. at 14d gestation. Within 24h of birth, pups and dams were randomized to normoxic (N) or hyperoxic (H) conditions (FiO2 0.21 or 0.65). At 28d, vascular remodelling was assessed in Masson trichrome and αSMA-stained sections (ImageScope). For analysis of vascular branching, lungs harvested at d60 were soaked in iodine for Synchrotron micro tomography, 3D reconstruction and in silico quantification (Imaris). In separate 28d mice, precision-cut slices were prepared to visualise arterial contraction by phase-contrast microscopy. Results: Hyperoxic mice developed severe BPD-like lung disease with fewer, larger alveoli accompanied by fewer small pulmonary blood vessels. Hyperoxic mice developed severe BPD-like lung disease with fewer, larger alveoli accompanied by fewer small pulmonary blood vessels. There was no difference in sub-endothelial collagen deposition or αSMA in the perivascular smooth muscle bundle of these arteries, compared with normoxic mice. Contraction to endothelin-1 was modest in both groups, and the thromboxane mimetic U46619 elicited contraction with similar maximum % reduction in lumen area (N 48 ± 9%; H 39 ± 4%). Conclusions: Perinatal inflammation and hyperoxia induces dysalveolarisation similar to BPD. We hypothesised that this would also lead to altered structure and contractile responses of the pulmonary vasculature, consistent with PAH.

Pulmonary TB patients with diabetes melitus, pregnancy and patients TB treatment. This study shows that there are significant differences in clinical changes in patient with tuberculosis after intensive phase treatment.

Background and Aims: To analyze the etiology and clinical characteristics of spasmodic cough children with respiratory tract infection in Hunan. Methods: Nasopharyngeal aspirate (NPA)s and Nasopharyngeal swab were collected from 280 spasmodic cough children with respiratory infection in Hunan from January 2015 to December 2015. Respiratory syncytial virus (RSV), human rhinovirus (HRV), Influenza virus A (IFVA), Influenza virus B (IFVB), parainfluenza virus (PIV1-3), Bordetella pertussis (BP), Mycoplasma (MP), Chlamydia pneumoniae (CP), adenovirus (ADV), human coronavirus (HCoV-229E, HCoV-OC43), human Boca virus (HBoV) were detected by Real-time fluorescence polymerase chain reaction (RT-PCR), and bacteria were detected by culture. Then combined with clinical data and through statistical analysis. Results: Among the 280 Nasopharyngeal swab and NPA, pathogen were detected in 219 sample (78.2%), BP (47.9%) was the most common pathogen, followed by RSV (10.4%), MP (6.6%), PIV3 (6.2%), and ADV (7.1%). 141 (64.4%) samples were simple infection, divided them into per-tussis and no-per-tussis groups. There was no significant difference between the two groups in the gender distribution, seasonal distribution, vaccination rate, utilization rate of macrolide (P > 0.05). There was significant difference between the two groups in coughs followed by a vigorous inspiratory and whoop, leucocyte count, Lymphocyte percentage, pulmonary rale, pneumonia image change and spas tic cough after leaving from hospital. Conclusions: BP predominate in the etiology of spasmodic cough children with respiratory tract infection in Hunan, and RSV, MP, HPIV3 and ADV is the main pathogens, compared to other pathogen, caused by Bordetella pertussis (BP) was more prone to coughs followed by a vigorous inspiratory effort, leucocyte count more than 10 × 10⁹/L, Lymphocyte percentage in 60-80%, but less pulmonary rale and Pneumonia image change than the non-pertussis group. These features are helpful in guiding the selection of clinical antibiotics.

ORAL PRESENTATION 9 - TUBERCULOSIS: TUBERCULOSIS AND HOST

INFLUENCES OF HEMOGLOBIN A1C TOWARDS SPUTUM ACID BACILLI SMEAR CONVERSION TIME AND CLINICAL SYMPTOMS IN PATIENTS WITH PULMONARY TUBERCULOSIS

D. WUJAYA, R. RATNAWATI, E. BURHAN
University of Indonesia Faculty of Medicine, Department of Pulmonology and Respiratory Medicine, Jakarta, Indonesia

Background and Aims: Hemoglobin A1c causes increased susceptibility to tuberculosis, as well as clinical symptoms, severity, and response to therapy. This study aims to determine the effect of HbA1c levels toward the treatment in patients with pulmonary tuberculosis new cases without diabetes mellitus at the Community Center for Lung Health (BBKPM) Bandung in 2014. Methods: A prospective cohort study was conducted in June 2014 until November 2014 at BBKPM Bandung. As the inclusion criteria is a new case of pulmonary TB patients aged ≥ 15 years and willing to participate in the study by signing a letter of approval. The exclusion criteria are pulmonary TB patients with diabetes mellitus, pregnancy and patients TB advancement. Results: The total number of subjects were 123 patients, consists of 63 female and 60 male. Patients with HbA1c levels < 6.5% at 111 subjects and levels of > 6.5% by 12 subjects. Subjects with smear positive are 69 and negative AFB as many as 54 subjects. Duration of sputum smear conversion time for more than 2 months were 9.9% while the conversion time for 2 months were 91.1%. Subjects with HbA1c levels > 6.5% were longer obtained sputum smear conversion of more than 2 months (50%) compared to HbA1c levels ≤ 6.5%, only 4.5% and the odds ratio found 21.2, with a confidence interval 0.047. Level of HbA1c did not show significant result in clinical changes after intensive phase treatment. Conclusions: This study shows that there are significant influence of HbA1c levels towards AFB sputum smear conversion in patients with new cases of pulmonary TB in BBKPM Bandung. However level of HbA1c did not show significant difference in clinical changes in patient with tuberculosis after intensive phase treatment.
DETERMINING THE EFFECTIVENESS OF SERUM NEUTROPHIL – LYMPHOCYTE RATIO (NLR) IN PATIENTS WITH PULMONARY TUBERCULOSIS

B.Y.M. SINAGA,1 P. SIAGIAN,1 S. SYAFRIL2, W. RAHARDJO1

Background and Aims: Differentiating pulmonary tuberculosis from the other lung infection is often difficult and challenging, because the microscopical examination from sputum is not sensitive nor specific to diagnose TB. Serum Neutrophil – lymphocyte ratio (NLR) is presumed to have a high discriminative capability to predict bacteria and thus can help to distinguish it from tuberculosis. The aim of this study is to determine the efficacy of serum neutrophil-lymphocyte ratio to diagnose tuberculosis.

Methods: We conducted a descriptive study with case series design from January 2015 to December 2015 in the Adam Malik General Hospital, Medan. From 100 patients with AFb (+) pulmonary TB with X Ray examination suggested for TB, excluding MDR TB, extrapulmonary TB, and patients with comorbid such as diabetes mellitus, HIV, pleural effusion, COPD/asthma, pneumonia, lung cancer, cardiovascular disease during follow up, receiving steroid therapy and antibiotic other than antituberculosis treatment (ATT).

Results: From 100 patients, with the highest neutrophil absolute count was 18.8x10^3/mm^3 an the lowest point was 0.67x10^3/mm^3. The highest lymphocyte absolute count was 31.5x10^3/mm^3 and the lowest point was 0.35x10^3/mm^3. We found that 88% of all TB patients had serum Neutrophil-Lymphocyte ratio below 7, and 12% had serum NLR above 7.

Conclusions: The serum NLR obtained at the initial diagnostic stage is a useful laboratory marker to discriminate patients with pulmonary TB from patients with other pulmonary infection in a high TB burden country.

VITAMIN D STATUS IN MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS COMPARED TO PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROLS IN MEDAN CITY, INDONESIA

H. HUTAGAOL,1 B.Y.M. SINAGA,3 E. MUTIARA2, W. RAHARDJO1

Background and Aims: Multidrug-resistant (MDR) tuberculosis (TB) is a serious public health problem worldwide. Its situation is worsened by the presence of multidrug resistant (MDR) strains of Mycobacterium tuberculosis (MTB), the causative agent of the disease. Recent studies have shown that vitamin D insufficiency is associated with a higher risk of active PTB, though no study has included MDR TB patients. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth. The aim of this study is to compare the serum vitamin D status in MDR TB patients, PTB patients, and healthy controls.

Methods: A case control study was conducted in 2015 at the Adam Malik General Hospital, Medan. Twenty five patients of MDR TB as a cases, thirty patients of PTB and thirty healthy subjects as a controls were selected. MDR TB was diagnosed by GeneXpert test with positive result. Vitamin D status was measured by ELISA technique and compared with healthy control group (p = 0.003). There was a significant difference between the levels of vitamin D in patients PTB-DMT2 with healthy controls, where levels of vitamin D in patients PTB-DMT2 is higher than the healthy controls, but no significant differences in vitamin D levels between PTB-DMT2 with PTB with healthy controls.

VITAMIN D STATUS IN MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS COMPARED TO PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROLS IN MEDAN CITY, INDONESIA

H. HUTAGAOL,1 B.Y.M. SINAGA,3 E. MUTIARA2, W. RAHARDJO1

Background and Aims: Multidrug-resistant (MDR) tuberculosis (TB) is a serious public health problem worldwide. Its situation is worsened by the presence of multidrug resistant (MDR) strains of Mycobacterium tuberculosis (MTB), the causative agent of the disease. Recent studies have shown that vitamin D insufficiency is associated with a higher risk of active PTB, though no study has included MDR TB patients. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth. The aim of this study is to compare the serum vitamin D status in MDR TB patients, PTB patients, and healthy controls.

Methods: A case control study was conducted in 2015 at the Adam Malik General Hospital, Medan. Twenty five patients of MDR TB as a cases, thirty patients of PTB and thirty healthy subjects as a controls were selected. MDR TB was diagnosed by GeneXpert test with positive result. Vitamin D status was measured by ELISA technique and compared with healthy control group (p = 0.003). There was a significant difference between the levels of vitamin D in patients PTB-DMT2 with healthy controls, where levels of vitamin D in patients PTB-DMT2 is higher than the healthy controls, but no significant differences in vitamin D levels between PTB-DMT2 with PTB with healthy controls.

VITAMIN D STATUS IN MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS COMPARED TO PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROLS IN MEDAN CITY, INDONESIA

H. HUTAGAOL,1 B.Y.M. SINAGA,3 E. MUTIARA2, W. RAHARDJO1

Background and Aims: Multidrug-resistant (MDR) tuberculosis (TB) is a serious public health problem worldwide. Its situation is worsened by the presence of multidrug resistant (MDR) strains of Mycobacterium tuberculosis (MTB), the causative agent of the disease. Recent studies have shown that vitamin D insufficiency is associated with a higher risk of active PTB, though no study has included MDR TB patients. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth. The aim of this study is to compare the serum vitamin D status in MDR TB patients, PTB patients, and healthy controls.

Methods: A case control study was conducted in 2015 at the Adam Malik General Hospital, Medan. Twenty five patients of MDR TB as a cases, thirty patients of PTB and thirty healthy subjects as a controls were selected. MDR TB was diagnosed by GeneXpert test with positive result. Vitamin D status was measured by ELISA technique and compared with healthy control group (p = 0.003). There was a significant difference between the levels of vitamin D in patients PTB-DMT2 with healthy controls, where levels of vitamin D in patients PTB-DMT2 is higher than the healthy controls, but no significant differences in vitamin D levels between PTB-DMT2 with PTB with healthy controls.

VITAMIN D STATUS IN MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS COMPARED TO PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROLS IN MEDAN CITY, INDONESIA

H. HUTAGAOL,1 B.Y.M. SINAGA,3 E. MUTIARA2, W. RAHARDJO1

Background and Aims: Multidrug-resistant (MDR) tuberculosis (TB) is a serious public health problem worldwide. Its situation is worsened by the presence of multidrug resistant (MDR) strains of Mycobacterium tuberculosis (MTB), the causative agent of the disease. Recent studies have shown that vitamin D insufficiency is associated with a higher risk of active PTB, though no study has included MDR TB patients. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth. The aim of this study is to compare the serum vitamin D status in MDR TB patients, PTB patients, and healthy controls.

Methods: A case control study was conducted in 2015 at the Adam Malik General Hospital, Medan. Twenty five patients of MDR TB as a cases, thirty patients of PTB and thirty healthy subjects as a controls were selected. MDR TB was diagnosed by GeneXpert test with positive result. Vitamin D status was measured by ELISA technique and compared with healthy control group (p = 0.003). There was a significant difference between the levels of vitamin D in patients PTB-DMT2 with healthy controls, where levels of vitamin D in patients PTB-DMT2 is higher than the healthy controls, but no significant differences in vitamin D levels between PTB-DMT2 with PTB with healthy controls.

VITAMIN D STATUS IN MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS COMPARED TO PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY CONTROLS IN MEDAN CITY, INDONESIA

H. HUTAGAOL,1 B.Y.M. SINAGA,3 E. MUTIARA2, W. RAHARDJO1

Background and Aims: Multidrug-resistant (MDR) tuberculosis (TB) is a serious public health problem worldwide. Its situation is worsened by the presence of multidrug resistant (MDR) strains of Mycobacterium tuberculosis (MTB), the causative agent of the disease. Recent studies have shown that vitamin D insufficiency is associated with a higher risk of active PTB, though no study has included MDR TB patients. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth. The aim of this study is to compare the serum vitamin D status in MDR TB patients, PTB patients, and healthy controls.

Methods: A case control study was conducted in 2015 at the Adam Malik General Hospital, Medan. Twenty five patients of MDR TB as a cases, thirty patients of PTB and thirty healthy subjects as a controls were selected. MDR TB was diagnosed by GeneXpert test with positive result. Vitamin D status was measured by ELISA technique and compared with healthy control group (p = 0.003). There was a significant difference between the levels of vitamin D in patients PTB-DMT2 with healthy controls, where levels of vitamin D in patients PTB-DMT2 is higher than the healthy controls, but no significant differences in vitamin D levels between PTB-DMT2 with PTB with healthy controls.
THE ASSOCIATION OF VITAMIN D RECEPTOR GENE FOKI POLYMORPHISM AND VITAMIN D LEVELS WITH PULMONARY TUBERCULOSIS IN MEDAN CITY, INDONESIA

D.O. MARPAUNG, B.Y.M. SINAGA, P. SIAGIAN
Medical Faculty University of North Sumatra, Department of Pulmonology and Respiratory Medicine, Medan, Indonesia

Background and Aims: Vitamin D has been known to have a role in developing pulmonary tuberculosis (TB). Vitamin D exerts several immunomodulatory effects by binding to Vitamin D Receptor (VDR). FokI polymorphism was one of the genetic variations within the VDR gene associated with pulmonary TB. In the present study we investigated the association of vitamin D receptor gene FokI polymorphism and vitamin D levels with pulmonary TB.

Methods: This is a case-control study in 70 pulmonary TB patients as a case and 70 healthy control. Vitamin D receptor gene FokI polymorphism was evaluated by PCR-RFLP technique. The association of vitamin D receptor gene FokI polymorphism and vitamin D levels with pulmonary TB were statistically analyzed.

Results: The frequencies of vitamin D levels were sufficient 37.1%, insufficient 45.7%, deficient 17.1% in pulmonary TB patients and sufficient 15.7%, insufficient 47.1%, deficient 37.1% in healthy control. There was a significant association between vitamin D levels and pulmonary TB (OR 5.1, 95% CI: 1.91-13.67 for sufficient vs deficient). There was no association between vitamin D levels and pulmonary TB (OR 2.1, 95% CI: 0.9-4.86 for insufficient vs deficient). The frequencies of FokI genotypes were FF 42.9%, Ff 44.3%, ff 12.9% for pulmonary TB patients and FF 41.4%, Ff 45.7%, ff 12.9% for healthy control. There was no significant association between vitamin D receptor gene FokI polymorphism and pulmonary TB (OR 1.03, 95% CI: 0.36-2.97 for FF vs Ff). There was also no significant association between vitamin D receptor gene FokI polymorphism and pulmonary TB (OR 0.96, 95% CI: 0.34-2.76 for FF vs ff).

Conclusions: There was a significant association between vitamin D levels and pulmonary TB. However, there was no significant association between vitamin D receptor gene FokI polymorphism and pulmonary TB.

RELATIONSHIP OF RADIOGRAPHIC MANIFESTATIONS OF TUBERCULOSIS IN DIABETIC PATIENTS AND HbA1C LEVELS

D.J. LAYALI
Medical Faculty University of North Sumatra, Pulmonology and Respiratory Diseases, Medan, Indonesia

Background and Aims: Diabetes mellitus is a known risk factor for tuberculosis. Radiographic manifestations of pulmonary TB in patients with DM have previously been reported. However, the results reported by different researchers have not been consistent. Several studies reported that TB patients with DM had an increased frequency of lower lung field lesions as compared TB patients without DM, but others did not. Some studies reported that TB patients with DM had a higher frequency of cavitation as compared with TB patients without DM while others did not.

Radiographic manifestation of pulmonary TB is likely to be associated with immune status and the risk of developing TB among patients with DM is likely dependent on glycemic control and glycemic control associated with HbA1C level.

The aim of this research is to see the relationship of radiographic manifestation of tuberculosis in diabetic patients and HbA1C levels.

Methods: In this case-control study we compared the radiographic manifestation of 40 patients of diabetic pulmonary tuberculosis and 40 patients of non-diabetic pulmonary tuberculosis. In diabetic pulmonary tuberculosis, we associated it with HbA1C levels. Diabetes Glycemic control was assessed by glycated hemoglobin A1C (HbA1C), chest radiograph was performed to examine tuberculosis radiographic manifestation.

Results: This research is on going research. We estimated that compared with those without DM, 15 TB patients with DM (not all patients) were more likely to have opacity over lower lung fields, extensive parenchymal lesions, any cavity, multiple cavities and large cavities. In diabetic tuberculosis patients with high level of HbA1C have extensive parenchymal lesions compared with low level of HbA1C.

Conclusions: We estimated that glycemic control influenced radiographic manifestations of pulmonary TB in patients with DM. But, further study and longer follow-up period were needed to make better conclusion.

COMPARATIVE STUDY OF EFFICACY, SELF-REPORTED SIDE EFFECTS AND PATIENT PREFERENCE ON Tiotropium, Glycopyruronum and Ipratropium in the Treatment of COPD

W. WAI MUI, C.H. CHAU, C.F. WONG, T.W.D. LUI
1 Grantham Hospital, Tuberculosis and Chest Unit, Wong Chuk Hang, Hong Kong, China, and 2 Queen Mary Hospital, Medicine, Hong Kong, Hong Kong, China

Background and Aims: Tiotropium and Glycopyruronum are two potent LAMA. This study aimed to assess the change in spirometry and symptoms control when atropine was switched to LAMA in stable COPD patients. Patient preference on individual LAMA was also evaluated.

Methods: Stable COPD patients on regular ipratropium (together with other inhalers) were included. Patients with prior use of LAMA or those with cognitive or functional impairment affecting the use the LAMA inhaler device were excluded. Patients were switched from ipratropium to randomly assigned glycopyruronum (breath) for 4 weeks followed by tiotropium (handihaler) for another 4 weeks, or vice versa. Spirometry, CAT and mMRC score were recorded at baseline and at the end of 4th and 8th week. Patients were questioned on their preference of anti-cholinergic and their reasons at the end of 8 weeks.

Results: Forty-six patients were enrolled into the study. Six dropped out during the study and data of the remaining 40 patients (M/F: 33/7; age: 74.6 ± 7 years) were analyzed. At baseline, their mean FEV1 was 0.87Litres (IQR: 0.71 L, 1.20 L), mean CAT score was 8 and mMRC grade 2. After 8 weeks of LAMA, there was no significant difference in the mean FEV1 (−0.03 L), CAT score (−0.5) and mMRC grade (−0.0) . On the preference of the inhalers, significantly more patients prefer glycopyruronum to tiotropium (65% (26 patients) vs 27.5% (11 patients), p < 0.0005 ) with the main reason being the preference of the inhaler device but not due to a difference in efficacy.

Conclusions: In our group of elderly stable COPD patients, switch from ipratropium to LAMA did not bring about significant improvement in spirometry and symptom control. More patients preferred glycopyruronum over tiotropium because of their preference in inhaler device.
COST AND UTILIZATION OF COPD MEDICATION IN KOREA

C.K. RHEE, 1 J.A. KIM, 2 J. LEE, 1 H.K. YOON 3
1Seoul St. Mary’s hospital, Internal Medicine, Seoul, Republic of Korea, 2Health Insurance Review and Assessment Service, Pharmaceutical Policy Evaluation Research Team, Seoul, Republic of Korea, and 3Yeouido St Mary’s Hospital, Internal Medicine, Seoul, Republic of Korea

Background and Aims: Nationwide data of COPD medication is rare and longitudinal follow up data has been extremely rare. The object of this study is to analyze the cost and utilization of COPD medication in Korea.

Methods: The Korean Health Insurance Review and Assessment Service database from 2008 to 2013 were used. COPD patients were defined by ICD-10 code and medication use.

Results: COPD patients in Korea were increased by 13.9% since 2008 until 2013 (from 184,059 to 209,579). The average number of prescribed medications for COPD were also increased, from 10.1 to 12.0. The total cost of COPD-related medication increased by 78.2% ($20,787,780). The cost of COPD medication per person increased from $138.4 in 2008 to $216.6, showing 56.5% increase over 6 years. In 2008, LAMA inhalers were dispensed to 26.2% (48,296) of COPD patients in Korea, and it is increased to 37.3% (78,227) in 2013. The total cost of LAMA increased from $9,738,800 in 2008 to $18,766,800, showing 92.3% increase over 6 years. In 2008, methylxanthine was high (N = 209,579). In 2013, methylxanthine was dispensed to 63.4% of patients.

Conclusions: Cost and utilization of COPD medication are increasing in Korea. Prescription rate of inhaler was low while methylxanthine was high in Korea. Use of inhaler was increased during 6 years.

INCIDENCE OF PNEUMONIA AMONG CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS ON INHALED CORTICOSTEROIDS ADMITTED AT PERPETUAL SUCCOUR HOSPITAL FROM JANUARY 1, 2010 TO DECEMBER 31, 2012

M.A. LETIGIO-UY, J.C. ARANAS
Perpetual Succour Hospital, Internal Medicine Section of Pulmonology, Cebu City, Philippines

Background and Aims: COPD is a leading cause of morbidity and mortality punctuated with exacerbations. ICS reduce the frequency of exacerbations in severe and very severe COPD. Pneumonia, a complication of COPD also predisposes to exacerbations. ICS have been reported to increase the risk for pneumonia in COPD patients.

The study aims to determine the incidence of pneumonia among COPD patients maintained on ICS admitted at Perpetual Succour Hospital from January 1, 2010 to December 31, 2012.

Methods: Medical records of 285 COPD patients over a three-year period were reviewed. Demographics, comorbid illnesses, smoking history, maintenance medications, chief complaint, spirometry, final diagnosis and outcomes were obtained. Association between pneumonia and ICS use were analyzed.

Results: Prevalence of COPD in Perpetual Succour Hospital was 0.55 percent. Two hundred fourteen (75.1 percent) of the COPD patients were males. Mean age on admission was 72.6 ± 9.702 years old. Hypertension was the most common comorbidity (N = 120; 85.7 percent). Most major current smokers (N = 134; 47 percent). Most common chief complaint was dyspnea (N = 149; 52.28 percent). One hundred eighteen (41.4 percent) patients were on ICS. Only 15 (6 percent) of the 285 COPD patients had documented spirometry results. The incidence of pneumonia was 35.8 percent. There was a significantly higher incidence of pneumonia among those on ICS (p = 0.001). Twenty-two (7.7 percent) COPD patients required invasive mechanical ventilation on admission while three (1.05%) required non-invasive mechanical ventilation. Mortality rate was low (N = 23; 8.1 percent). There were no significant differences on mortality whether the COPD patients were admitted for pneumonia or not.

Conclusions: The incidence of pneumonia among COPD patients maintained on ICS was 35.8 percent and this was significantly higher among patients receiving ICS.

COPD BEING DIAGNOSED IN LUNG CANCER PATIENTS WITH THORACIC OPERATION

W. GUFANG
Huashan hospital, department of respiratory diseases, Shanghai, China

Background and Aims: Chronic obstructive pulmonary disease (COPD) is a risk factor and important coexisting disease for lung cancer. At the same time, coexisting COPD poses unfavorable effect on management of lung cancer. However, the current status of management of COPD in lung cancer patients with operable sites is not fully described.

Methods: All patients with lung cancer underwent surgery were collected retrospectively from Jan. 2002 to Dec. 2008. Medical records were reviewed about clinical information, pathological records, lung functions, etc., to analyze comorbidity rate about COPD and characters. The definition of COPD was according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) document. The diagnostic rate (COPD recorded as a discharge diagnosis/spirometry-defined percentage) and conformity to GOLD treatment guidelines were investigated. The factors influencing diagnosis were analyzed.

Results: Among all 437 undergone surgery patients aged older than 40 years old, 94 patients were diagnosed COPD, the prevalence of COPD was 21.36% (41 as GOLD 1, 52 as GOLD 2, and 1 as GOLD 3). Among them, 89.36% was male, with average age being 63.3 years old. Only 9 patients were diagnosed as COPD, the rate of misdiagnosis was 90.4%, and all of them didn’t receive pulmonary function test. 71.3% of those patients with COPD had smoke history; average smoke intensity was 26.7 pack-year. All surgery of pathological staging were classified as followed according to the standards of the Union International Contre le Cancer (UICC):Istage (A + B:38 + 119); II (A + B:14 + 83); III (A + B:100 + 32); IV: 31; No specific: 20 cases. And patients complicated with COPD presented stages as followed: Istage (A + B:6 + 236)(B:21); III(A + B:33 + 7); IV: 1; No specific: 3 cases. The rate of lung cancer complicated with COPD was 24.8%, 21.6%, 30.3% respectively.

Conclusions: Patients of lung cancer undergone surgery have high risk morbidity of COPD. To improve the result of peri-operation period management, COPD should be pay attention to treat for these patients.
FACTORS ASSOCIATED WITH DEVELOPMENT OF CORPULMONALE IN COPD

C. S K, J. B S, M. M, L. K S, M. P A
JSS Medical College - Mysore., pulmonary medicine, Mysore, India

Background and Aims: It is observed that not all patients with COPD with low lung functions develop corpulmonale. The factors associated with corpulmonale needs further elucidation in our population.

Methods: Subjective measures such as St. George’s questionnaire (SGRO), MMRC dyspnea scores, objective measures such as spirometry, 6MWT, Arterial blood gases, Echocardiography and clinical variables such as smoking (pack years), number of exacerbations per year, co morbidities and BMI were evaluated in consecutive patients with COPD as risk factors for Corpulmonale.

Results: one twenty consecutive patients with COPD were included in the study and there were 22 patients with corpulmonale. Of the variables tested only pulmonary hypertension was found to be significantly associated with development of Corpulmonale. No significant association was observed with pack years of smoking, severity of COPD, spirometry (FVC, FEV1 as continuous variables), arterial blood gases or 6MWT with corpulmonale.

Conclusions: Factors leading to Corpulmonale needs further elucidation. Severity of COPD and low lung functions are not associated with corpulmonale.

A SMART MOBILE-PHONE BASED SYSTEM TO ASSIST IN THE DIAGNOSIS OF COPD PATIENTS

P.D. DESHPANDE, R. VEMPADA, A. SINHARAY
1TRDDC, TCS- Research and Innovation, Pune, India, and 2TCS, Research and Innovation, Kolkata, India

Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) is the second largest cause of death in India in non-communicable diseases. However, till date there is limited medical equipment and awareness of the severity of this disease largely aggravated due to prevalence of smoking, bio-mass and air-pollution. Furthermore, the symptoms of cardiac patients and COPD patients are similar and hence likely to be mis-classified. The symptoms of this disease are specific lung sounds like wheezes and crackles which progress into breathlessness and a full blown COPD, which unfortunately is irreversible.

Methods: We at TCS, Research and Innovation (R & I) are developing a smart mobile-phone based, cost-effective and non-invasive system to assist diagnosis of such pulmonary diseases. There is immense positive societal impact of such a mobile-phone based system with an aim to assist medical practitioners to diagnose early signs of this disease and to allow for administering timely treatment and prevent irrevocable damage. We have developed a low-cost eStethoscope (http://www.wearabletechworld.com/topics/newsfeed/articles/416367-winners-the-2016-wearable-technology-product-the-year.htm) which will be used to collect lung sounds from various patient-body locations and processed for detecting acoustic anomalies and flagged as COPD indications for further investigations.

Results: Our data-driven approach enables visualization of sound signals and captures specific features via our machine learning algorithms to assist medical practitioners in detecting COPD specific sounds and mark these patients for further investigation such as Spirometry tests. Preliminary results are presented.

Conclusions: The accuracy of these machine learning algorithms and success of this program depends on availability of annotated quality data and are currently in the process of continuous supervised learning and improvement.
ANAPLASTIC LYMPHOMA KINASE GENE REARRANGEMENT IN MALAYSIAN PATIENTS WITH EGFR WILD TYPE LUNG ADENOCARCINOMA

N. MOHAMAD,1 J. TAN2 J. PAILOOR,1 P. RAJADURAI3, C.K. LIAM2
1University of Malaya, Department of Pathology, Kuala Lumpur, Malaysia, 2University of Malaya, Department of Medicine, Kuala Lumpur, Malaysia, and 3Subang Jaya Medical Center, Department of Pathology, Selangor, Malaysia

Background: Anaplastic lymphoma kinase (ALK) gene rearrangements in adenocarcinoma of lung are predictive of treatment response to targeted therapy with ALK tyrosine kinase inhibitors.

Objectives: This study aimed to determine the incidence of ALK gene rearrangement using immunohistochemistry method (IHC) in lung adenocarcinomas; which were negative for epidermal receptor growth factor (EGFR) mutation and to determine the clinic-pathological features of patients with ALK-positive tumours.

Materials and Methods: The Ventana anti-ALK (DSF3) immunohistochemistry (IHC) was performed on formalin fixed paraffin embedded tissue sections of primary lung adenocarcinoma biopsy specimens from 92 patients which were negative for EGFR mutation. ALK-positive cases were subsequently tested with fluorescent in-situ hybridization (FISH) using Vysis ALK break Apart FISH probe kit.

Results: Twelve of 92 cases (13%) were IHC positive for ALK protein. Seven of these cases were confirmed positive by FISH. Five others were not suitable for FISH test interpretation because of insufficient tumour cells or the presence of fibrous tissue. ALK protein expression was found significantly more common in females than in males (29.6% versus 6.2%; p = 0.005). All 12 ALK-positive lung adenocarcinoma patients were never smokers. There was no significant difference in the prevalence of ALK rearrangement in patients of different ethnicities (p = 0.485).

Conclusions: In Malaysian patients with EGFR mutation-negative lung adenocarcinoma, the incidence of ALK rearrangement was similar to that of other Asian populations. ALK rearrangements are significantly more common in female patients and exclusively in never smokers. The IHC method using DSF3 antibody is a valuable screening tool in detecting ALK rearrangement in lung adenocarcinoma before testing with FISH method.

RISK OF SECOND PRIMARY MALIGNANCIES IN LUNG CANCER SURVIVORS – THE INFLUENCE OF DIFFERENT TREATMENTS: DATA FROM 18,372 PATIENTS

V.V.F. SU
Taipei Veterans General Hospital, Department of Critical Care Medicine, Taipei, Taiwan

Background and Aims: There was no large study addressing the relationship of lung cancer patients with different therapies and second primary malignancy (SPM).

Methods: Using the Taiwan National Health Insurance Research Database; we conducted a population-based cohort study. Patients newly diagnosed with lung cancer during 1997 to 2005 were enrolled and followed up until Dec. 31, 2011. The endpoint of the study was SPM occurrence. Standardized incidence ratios (SIRs) of cancers were calculated to compare the risk of cancer increased with treatments; tyrosine kinase inhibitors (TKIs) statistically significantly reduced SPM (HR: 0.41; 95% CI: 0.21–0.79; p = 0.008).

Conclusions: Our study indicates that lung cancer may be a risk factor for SPM. TKI was associated with a significantly lower risk of SPM development.

THE RELATIONSHIP BETWEEN SERUM CARCINOEMBRYONIC ANTIGEN (CEA) AND ENDOTHELIAL GROWTH FACTOR RECEPTOR (EGFR) MUTATIONS IN LUNG ADENOCARCINOMA PATIENTS

N. WATI1, S.D. PRATIWI2, N. SETIJOWATI2
1Universitas Brawijaya/Saiful Anwar Hospital, Pulmonology and Respiratory Medicine, Malang, Indonesia, and 2Universitas Brawijaya/Saiful Anwar Hospital, Public Health Department, Malang, Indonesia

Background and Aims: Adenocarcinoma is the most often type of lung cancer found in Dr. Saiful Anwar General Hospital Malang. EGFR mutation and increased level of CEA are found in Lung adenocarcinoma. EGFR mutations is associated with sensitivity to tyrosine kinase inhibitors (TKIs) therapy. There are some limitations in detecting EGFR mutation. The best specimens to examine EGFR mutation are obtained from open biopsy but 70 – 80% of lung cancer patient can’t undergo open biopsy. CEA is also expected to predict treatment efficiency of EGFR-TKIs therapy. In this study; we investigated the relationship between serum Carcinoembryonic antigen (CEA) and Endothelial Growth Factor Receptor (EGFR) Mutations in Lung Adenocarcinoma patients.

Methods: The research was conducted in Dr. Saiful Anwar General Hospital Malang. From May 2014 to November 2015; 54 lung adenocarcinoma patients who had underwent measurements of EGFR mutation and serum CEA level in Dr. Saiful Anwar General Hospital Malang were retrospectively recruited. None of them had surgery; radiotherapy; chemotherapy and targeted therapy before. EGFR mutation was detected using PCR; while the serum CEA levels were analyzed using electrochemical luminescence.

Results: Abnormal serum levels of CEA were significantly associated with EGFR mutation (95% CI; P = 0.043) with an odds ratio of 3.4 (95% CI; 1.010-11.451). The area under the ROC curve for CEA was 0.558 (95% CI; P = 0.078).

Conclusions: Serum CEA is associated with mutation of EGFR in lung adenocarcinoma patients. Patients with EGFR mutations are 3.4 more times more at risk to had increased levels of CEA than patients without EGFR mutations.

Keywords: Lung cancer; adenocarcinoma; EGFR; CEA

Respirology (2016) 21 (Suppl. 3), 3–213 © 2016 Asian Pacific Society of Respirology
Background and Aims: Because of small patient populations; the full genetic alteration profile of lung adenocarcinomas (LADCs) driven by oncogenic ALK; RET and ROS1 kinase gene fusions has not been investigated; even in recent large-scale studies. To address this issue; genetic alteration profile of 31 LADCs driven by these oncogenic fusions was obtained and compared to those of 169 other LADCs.

Methods: Among 608 LADC specimens collected consecutively from Japanese patients; 200 cases were selected; including 31 with ALK (n = 11); RET (n = 11) or ROS1 fusions (n = 9) (driver fusion cases); 96 with oncogenic EGFR; KRAS; BRAF; HER2; or HRAS mutations (driver mutation cases); and 73 without known fusions or mutations (pan-negative cases). The tissues were subjected to whole exome sequencing and copy number variation analyses. Deep re-sequencing was performed on 26 genes for validation.

Results: The driver fusion cases showed a distinct profile with small numbers of non-synonymous mutations compared to the driver mutation and pan-negative cases (non-synonymous mutations/Mb = 0.39 vs 0.87 and 2.8; respectively; P < 0.0001 by t-test). Mutations in genes involved in lung carcinogenesis; such as TP53; CDKN2A; KEAP1; STK11/LKB1; and RB1; as well as truncating mutations in SWI/SNF chromatin remodeling complex genes; were only rarely detected in driver fusion cases. This result was validated in LADCs collected from US patients.

Conclusions: The development of LADCs with ALK; RET; and ROS1 fusions includes few additional genetic aberrations. This finding supports the present LADC therapeutic strategy; which relies on drugs suppressing the kinase activity of fusion gene products.

EPIDERMAL GROWTH FACTOR RECEPTOR MUTATION STATUS ON RESPONSE TO FIRST-LINE CYTOTOXIC CHEMOTHERAPY IN ADVANCED LUNG ADENOCARCINOMA

C.S. Chai; C.K. Liam; Y.K. Pang; K.S. Kow; C.K. Wong; M.E. Poht; J.L. Tan

Background and Aims: The presence of activating epidermal growth factor receptor (EGFR) mutations in advanced lung adenocarcinoma predicts a good response to EGFR-tyrosine kinase inhibitor (TKI). Nevertheless; it remains uncertain whether the presence of similar mutation confers survival and treatment response benefits in patients receiving first-line cytotoxic chemotherapy.

This study aims to compare the progression-free-survival (PFS); overall survival (OS); objective response rate (ORR) and disease control rate (DCR) of patients with EGFR mutant versus EGFR wild-type advanced lung adenocarcinoma; both on first-line cytotoxic chemotherapy.

Methods: A retrospective observational study of patients with EGFR mutant and those with EGFR wild-type advanced lung adenocarcinoma (stage IIIIB and stage IV) receiving first-line cytotoxic chemotherapy at the University of Malaya Medical Centre from 1st August 2010 to 31th July 2014.

Results: Of 104 patients with advanced lung adenocarcinoma receiving first-line chemotherapy; 19 patients (18.5%) had activating EGFR mutation-positive tumours (exon 19 deletion and exon 21 L858R point mutations) and 85 patients (81.7%) had EGFR wild-type tumours. Although the PFS and OS were numerically shorter in patients with EGFR mutant than those with EGFR wild-type adenocarcinoma (PFS; 2.23 months versus 2.93 months [HR; 1.16; 95% CI; 0.64-1.20; p = 0.630]) [OS; 9.63 months versus 10.43 months [HR; 1.20; 95% CI; 0.55-2.64; p = 0.649]]; the differences were not statistically significant (figure 1 and 2). The ORR and DCR were also numerically inferior in patients with EGFR mutant compared to those with EGFR wild-type tumours [ORR; 10.5% versus 16.5% [OR; 0.58; 95% CI; 0.17-2.93; p = 0.164];[DCR; 36.8% versus 51.8% [OR; 0.54; 95% CI; 0.17-2.69; p = 0.291]) but the differences were not statistically significant.

Conclusions: Advanced lung adenocarcinoma patients receiving first-line cytotoxic chemotherapy appeared to have similar PFS; OS; ORR and DCR irrespective of the EGFR mutation status. However; the apparent lack of differences could have been due to the small sample size.
MIR-26A DESENSITIZES NON-CELL SMALL CELL LUNG CANCER CELLS TO TYROSINE KINASE INHIBITORS BY TARGETING PTPTN13

Z. NING, S. LI, S. XU, T. WANG, Z. YANG, Y. LI
1Huashan Hospital, The Department of Respiratory Medicine, Shanghai, China, 2Shaanxi Provincial People’s Hospital, Department of Neurology, Xi’an, China, 3Xi’an Jiaotong University, Department of Applied Physics, Xi’an, China, and 4Shaanxi Provincial Second People’s Hospital, Department of Respiratory Medicine, Xi’an, China

Background and Aims: Epidermal growth factor receptor (EGFR)-targeted tyrosine kinase inhibitors (TKIs) have emerged as first-line drugs for non-small cell lung cancers (NSCLCs). However, resistance to TKIs represents the key limitation for their therapeutic efficacy. This paper is going to study the molecular mechanism and the effect of mir-26a on the development of EGFR-TKI resistance in NSCLCs.

Results: We found that mir-26a was upregulated in gefitinib-refractory NSCLCs; mir-26a is downstream of EGFR signaling and directly targets and silences protein tyrosine phosphatase non-receptor type 13 (PTPN13) to maintain the activation of Src; a dephosphorylation substrate of PTPN13; thus reinforcing EGFR pathway in a regulatory circuit. mir-26a inhibits efficiently p38 MAPK phosphorylation to get gefitinib-refractory NSCLC responses to gefitinib.

Conclusions: This study unravelled the regulatory roles of miRNA(s) in EGFR-TKI responsiveness of NSCLCs; and thus hold out great promise for miR-26a as a potential target for treatment of EGFR-TKI resistant NSCLCs.

REFERENCE VALUES OF impulse OSCILLOMETRY IN HEALTHY PRESCHOOL CHILDREN FROM SOUTHEAST CHINA

Y. SHI
Children’s Hospital of FuDan University, Respiratory Department, Shanghai, China

Background and Aims: The impulse oscillometry system (IOS) is a simple and noninvasive technique for measuring lung function during tidal breathing. However, the reference values available in Chinese preschool children are limited. The purpose of our study was to present the reference equations of IOS parameters in healthy preschool children in Southeast China.

Methods: IOS was performed in 537 (287 boys, 250 girls) healthy Chinese preschool children from Southeast China in the first 2 years of life, highlighting the importance of using population-specific ventilatory parameters and could be used to assess lung functions in Sri Lankan children.

Results: There were significant correlations between spirometry parameters and height and weight in both genders. There were significant correlations between age and PEFR, FEV25 and FEF50 in males and age and FEV1, PEF and FEV25-75% in females. The prediction equations in males for FVC: 0.047height + 0.007age – 4.66; for FEV1: 0.016height + 0.016age – 4.22; for PEFR: 0.074height + 0.123age – 7.59 and FEF25-75%: 0.042height + 0.066age – 4.36. The equations in females for FVC: 0.028height + 0.031age – 2.36; for FEV1: 0.027height + 0.047age – 2.57; for PEFR: 0.038height + 0.159age – 2.93 and FEF25-75%: 0.026height + 0.136age – 3.18.

Conclusions: This study provided reference standards for BabyBody-plethysmographic measurements in healthy Chinese children in the first 2 years of life, highlighting the importance of using population-specific data.
DIAGNOSTIC ACCURACY OF REVERSED HALO SIGN WITH SPECIFIC CRITERIA ON SPIRAL CHEST COMPUTED TOMOGRAPHY TO PREDICT PULMONARY INFARCTION

A. GHAFARI ANVAR,1 S. KAHKOUEE1, T. FAGHIHI LANGERUDI2
1National Institute of Tuberculosis and Lung Diseases, radiology, tehran, Iran, and 2shahid beheshti university of medical science, radiology, tehran, Iran

Background and Aims: To determine the diagnostic accuracy of reversed halo sign with specific criteria for diagnosis of pulmonary infarction in spiral chest computed tomography performed in patients with low clinical suspicion for pulmonary thromboembolism.

Methods: In a retrospective study, 1584 spiral chest CT scan which was performed in patients with clinical concern of pulmonary diseases other than pulmonary thromboembolism were reviewed. In the next step those CT scans which revealed subpleural consolidation were included in study provided that a pulmonary CT angiography had also been performed for patient in following 96 hours.

Then including CT scans had been divided into to two distinct groups according to presence of peripheral consolidation with reversed halo and specific predefined criteria (clear margin, central streaks of air lucency, located in lower lung fields and healthier area oriented toward the hilum with or without pleural reaction) as group A and simple peripheral consolidation as group B.

Our gold standard for confirmation of pulmonary infarction was presence of pulmonary emboli on CT angiography or infarction on tissue diagnosis.

Results: Among firstly reviewed 1584 CT- scans, 73 cases with peripheral consolidation, had available recent pulmonary CT angiography. Among these CT scans, 44 cases had our predefined CT scan criteria which were placed in group A and 29 cases were placed in group B. According to our gold standard from group A 42 patient and from group B 5 patient had pulmonary infarction.

The results revealed a diagnostic accuracy = 90/4%, specificity = 89/4%, sensitivity = 92/3%, positive predictive value = 95/5% for our specific criteria, in diagnosis of pulmonary infarction.

Conclusions: Presence of the described imaging criteria on spiral chest CT scan may strongly predict pulmonary infarction. It may be particularly helpful in the medical centers without emergency access to multi-detector CT angiography.

EFFECTIVENESS OF CLARITHROMYCIN IN PATIENTS WITH YELLOW NAIL SYNDROME

S. MATSUBAYASHI, M. SUZUKI, Y. HAYASHI, A. SHIOZAWA,
K. Kobayashi, S. Ishii, E. Morino, T. SATO, J. TAKASAKI,
G. Naka, M. Ikura, S. Izumi, Y. Takeda, M. Hojo, H. Sugiyama
National Center for Global Health and Medicine, Respiratory Medicine, Tokyo, Japan

Background and Aims: Yellow Nail Syndrome (YNS) is a rare disease characterized by the triad of thickened, slow-growing yellow nails, lymphedema and chronic respiratory manifestations. What causes YNS is unknown, however, is suggested as congenital lymph abnormality. Any Stress such as infection may make this abnormality obvious. As, 20-25% of YNS accompanies chronic sinusitis, or bronchiectasis, the treatment with clarithromycin (CAM) can be considered. Some reports showed that improvement in the nail abnormalities corresponds to better control of respiratory manifestations. We speculated the effect of CAM against nail discoloration.

Methods: We conducted an observational study involving patients diagnosed as YNS from January 2005 to January 2016 treated at our institution. We extracted the data of their age, sexuality, comorbid diseases, medication, respiratory manifestations, and the color of nails.

Results: Five YNS patients were included, and the mean age of the patients was 71.6 years old, and 2 (40%) were male. Four patients had sinusits, and 2 had rheumatoid arthritis. CAM (400-600 mg/day) was prescribed for every patient. As of respiratory manifestations, 4 patients had sinobronchial syndrome, and 2 had pleural effusion. Four patients had improvement in their respiratory manifestations. The improvement of nail discoloration was seen in every patient within a year after started on CAM.

CONCLUSIONS:

Conclusions: In YNS patients, long-term macrolide treatment may improve not only respiratory manifestations but yellow nail itself, also. Anti-inflammatory activity of macrolide may improve lymphedema, and set off growing of nails.
Thy-related cytokines in asthmatics with CRS may contribute to a recalcitrant status.

**Therapeutic effects of histone deacetylase inhibitors in a murine asthma model**

R. Yuan  
The first hospital of China Medical University, Department of Respiratory Disease, Shenyang, China

**Background and Aims:** Present studies have confirmed that broad-spectrum histone deacetylase inhibitors can effectively relieve airway inflammation, airway remodeling and airway hyperresponsiveness in asthma. But which histone deacetylase (HDACs) members play a key role in asthma pathogenesis is still unknown. In this study, we investigated the therapeutic effects of various HDAC inhibitors on the development of chronic allergic airway disease in mice with airway inflammation, airway remodeling, and airway hyperresponsiveness.

**Methods:** Wild-type BALB/c mice were divided into 6 groups: control, asthma, dexamethasone (positive control), TSA (Tubastatin A HCl, a selective histone deacetylases 6 (HDAC6) inhibitor), PFI-34051 (a selective HDAC8 inhibitor), and Givinostat (a broad-spectrum HDAC inhibitor that inhibits class I and class II HDACs and several pro-inflammatory cytokines). Twenty-four hours after OVA nebulization, airway hyperresponsiveness, inflammation, and remodeling was assessed.

**Results:** Administration of PFI-34051 and dexamethasone reduced the eosinophilic inflammation and airway hyperresponsiveness in asthma to reduce the airway remodeling. Treatment with Tubastatin A HCl reduced airway inflammation and was associated with decreased IL-4, IL-5 and total inflammatory cell count, as well as goblet cell metaplasia and subepithelial fibrosis; however, this outcome was not as effective as that with dexamethasone. TGF-β1 expression in the cytoplasm of airway epithelium of mice in the Tubastatin A HCl group was reduced and expression of α-SMA in the airway smooth muscle was also decreased.

**Conclusions:** The results suggested that treatment with HDAC inhibitors can reduce airway inflammation, airway remodeling, and airway hyperresponsiveness in chronic allergic airway disease in mice. HDAC6 may play a key role in the process of airway remodeling, and HDAC8 may play a key role in airway inflammation.

**Impact of ILC2 cells and Th2 cytokines in chronic rhinosinusitis on patients with severe asthma**

C.H. Wang, T.J. Lee, T.F. Sheng, H.P. Kuo  
Chang Gung Memorial Hospital, Department of Thoracic Medicine, Taoyuan, Taiwan, and Chang Gung Memorial Hospital, Division of Rhinology-Department of Otolaryngology, Taoyuan, Taiwan

**Background and Aims:** Coexistence of chronic rhinosinusitis (CRS) with asthma appears to impair asthma control, especially in severe asthma. Th2-driven cytokines are the major drivers in CRS. Type-2 innate lymphoid cells (ILC2s) respond to the cytokines of thymic stromal lymphopoietin (TSLP), interleukin (IL)-25 and IL-33 and may contribute to airway diseases such as CRS and asthma. To investigate whether the augmented Th2-cytokines in CRS might be related to sinusal tract ILC2s in response to enhanced IL-25, IL-33 and TSLP release in severe asthmatics, and be involved in asthma control.

**Methods:** Twenty-eight asthmatics (12 non-severe and 16 severe) with CRS receiving nasal surgery were enrolled. CRS severity was scored by endoscopy and CT scans. Lung function was measured before and after nasal surgery. Cytokine and ILC2s in nasal tissue were determined by real-time PCR and immunostaining.

**Results:** The predicted FEV1, inversely associated with CRS severity of CT or endoscopy scores. Higher expression of Th2-driven cytokines (IL-4, IL-5, IL-9, and IL-13), TSLP, IL-25 and IL-33 in nasal tissues was observed in severe asthma. Severe asthmatics had higher ILC2 cell counts in their nasal tissues. ILC2 counts were positively correlated with Th2-cytokines. Nasal surgery significantly improved asthma control and lung function decline in severe asthma and CRS.

**Conclusions:** The higher expression of IL-33/ILC2 axis-directed type 2 immune response in nasal tissue of CRS brought the greater decline of lung function in severe asthma. ILC2-induped the upregulated activity of...
**ORAL PRESENTATION 14 • RESPIRATORY INFECTIONS (NON-TUBERCULOUS): TOPICS IN LUNG INFECTION 2**

**THE EXISTENCE OF PSEUDOMONAS AERUGINOSA ISOLATION WAS ASSOCIATED WITH WORSE PROGNOSIS IN BRONCHIECTASIS**

H. WANG, X.B. JI, B. MAO
Shanghai Pulmonary Hospital, Respiratory and Critical Care Medicine, Shanghai, China

**Background and Aims:** Pseudomonas aeruginosa (P. aeruginosa) occupies an important niche in the pathogenic microbiome of bronchiectasis. The objective of this study is to evaluate the clinical characteristic and prognostic value of Pseudomonas aeruginosa in Chinese adult bronchiectasis patients.

**Methods:** This study enrolled 1188 patients diagnosed with bronchiectasis at Shanghai Pulmonary Hospital between January 2011 and December 2012. Patients related clinical data were reviewed and analyzed carefully. Following a median (interquartile range) follow-up duration of 44 (40-54) months, the data of 899 patients were collected and analyzed for the outcomes of mortality, annual exacerbation frequency, and health-related quality of life.

**Results:** P. aeruginosa was isolated from 232 patients, alongside other pathogens such as Aspergillus (n = 75) and Candida albicans (n = 72). There were a total of 74 deaths (12% of patients with P. aeruginosa, 7.3% of those without) during follow-up. The isolation of P. aeruginosa was a risk factor for all-cause mortality (HR, 3.07; 95% CI, 1.32-7.15; P = 0.009) and associated with suffering ≥3 exacerbations per year of follow-up (HR, 2.40; 95% CI, 1.20-4.79; P = 0.013). Patients with P. aeruginosa also scored worse on the Hospital Anxiety and Depression Scale (HADS) (anxiety, P = 0.005; depression, P = 0.001), Leicester Cough Questionnaire (LCQ) (P = 0.033) and modified medical research council (mMRC) scale (P = 0.001) compared to those without.

**Conclusions:** Isolation of P. aeruginosa in Chinese bronchiectasis patients is a significant prognostic indicator and should be a major factor in clinical management of the disease.
THE STUDY OF FACTORS ASSOCIATED WITH HOSPITAL ADMISSIONS IN BRONCHIECTASIS

D. R. U. DEVARAJ, P. RAMACHANDRAN, U. MAHESWARI, G. D’SOUZA
St John’s Medical College and Hospital, Department of Pulmonology, Bangalore, India

Introduction: Bronchiectasis continues to be a common chronic respiratory problem. Scant data is available about bronchiectasis with regards to microbiological profile and its relation to hospital admissions in South India.

Aims: To describe microbiological profile, etiology and frequency of hospital admissions in bronchiectasis patients.

Methods: All adults with bronchiectasis, between Jan 2015 to May 2016, were included in the study. Subjects with other structural lung diseases were excluded. Ethics committee approval and written informed consent from patients was obtained.

Demographic data, number of hospital admissions and sputum culture were recorded. Severity of bronchiectasis on HRCT using modified Reiff score (MRS) was assessed. Severe disease was defined as MRS of ≥7. Statistical analysis was done using SPSS 16.

Results: Seventy seven patients were studied. Mean age was 48.4 ± 13 years (range-22-82). M:F = 4:3. Most common cause of bronchiectasis was tuberculosis 23(29.8%), followed by pneumonia 8(10.3%), miscellaneous pneumonia 1(1.3%), and unknown in 22 patients. Pseudomonas was most common organism cultured 22 (28.5%), followed by Klebsiella 9(11.6%) and 8(10.3%) E.coli; 36 (46.7%) patients did not isolate any organism. Mean number of hospital admissions was 2 (Range – 2 to 7). In patients with pseudomonas infection, 13 were colonizers and had more number of hospital admissions as compared to other etiologic agents (p = 0.001).

There was no correlation between duration of illness and hospital admissions by ROC analysis. Number of hospital admissions increased as MRS score increased, (p = 0.001).

Conclusions: There was no correlation between duration of illness and hospital admissions. Frequency of hospital admissions was higher in patients with pseudomonas colonisation. Higher the MRS (>7 Reiff score) on HRCT, greater was the frequency of hospital admissions.

EXPERIMENTAL STUDIES ON TRACHEAL EPITHELIAL CELLS IN VITRO BY NONTYPEABLE HAEMOPHILUS INFLUENZAE

W. GUIFANG
huashan hospital, department of respiratory diseases, shanghai, China

Background and Aims: To explore the interaction of nontypeable Haemophilus influenzae (NTHi) strain ATCC49247 with primary rabbit tracheal epithelial (TE) cells.

Methods: (1) TE cells were isolated using low temperature protease digestion. TE cells were cultured on collagen gel-coated membranes at an air-liquid interface in serum-free medium. Under these conditions, TE cells first proliferated and then differentiated into a pseudostratified mucociliary epithelium. Then, TE cells were infected by NTHi. After 24 h, fixed cell cultures were processed for Scanning electron microscopy(SEM); (2) HBEC were isolated by using low temperature protease digestion and cultured in serum-free medium. Confluent epithelial cell were incubated with NTHi, NTHi + erythromycin(0.1 mg/L), NTHi + erythromycin(10 mg/L), NTHi + gentamicin(100 mg/L), NTHi + dexamethasone(0.1 mM) and normal untreated control cells after 24 h, respectively. Release of interleukin(IL)-8 and tumor necrosis factor(TNF)-α from the supernatant was assayed by enzyme-linked immunocorrent assay. The expression of ICAM-1 was examined by immunohistochemistry staining.

Results: (1) SEM indicated that bacteria adhered to nonciliated cells in the population. 90 percent of TE cells were either died or apotosised and cilia appeared to be broken. (2) NTHi-induced cells released significantly greater amounts of IL-8 and TNF-α (2172.18 ± 131.83, 7.22 ± 2.17 pg/ml, respectively) than normal untreated cells (115.76 ± 57.6322.84 ± 1.04 pg/ml) (p < 0.001). NTHi also significantly increased the total number of ICAM-1 positive cells from 10 ± 5%(in control untreated cultures) to 80 ± 5%(p < 0.001). Similarly, incubation of HBEC with 0.1 mg/L erythromycin and gentamicin significantly induced bronchial release of IL-8, TNF-α and the expression of ICAM-1, which was blocked by 10 mg/L erythromycin and 100μM dexamethasone.

Conclusions: (1) These studies indicated that NTHi could attach to nonciliated cells, devouring the bacteria by lamellipodia and microvilli, and that NTHi were toxic to TE cells and resulted in the death of TE cells. (2) HBEC can release IL-8 and TNF-α. NTHi may increase significantly the secretion and expression of proinflammatory cytokines. Erythromycin may have anti-inflammatory effects. Dexamethasone has distinct anti-inflammatory effects.
THE APPLICATION OF EBUS IN THE BRONCHI DIEULAFOY’S DISEASE

W. JIN
First People’s Hospital of Hangzhou, respiratory medicine, Hangzhou, China

Background and Aims: Dieulafoy’s disease in airway is one of many causes of recurrent and sometimes massive hemoptysis. Biopsy of the lesion may prove fatal. It's very important to recognize the disease rapidly. Endobronchial ultrasound (EBUS) can be of value in prompt diagnosis of the disorder.

Methods: The elevated lesion in bronchus were detected by using of EBUS before biopsy.

Results: Based on the EBUS, we currently have made diagnosis of Dieulafoy’s disease of bronchi in three patients with unexplained hemoptysis. Of which these patients, one was a 44-year-old male suffered from recurrent hemoptysis. Computed tomography of bronchial artery showed an absence of left upper pulmonary artery and patchy shadows in the left lower lobe. The segmental lobe on CT scan, flexible bronchoscopy revealed an elevated lesion in the left lower bronchus. The radial probe endobronchial ultrasound showed a circular anechoic area within the submucosa, circumscribed with a hyperechoic margin highly suggestive of vascular structures. Of note, the anechoic area beat rhythmically in keeping with the pulse. The DSA revealed a left tortuous bronchial artery. The diagnosis was established. After transcatheater embolization of the hyperplastic bronchial artery, DSA revealed complete disappearance of the abnormal bronchial artery.

Conclusions: EBUS is competent to the diagnosis of Dieulafoy’s disease of bronchi.

A CASE OF BRONCHIAL PYOGENIC GRANULOMA TREATED SUCCESSFULLY WITH AFTERLOADER RADIOTHERAPY

Y.P. LI,1 J.S. OUYANG,1 K.Y. YANG,2 M. YE,1 X.L. TIAN,2 C.S. CHEN1
The First Affiliated Hospital of Wenzhou Medical University, the department of respiratory and critical medicine, wenzhou, China, 2The First Affiliated Hospital of Wenzhou Medical University, the department of pathology, wenzhou, China, and 3Peking union medical college hospital, Department of Respiratory Medicine, Beijing, China

Background and Aims: Pyogenic granuloma (PG) is a benign polyvacular growth due to local chronic low-grade irritation or trauma, and characterized by excessive and exuberant tissue repair response with an inflammatory component, it often located on the skin and the mucosa of the alimentary, urinary and genital tracts. It is extremely rare on the respiratory tract. Pyogenic granuloma was established instead of bronchoscopic intervention therapy.

Methods: The patient received endobronchial radiotherapy of 15Gy-afterloader in Peking Union medical college Hospital, a total radiation exposure of 51Gy for each of three visits. His dyspnea and cough were dissolved, bronchoscopy examination showed that the left main bronchial lesions were smaller in June 2016 (Figure 2016-6-A;2016-6-B).

Conclusions: PG should be considered in the differential diagnosis of occupying lesion on respiratory tract. Local afterloader radiotherapy is a suggested treatment option for pyogenic granuloma on respiratory tract instead of bronchoscopic intervention therapy.
STUDY OF THE PATIENTS UNDER TREATMENT OF RESPIRATORY DISORDERS THAT WERE COMPROMISED WITH MEDIASTINAL EMPHYSEMA

A. ONG, K. DOBASHI, Y. KOGA, Y. HACHISU, H. TSURUMAKI, M. YATOMI, N. KASHARAYA, Y. TSUKAGOSHI, N. SUNAGA, T. MAENO, T. HISADA
Gunma University Graduate School of Medicine, Allergy and Respiratory Medicine, Maebashi, Japan

Background and Aims: We have experienced the complication of mediastinal emphysema relatively with high frequency, although the detail of this complication has not been well studied. So we tried to clarify the therapeutic experience in our department.

Methods: We have retrospectively studied the medical records of admitted patients with a diagnosis of mediastinal emphysema by CT findings since April 2008.

Results: 15 patients, 8 males and 7 females had an onset of mediastinal emphysema. Average age, body-mass index and serum albumin concentration were 66.8, 19.1, 3.3 g/dl. 7 patients were diagnosed as idiopathic interstitial pneumonia(IIP), 6 idiopathic pulmonary fibrosis(IPF) and one fibrotic non-specific interstitial pneumonia(NSIP). 4 patients were collagen vascular disease-associated interstitial pneumonia(CVID-IP), 2 rheumatoid arthritis and 2 dermatomyositis. 2 patients were bird-related chronic hypersensitivity pneumonia(BR-CHP), another patient was combined pulmonary fibrosis and emphysema(CPFE). Twelve patients had already been in condition to need home oxygen therapy. 5 patients were accompanied by subcutaneous emphysema, and 4 were concurrently and 3 were intertemporally accompanied by pneumothorax. It was notable that 12 patients were developed mediastinal emphysema after treatment with corticosteroids, including 5 patients who unfortunately resulted in death.

Conclusions: Our study indicates that interstitial lung diseases are associated with a significant rate of complication of mediastinal emphysema, almost after administration of corticosteroid therapy. Furthermore this complication have a possibility to be associated with poor prognosis. For fibrotic lung diseases which organized structures such as elastic fiber layer are damaged, corticosteroids may accelerate the tissue injury due to development of mediastinal emphysema. We must pay attention carefully to the complication of mediastinal emphysema during treatment of respiratory diseases notably there are fibrotic lung diseases. It is also thought to be quite important that we should adequately consider the patients’ risk and benefit on the occasion of decision of the start of treatment for interstitial lung disease especially with corticosteroids.

MDS was 0.1%. As the median survival time was 17 months after diagnosis of MDS-sPAP, the prognosis of MDS-sPAP was very poor.

Conclusions: The onset of MDS-sPAP could be high prevalence in Japan, compared as Caucasian countries. This suggests that MDS-sPAP in Japanese cases has some specific gene mutant, probably.

A LESSON FROM A CASE: RECURRANCE OF PULMONARY ALVEOLAR PROTEINOSIS AFTER BILATERAL LUNG TRANSPLANTATION IN A PATIENT WITH A NONSENSE MUTATION IN CSF2RB

T. TANAKA, M. TAKAKI, Y. KOMOHARA, Y. TSUCHIHASHI, D. MORI, K. HAYASHI, J. FUKUDA, N. YAMASAKI, T. NAGAYASU, K. ARIYOSHI, K. NAKATA, K. MORIMOTO
Nagasaki University Hospital, Department of Infectious Diseases, Nagasaki City, Japan, Kumamoto University, Department of Cell Pathology-Graduate School of Medical Sciences, Kumamoto City, Japan, Juzenkai Hospital, Department of Internal Medicine, Nagasaki City, Japan, Saga-ken Medical Centre Koseikan, Department of Pathology, Saga City, Japan, Nagasaki University, Department of Pathology, Nagasaki City, Japan, Nagasaki University Graduate School of Biomedical Sciences, Division of Surgical Oncology-Department of Translational Medical Science, Nagasaki City, Japan, and Nigata University Medical and Dental Hospital, Bioscience Medical Research Center, Niigata City, Japan

Background and Aims: Hereditary pulmonary alveolar proteinosis (hPAP) is a rare disease, caused by mutations in CSF2RA or CSF2RB, which encode GM-CSF receptor α and β respectively. Although some experimental therapeutic strategies have been proposed, no clinical case with treatment intervention has yet been reported.

Methods: We report a case of the recurrent PAP following lung transplantation. A 36-year-old woman developed PAP without serum GM-CSF autoantibodies. She was complicated with progressive pulmonary fibrosis, which required bilateral lung transplantation from living donors at the age of 42 years. The etiology of this PAP case was later attributed to a nonsense mutation in CSF2RB (Tanaka et al., J Med Genet 2011). Patient’s alveolar macrophages characteristics was assessed by Fluorescence in situ hybridization (FISH) and immunohistochemistry method during the clinical course after the lung transplant.

Results: PAP recurred 9 months after the lung transplantation. FISH revealed that donor-origin alveolar macrophages had been almost completely replaced with recipient-origin macrophages. PAP progressed with fibrosis in both transplanted lungs, and the patient died of respiratory failure complicated with bronchiolitis obliterans syndrome and Aspergillus infection 5 years after.

Conclusions: The clinical course of this case indicates that human alveolar macrophages do not maintain their population only by self-renewal but depend on a supply of precursor cells from the circulation. Our experience raises a possibility that bone marrow transplantation might be an option for treatment of severe PAP with GM-CSF receptor gene deficiency. However, indication for the feasibility of bone marrow transplantation is still controversial among hematologists because of a lack of precedent. This case report should enhance discussion over the new treatment approach for hPAP.

Acknowledgements:Supported by a grant, “Rare lung diseases (pulmonary alveolar proteinosis, congenital interstitial lung disease and hereditary hemorrhagic telangiectasia) (H24-Nanchitou[Nanchi]-Ippan-035),” from the Ministry of Health, Labour and Welfare, Japan.
CONCLUSIONS:

Class II-dependent disease.

Methods: We first showed that the anti-GM-CSF autoantibody was reported not to correlate with the disease severity score (DSS) of aPAP. Recently, we have reported that HLA class II molecule transports and presents misfolded full-length self-protein on the cell surface, and the protein/HLA class II complex could be the target of autoantibodies in autoimmune diseases (Jin et al., Proc Natl Acad Sci USA 2014; Tanimura et al., Blood 2015). The aim of this study was to investigate the role of anti-GM-CSF/HLA class II complex autoantibody in aPAP.

Results: After transfection, full-length GM-CSF was presented by HLA-DR on the cell surface. The efficiency of GM-CSF presentation was different depending on applied HLA-DR alleles, especially two critical amino acids (b47 and b71) in HLA-DRb. Immunohistochemistry showed that HLA-DR was highly expressed in alveolar macrophages and respiratory epithelial cells in aPAP lung. The titer of serum anti-GM-CSF autoantibody distinguished patients with aPAP from healthy controls (sensitivity, 100%; specificity, 90.5%). Anti-GM-CSF autoantibody levels measured by ELISA did not correlate (r = 0.36, p = 0.11) with anti-GM-CSF/HLA-DR complex autoantibody levels measured by ELISA did not correlate (r = 0.36, p = 0.11), while anti-GM-CSF/HLA-DR complex autoantibody levels significantly correlated with DSS among aPAP patients (p = 0.08, p < 0.01).

Conclusions: All these results suggested that GM-CSF/HLA class II complex is the target of autoantibody in aPAP and that aPAP is a HLA class II-dependent disease.

ORAL PRESENTATION 16 - COPD: IMPROVING MANAGEMENT IN COPD

DETECTION OF MICROBIAL PATHOGENS USING A MULTIPLE TARGET QUANTITATIVE POLYMERASE CHAIN REACTION (qPCR) ARRAY IN PATIENTS WITH ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

H. CUTCHELL, J. SHAW, F. GOH, R. BOWMAN, K. FONG, I. YANG
The Prince Charles Hospital, University of Queensland Thoracic Research Centre, Chermside, Australia

Background and Aims: Acute exacerbations of chronic obstructive pulmonary disease (COPD) lead to morbidity and mortality. Culture-independent methods, such as quantitative PCR (qPCR) may be more sensitive for detecting potentially pathogenic microorganisms in exacerbations. This project aimed to identify bacterial and fungal load of specific pathogens in sputum during COPD exacerbation and the stable state, using qPCR compared to conventional culture.

Methods: 40 COPD patients provided sputum and blood samples during exacerbation (n = 24) and stable state (n = 16). Sputum was selected for sputum plugs without saliva contamination, extracted for nucleic acids and tested by qPCR for 47 targets (16S rRNA of bacterial, 18S rRNA fungal pathogens and antibiotic resistance genes).

Results: qPCR detected target genes in 38 (95%) of the 40 sputum samples, and was more sensitive than culture, which was positive for bacterial species in 11/31 (35%) samples cultured. The most prevalent bacterial species detected by qPCR were Streptococcus pneumoniae (80%), Pseudomonas aeruginosa (47%), Pseudomonas stutzeri (36%) and Haemophilus influenzae (25%). Mean bacterial 16S copies and numbers of bacterial species detected by qPCR were similar between exacerbation and stable patients (Figure 1). No statistically significant correlation was observed between total 16S bacterial copy number per mL sputum and smoking status or disease severity based on lung function impairment.

Conclusions: Use of a comprehensive qPCR array for bacterial and fungal pathogens is feasible for COPD sputum, and is a more sensitive measure of sputum pathogens, in both exacerbation and stable patients, compared to conventional culture methods. Implementation of qPCR in routine clinical practice for pathogen detection in COPD sputum warrants further investigation, to improve diagnostic techniques and understanding of the pathogenesis of COPD exacerbations.

EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON RESPIRATORY MECHANICS AND NEURAL RESPIRATORY DRIVE IN PATIENTS WITH STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

L. YUN, P. LUO, L. YUWEN, C. YITAI, H. XIA, W. KAI, X. CHEN
Zhujiang Hospital- Southern Medical University- Guangzhou -Guangdong province- C, Department of Respiratory Medicine, Guangzhou, China

Background and Aims: For non-hypoxic individuals with stable chronic obstructive pulmonary disease (COPD), early intervention of continuous positive airway pressure (CPAP) as a form of pulmonary rehabilitation may alleviate the intrinsic positive end-expiratory pressure (PEEP), rectify the abnormal pathophysiologic changes and help postpone the disease progression. However, it lacks relevant evidence. Therefore, we aim to investigate the effects of CPAP on respiratory mechanics and neural drive in these patients.

Methods: 22 patients with moderate-to-severe COPD were enrolled and they received CPAP with 4 cmH2O initially and increased in increments of 1 cmH2O to a maximum of 10 cmH2O. During rested tidal breathing and during different levels of CPAP, we monitored and calculated some indices including minute ventilation (Ve), end expiratory lung volume (EELV), dynamic PEEPi (PEEPi, dyn), airway resistance (Raw), and pressur-time product of transdiaphragmatic pressure (PTPdi).

Results: 19 patients successfully completed the experiment. After CPAP was applied, Raw, PTPdi, and PTPes decreased first and then increased after 7 cmH2O, but there were no marked differences among 5 ~ 10 cmH2O groups (all P > 0.05). In comparison with at rest condition, EELV decreased significantly at CPAP 4 ~ 8 cmH2O, but increased markedly after 8 cmH2O. PEEPi, dyn decreased from 2.18 ± 0.98 cmH2O to 1.37 ± 0.55 cmH2O. As CPAP increased, RMS increased gradually, but there were no marked differences among different groups. Ve and Ve/RMS increased gradually as the increment of CPAP level, but it decreased at 8 cmH2O. Ve correlated negatively with Raw, PTPdi and PEEPi, dyn (all P < 0.05).

Conclusions: In COPD patients without respiratory failure, appropriate application of CPAP can decrease PEEPi, airway resistance and work of breathing, as well as reducing lung hyperinflation, increasing minute ventilation and improving the ventilation-drive coupling. This study may assist decision-making in the application of CPAP in patients with stable COPD.
SPUTUM BACTERIAL AND FUNGAL DYNAMICS DURING EXACERBATIONS OF SEVERE COPD

S. JIN1, L. ZHENGYU2, C. RONGCHANG2
1Nanfang Hospital- Southern Medical University-, Department of Respiratory and critical care medicine-, guangzhou, China, and 2First Affiliated Hospital of Guangzhou Medical University, State Key Laboratory of Respiratory Disease- Guangzhou Institute of Respiratory Disease, guangzhou, China

Background and Aims: The changes in the microbial community structure during acute exacerbations of severe chronic obstructive pulmonary disease (COPD) in hospitalized patients remain largely uncharacterized. Therefore, further studies focused on the temporal dynamics and structure of sputum microbial communities during acute exacerbation of COPD (AE-COPD) would still be necessary. Our findings highlight that COPD patients have personalized structures and varieties in sputum microbial community during hospitalization period.

Methods: In our study, the use of molecular microbiological techniques provided insight into both fungal and bacterial diversities in AE-COPD patients during hospitalization. In particular, we examined the structure and varieties of lung microbial community in 6 patients with severe AECOPD by amplifying 16S rRNA V4 hyper-variable and internal transcribed spacer (ITS) DNA regions using barcoded primers and the Illumina sequencing platform.

Results: Sequence analysis showed 261 bacterial genera representing 20 distinct phyla, with an average number of genera per patient of >157, indicating high diversity. Acinetobacter, Prevotella, Neisseria, Rothia, Lactobacillus, Lepotrichia, Streptococcus, Veillonella, and Actinomyces were the most commonly identified genera, and the average total sequencing number per sputum sample was >10000 18S ITS sequences. The fungal population was typically dominated by Candida, Phialocephala, Aspergillus, Penicillium, Cladosporium and Euphelia.

Conclusions: Our findings highlight that COPD patients have personalized structures and varieties in sputum microbial community during hospitalization period.

BLOOD EOSINOPHILIA AS PREDICTOR FOR PATIENT OUTCOMES IN COPD EXACERBATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

R.E. VILLALOBOS, J. MAGALLANES, A. DAVID-WANG
University of the Philippines-Philippine General Hospital, Department of Medicine, Manila, Philippines

Background and Aims: COPD exacerbations are associated with significant morbidity, mortality, and substantial healthcare cost. The eosinophilic phenotype of COPD has been demonstrated to respond better to corticosteroids thus providing better clinical outcomes. This review aims to elucidate further the correlation between blood eosinophilia and outcomes in hospitalized COPD exacerbations.

Methods: We systematically searched published and unpublished literature for potential studies that fulfilled our eligibility criteria. Inclusion criteria include any cohort (prospective or retrospective), case-control or randomized trials that looked into the association of blood eosinophilia and outcomes in hospitalized COPD exacerbation patients. The primary study outcome was length of hospitalization; other outcomes include readmission and mortality rate within 1 year, in-patient mortality, and need for mechanical ventilation. An extensive eligibility, methodological and risk of bias assessments were performed independently by two authors adhering to the MOOSE and Cochrane standards.

Results: Six studies, with a total of 7293 patients, were included in the review. Five are retrospective cohorts and one is a retrospective analysis of a subgroup of a randomized trial.

Patients with blood eosinophilia had significantly shorter hospital stay compared to non-eosinophilic patients (mean difference 0.68 days [95% CI 1.09, 0.27]). Eosinophilic patients had significantly less frequent readmissions (odds ratio/OR 0.69 [95% CI 0.55, 0.87]) but there was no statistically significant difference in the 1-year mortality rate (OR 0.88 [95% CI 0.73, 1.06]). Analysis showed a trend toward lower in-patient mortality among eosinophilic patients, although this difference is not statistically significant (OR 0.53 [95% CI 0.27, 1.00]). Furthermore, COPD patients with eosinophilia had significantly less need for mechanical ventilation during an exacerbation (OR 0.56 [95% CI 0.35, 0.89]). Only the primary outcome was significantly heterogeneous.

Conclusions: COPD patients with blood eosinophilia had significantly shorter hospital stay, less frequent readmissions, and are less likely to require mechanical ventilation compared to the non-eosinophilic phenotype.
COLLABORATIVE PARTNERSHIPS BETWEEN A HOSPITAL AND LOCAL GYM FACILITIES TO SUCCESSFULLY FACILITATE LONG-TERM PHYSICAL ACTIVITY SELF-MANAGEMENT

M. TRAN
St Vincent’s Hospital, Subacute Ambulatory Care Services, Fitzroy, Australia

Background and Aims: All types of cardiopulmonary rehabilitation, including pulmonary rehabilitation, improve and optimise client health status, quality of life and even influences morbidity and mortality. They form an essential part of a client’s comprehensive management plan. However, the initial benefits are known to reduce over 6-12 months post rehabilitation. This study provides insight into the viability and benefits of a hospital-gym collaboration to ensure longer-term outcomes.

Methods: Prospective observation cohort study of 63 clients recruited post cardiopulmonary rehabilitation to continue their exercise program in a local community gym. Clients were given appropriate skill development to enable them to safely exercise in a gym environment and financial assistance for gym-memberships was provided. Professional development support was provided to gym instructors to increase their knowledge and confidence with this cohort. Physical and psychosocial data collected before and after hospital rehabilitation, at commencement at the gym and at 3 months post participation.

Results: Clients’ mean age was 66 (62% male). At 3 months post gym commencement, 6-Minute-Walk-Test distance improved from 501 m to 549 m (p = 0.006), 1 Repetition-Max (1RM) seated-row improved from 40.0 kg to 43.6 kg (p = 0.055), 1RM leg-press improved from 111 kg to 130 kg (p = 0.001). All SF-36 domains and the physical and mental component scores remained unchanged in the gym setting, while PHQ-9 score (depression screening tool) improved (p = 0.001). There were zero safety incidents during this trial.

Conclusions: Guided gym transition post hospital rehabilitation by hospital staff has been safe and effective for people with chronic cardiopulmonary conditions. Physical and psychological outcomes show marked improvements beyond the initial hospital rehabilitation program. Gym facilities are an ideal location for chronic cardiopulmonary clients to continue their exercise regimes and provide a positive therapeutic influence on clients’ exercise capacity and mood. Collaborations between hospital and local gym facilities can assist with establishing longer-term continuous adherence to exercise for this cohort.

THE CLINICAL AND PSYCHOSOCIAL IMPACTS ON MANAGEMENT TO PATIENTS WITH COPD IN HARP SETTINGS

R. PANG, P. VAN LEUR, S. SULLIVAN, C. WOTHERSPOON
Peninsula Health, Hospital Admission Risk Program, Frankston, Australia

Background and Aims: COPD patients follow the GOLD guidelines and evidenced based practice to manage their condition, however, adherence can be challenging once discharged from hospital. Community supports vary depending on completion of referral, patient compliance; patient and carer supports and COPD management. The Hospital Admission Risk Program (HARP) at Peninsula Health developed a respiratory management package for COPD patients frequently presented to hospital. It aims to provide holistic approach to patients in the community in order to manage them clinically with better quality of life.

Methods: HARP employs specialist respiratory clinical nursing consultants (CNCs) who review all referred COPD clients, especially those newly commenced on long-term home oxygen therapy. CNCs develop a COPD management package. CNCs complete comprehensive assessment, provide education and organise multidisciplinary support. Lung function test, pulmonary rehabilitation program and smoking cessation referrals are organised per needs. They liaise with hospital specialists; GPs and help manage any psychosocial implication associated with COPD.

Early discussion on advance care planning (ACP) and palliative care approach on COPD management was identified as better patient-centred care. In 2014, CNCs worked closely with ACP clinicians and developed partnership with Peninsula Home Hospice to facilitate better quality of life management of patients in the community.

Results: Between 1/7/2015-30/6/2016, CNCs provided 1466 contacts to 216 patients through this management package. Pharmacist reviewed 111 patients’ medication use; 103 patients (47.7%) have minimum of 2-additional allied health consultations during the care period. Of interest, 106 patients had their ACP related documentation completed. Recent ACP survey with respiratory patients showed that they felt less anxious about their future health-care and more control in direct medical care with having an ACP in place.

Conclusions: The COPD management package at HARP provides holistic management and care in the community; the early interventions in ACP support patients with good symptoms management and better quality of life.
PRODUCTIVE COUGH AS A PREDICTOR OF EXACERBATIONS AND MORTALITY IN THE UPLIFT® TRIAL

L. MCGARVEY,1 N. METZDORF,2 A. MUELLER,3 D.P. TASHKIN4
1Queen’s University, Centre for Infection and Immunity, Belfast-Northern Ireland, United Kingdom, 2Boehringer Ingelheim Pharma GmbH & Co. KG, Respiratory Medicine, Ingelheim am Rhein, Germany, 3Boehringer Ingelheim Pharma GmbH & Co. KG, Biostatistics and Data Sciences Europe, Biberach an der Riss, Germany, and 4David Geffen School of Medicine UCLA, Department of Medicine, Los Angeles, CA, USA

Background and Aims: Productive cough is a common symptom of chronic obstructive pulmonary disease (COPD); however, its role in predicting clinical and treatment outcomes is unclear. We assessed risks of exacerbation and mortality relative to productive cough, using data from the Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT®) trial.

Methods: UPLIFT® was a 4-year randomized clinical trial, evaluated tiotropium HandiHaler® 18 μg versus placebo in patients with COPD. Patients were categorized by treatment and presence of baseline productive cough. Hazard ratios (HR) and confidence intervals (CI) were calculated using a Cox regression model with factors for treatment, productive cough and interaction term.

Results: Overall, 5991 patients were analyzed. Patients with productive cough were more likely to be current smokers, GOLD Group D (Table 1), and to have had ≥2 moderate-to-severe or severe exacerbations in the year prior to study enrolment than those without (Table 2). Risk of moderate-to-severe exacerbations was increased with productive cough (P = 0.001 versus no productive cough), reduced with tiotropium (P < 0.0001 versus placebo); treatment effect was independent of productive cough (HR versus placebo [95% CI]: Productive cough, 0.869 [0.808-0.935], P = 0.0002; no productive cough, 0.835 [0.742-0.939], P = 0.0027); results were similar for severe exacerbations (Figure 1). Patients with productive cough were at higher risk of cardiovascular death (P = 0.0006 versus no productive cough), which was reduced with tiotropium (P = 0.01 versus placebo); treatment effect was independent of productive cough (HR versus placebo [95% CI]: Productive cough, 0.834 [0.632-1.101], P = 0.2002; no productive cough, 0.512 [0.285-0.919], P = 0.0250). All-cause mortality showed a similar pattern (Figure 2), but there was no effect of productive cough or treatment on respiratory death.

Conclusions: Productive cough was associated with increased risk of exacerbations and mortality, in particular cardiovascular mortality. Tiotropium improved exacerbation outcomes independently of productive cough.

Acknowledgements: Editorial and writing support was provided by Jennifer Fuchs of PAREXEL, funded by Boehringer Ingelheim.

Table 1: Baseline characteristics of participants by treatment and presence of productive cough.

Table 2: Exacerbation incidence by treatment and presence of productive cough.

Figure 1: Analysis of time to first moderate-to-severe exacerbation by treatment and presence of productive cough at baseline.

Figure 2: Analysis of time to death (vital status) by treatment and presence of productive cough at baseline.

Respirology (2016) 21 (Suppl. 3), 3–213 © 2016 Asian Pacific Society of Respirology
Background and Aims: Leptin is an important adipocyte-derived cytokine which regulates metabolic, endocrine and immune function. Mounting evidences have demonstrated that leptin is closely related to various allergic diseases, such as asthma and allergic rhinitis. This study aimed to examine the relationship between serum leptin and airway eosinophil in patients with asthma.

Methods: The study included 107 subjects: 78 patients with asthma (8 obese and 70 non-obese) and 29 health controls. All subjects were prospectively evaluated and analyzed. Serum leptin levels in all subjects, percentages of eosinophils and neutrophils in induced sputum in patients were measured.

Results: Obese asthmatic patients had significantly higher leptin levels (29.7 ± 10.8 ng/ml) than non-obese asthmatic patients (13.3 ± 9.0 ng/ml, P < 0.001) and health controls (15.2 ± 11.7 ng/ml, P = 0.003) (Figure 1). In patients with asthma, serum leptin levels were positively related to percentages of eosinophils in induced sputum (r = 0.332, P = 0.026) (Figure 2), but not related to percentage of neutrophils in induced sputum (r = -0.215, P = 0.16) and blood eosinophils (r = -0.056, P = 0.679). Percentage of induced sputum eosinophils was related to ACT Score (r = -0.356, P = 0.016) (Figure 3). In general linear model analysis, after adjustment for BMI, count of blood eosinophils, serum IgE, allergic rhinitis, using inhaled corticosteroids and positive allergen test, serum leptin levels remained independently related to percentages of eosinophils in induced sputum (P = 0.007).

Conclusions: Serum leptin levels are significantly elevated in obese patients with asthma. Additionally, serum leptin is positively and independently related to increased airway eosinophils in patients with asthma. Leptin may play an important role in pathogenesis of asthma.

Acknowledgement: This study was supported by the National Natural Science Foundation of China-Youth Fund Project (81400017) and Peking University Third Hospital Starting Foundation for Returned Overseas Scholars (Y77429-01).
Conclusions: The decrease of FEV1 and the slope of the linear regression curve. We divided patients into two groups based on exacerbation histories. Results: 64 of 135 asthma patients were enrolled in this study. The mean follow up period was 55.2 months (48-60 months). The annual changes of forced expiratory volume in one second (FEV1), resistance at 5Hz (R5), reactance at 5Hz (X5), resonant frequency (Fres) were 6.2 ml/year, 0.033 \( \pm \) 0.028 cmH2O/L/s/year, 0.012 \( \pm \) 0.020 cmH2O/L/s/year, -0.011 \( \pm \) 0.048 cmH2O/L/s/year, -0.068 \( \pm \) 0.023 cmH2O/L/s/year and 0.570 \( \pm \) 0.0868 Hz, respectively. 31 (48.4%) patients experienced exacerbations. The decrease of FEV1 and the increase of R5 and Fres were greater in patients with exacerbations than patients experienced exacerbations. The number of peripheral blood basophils was greater in patients with exacerbations than patients without. Conclusions: Exacerbations of asthma lead not only lung function decline but also increase of resistance and reactance of airway.

MAJOR GRASS POLLEN ALLERGENS AND COMPONENTS DETECTED IN A SOUTHERN CHINESE COHORT OF PATIENTS WITH ALLERGIC RHINITIC AND/OR SATHMA

W. LUO, B. SUN
State Key Laboratory of Respiratory Disease- National Clinical Research Center o, Guangzhou Institute of Respiratory Diseases, Guangzhou, China

Background and Aims: There is so far a paucity of data about allergen component-resolved diagnosis, and the prevalence of grass pollen allergen components in China, in contrast to those from western countries. Even in this country, allergies to grass pollen allergen components in the vast south are inadequately described. This study aimed to determine the major sensitizing grass pollens in Guangzhou, the largest city in southern China.

Methods: Included in this study were 258 patients having allergic rhinitis with or without asthma and 88 healthy controls. ImmunoCap® was used to examine the serum sIgE to Bermuda, Timothy, and Japanese hop. Subjects who tested positive were further examined for sIgE to Bermuda antigen Cyn d 1, Timothy antigens Phl p 1/4/5/6/7/11/12, and CCD. The relationship of grass pollen allergy to specific antigen sensitization was assessed.

Results: 22.5% of patients with allergic rhinitis and/or asthma were positive for Bermuda-sIgE, 13.6% for Timothy-sIgE, and 7.0% for Japanese hop-sIgE. These patients were more likely to be sensitized compared with controls (p < 0.001). Of the Bermuda-sIgE positive patients, 53.4% were Cyn d 1 positive and 60.3% were Timothy-sIgE positive. Of the Timothy positive patients, 100% were positive for Phl p 4, 17.1% were positive for Phl p 1 and 8.6% tested positive for Phl p 5/6/7/11/12. Patients with high Bermuda-sIgE levels were more likely to be positive for pollen. In 41.4% of Bermuda grass positive patients, CCD-sIgE was also positive. Sensitization to Phl p 4 was significantly correlated with CCD (r = 0.32).

Conclusions: In summary, we found that these southern Chinese patients with allergic rhinitis and/or asthma tested positive for Bermuda, Timothy, and Japanese hops sIgE. A high Bermuda-sIgE level may predict sensitization to other grasses. Correlations between sensitization to CCD and grass pollen allergens suggested a likelihood of cross-reactivity. Further in vitro inhibition assays are required to confirm this relationship.
Background and Aims: Data on adult asthma is scarce in Sri Lanka. The objective of this study was to estimate the prevalence of asthma and related symptoms amongst adults in the general population.

Methods: A multi-centered, cross-sectional study was conducted using an interviewer-administered translated version of the screening questionnaire of the European Community Respiratory Health Survey from June to December 2013 in 7 provinces of Sri Lanka. Subjects were selected randomly from different regions by stratified sampling. The prevalence of asthma was defined as "wheezing in the past 12 months (current wheeze)", "self-reported attack of asthma in the past 12 months" or "current asthma medication use".

Results: The study comprised 1872 subjects (45.1% males, 48.8% aged 18-45 years) of which 12.2% were current smokers. In the total population, the prevalence of current wheeze was 23.9% (95% CI: 22.0%-25.9%), of self-reported asthma was 11.8% (95% CI: 10.3%-13.2%) and of current asthma medication use was 11.1% (95% CI: 9.6%-12.5%). The prevalence of asthma according to a positive response to either of the above questions was 31.4% (95% CI: 29.3%-33.4%). The prevalence of symptom was higher in adults aged >45 years. Of those with current wheeze, 60.9% denied a diagnosis of asthma and only 38.2% admitted to use of asthma medication.

Conclusions: The prevalence of asthma in Sri Lankan adults is high in comparison with global data. A significant percentage of symptomatic individuals deny having asthma and are not on medication.

THE PREVALENCE OF ASTHMA IN SRI Lankan ADULTS

D.L. AMARASIRI,1 U.C.M. UNDUGODAGE,2 H.K.M.S. SILVA,3 A. SADIEKEN,4 W. GUNASINGHE,4 A. FERNANDO,4 A.R. WICKRAMASINGHE,4 A. SADIKEEN,4 W. GUNASINGHE,4 A. FERNANDO,4 D.L. AMARASIRI,1 U.C.M. UNDUGODAGE,2 H.K.M.S. SILVA,3 A. SADIEKEN,4 W. GUNASINGHE,4 A. FERNANDO,4 A.R. WICKRAMASINGHE,4 A. SADIKEEN,4 W. GUNASINGHE,4 A. FERNANDO,4

ASSOCIATION BETWEEN REVERSIBILITY ON SPIROMETRY AND INTERLEUKINS IN ASTHMA WITH FOOD SENSITIZATION

N. MALHOTRA, R. KUMAR
Vallabhbhai Patel Chest Institute, Department of Pulmonary Medicine, New Delhi, India

Background and Aims: Asthma is a common respiratory illness involving airway inflammation and hyper responsiveness. Previously, it was found that 29% asthmatics in India have food allergen sensitization. Serum values of interleukins are raised in patients of asthma. But there is little data about interleukin levels in the Indian asthmatic population with food sensitization. In the present study we looked for any association between inflammatory marker levels and bronchodilator induced reversibility on spirometry in patients of food sensitized asthmatics.

Methods: This was a prospective study, done in the outpatient department at a respiratory specialty hospital. A total of 203 patients diagnosed with bronchial asthma according to GINA guidelines were enrolled. These patients underwent spirometry and reversibility response evaluation, skin prick testing against food allergens, and quantitative serum ILs 5, 6, 13 and 13 levels.

Results: Out of 203 asthma patients, 94 were sensitized to at least one food allergen. On spirometry, 24.5% food sensitized asthmatics showed a positive reversibility response. Patients with reversibility were sensitized to a higher number of allergens (6.8 vs 3.1, p value 0.0018), and had a higher serum IL 5 level (15.4 vs 11.3 pg/ml, p value 0.0428). These patients showed a higher level of IL 13 (25.6 vs 22.1, p value 0.13), and lower values of IL 4 (14.1 vs 15.5, p value 0.57) and IL 6 (35.0 vs 40.8, p value 0.42).

Conclusions: Asthmatic patients with food sensitization who had a positive bronchodilator reversibility response on spirometry were sensitized to a significantly higher number of allergens. These patients had a significantly higher serum levels of ILs 5 and 13.

EARLY NON-INVASIVE VENTILATION VERSUS CONVENTIONAL OXYGEN THERAPY IN IMMUNOCOMPROMISED PATIENTS WITH RESPIRATORY FAILURE: A META-ANALYSIS

R.E. VILLALOBOS, U.K. GOPEZ, K. FLORES
University of the Philippines-Philippine General Hospital, Department of Medicine, Manila, Philippines

Background and Aims: Respiratory failure is common in immunocompromised patients. Intubation and mechanical ventilation (MV) is the mainstay of treatment but is associated with increased risk of pneumonia and other complications. Non-invasive ventilation (NIV) is an alternative to MV in a select group of patients and aims to avoid the complications of MV. In these patients, we performed a meta-analysis on the effect of early NIV versus conventional oxygen therapy in immunocompromised patients with respiratory failure. Risk of bias and acceptability assessment were independently performed by the authors.

The primary outcome of interest was intubation and MV rate. The secondary outcomes were ICU and all-cause mortality, ICU length of stay and duration of mechanical ventilation.

Results: Four studies with a total of 553 patients met the criteria for inclusion and were included in the analysis. Rate of intubation and mechanical ventilation was significantly lower in the patients treated with early NIV versus those given oxygen alone (RR = 0.73[0.59-0.89]). This result of the primary outcome was significantly heterogeneous (I2 = 55%). Upon sensitivity analysis and removal of source of heterogeneity, the benefit of early NIV in reducing intubation and mechanical ventilation rate was preserved (RR = 0.49[0.33-0.73]). Early NIV also significantly decreased ICU mortality rate (RR 0.52 [0.28-0.97]) and ICU length of stay (mean decrease of 1.08 days [range 1.50-0.65]). However, it did not decrease all-cause mortality but showed a trend toward reduction (RR = 0.77[0.53-1.11]). It also did not reduce the days on mechanical ventilator (mean decrease of 0.08 [range: -0.49-0.33]).

Conclusions: In immunocompromised patients with respiratory failure, early NIV reduced intubation rates and decreased ICU mortality and length of stay compared to standard oxygen therapy.
ACCURACY OF PREDICTIVE EQUATIONS FOR RESTING ENERGY EXPENDITURE ESTIMATION IN THAI MECHANICALLY VENTILATED PATIENTS

N. KONGPOLPROM
Chulalongkorn University- Thai Red Cross, Division of Pulmonary and Critical Care Medicine- Department of Medicine- Faculty of Medicine, Bangkok, Thailand

Background and Aims: Indirect calorimetry is the gold standard for determining calorie-need in critically-ill patients. However, it is rarely affordable in our country. Predictive equations are the alternatives. We aimed to evaluate accuracy of 11 equations for estimating resting energy expenditure (REE) in ventilated-patients.

Methods: This study included ventilated-patients, who underwentREE-measurement by indirect calorimetry using an ECOVX-module integrated in Engstrom ventilator, in medical intensive care units in Chulalongkorn hospital from January 2014 to May 2016. Patients receiving continuous hemo dialysis, or assisted with high ventilator settings; FIO2 ≥ 60% or PEEP ≥ 12 cmH2O, or an air leak were excluded. Estimated REE-values were calculated by 11 predictive-equations shown in figure1. Accuracy of the equations, defined as calculated-values within 90% and 110% of measured-REE, was analyzed. Correlation and agreement between predictive-values and measured-values were tested by Spearman’s ρ and Bland-Altman methods.

Results: Data from 24 ventilated-patients with a median age of 64.5 years, a median height of 160 cm, and a median body mass index (BMI) of 22.95 Kg/m² were collected. Fifty-percent of the patients were male and 40% of them had BMI of more than 30 Kg/m². The accuracy of all equations varied from 6.7% to 48.1%. Regardless of BMI, the predictive precision among these equations was poor. Penn state-2010 equation had the maximal accuracy (48.1%) with mean bias of 97.6 Kcal/day and 11.64% of measured-REE. Ireton-Jones 1992 and 2002, Penn State-2003(MSJ), Penn State-2010, Swinamer-1990, Faisy and Brandi equations tended to overestimate REE, while ACCP, HBE, MSJ, and Penn State-2003(HBE) tended to underestimate energy-requirements. Moreover, despite significant positive correlations (r = 0.445-0.778), the Bland-Altman plots showed wide intervals of limits of agreement (larger than 10% of the measured-REE), indicating clinically unacceptable differences between measured-REE and REE estimated by each equation.

Conclusions: No predictive-equations precisely estimated REE or substituted for indirect calorimetry in mechanically ventilated-patients.

ANTENATAL DIAGNOSIS OF CONGENITAL CYSTIC ADENOMATOID MALFORMATION OF THE LUNG: A CASE REPORT

K. ALCANTARA
Cebu, Philippines

Background and Aims: Congenital cystic adenomatoid malformation (CCAM) is a rare developmental abnormality with an incidence of 1 in 25,000 to 1 in 35,000 live births. Increasing sophistication of ultrasonography has allowed for its antenatal diagnosis and better surveillance. Prenatal diagnosis of CCAM has provided better understanding of tumor evolution and predicts its management. Confirmation of diagnosis can be achieved via CT scan. Surgical intervention can be safely considered in symptomatic CCAM.

THE RESEARCH OF EPIDEMIOLOGY OF SEROUS CAVITY IN SEVERE SEPSIS AND THE PATHOGENESIS OF BLOODY EFFUSION

M. XUE
Zhongshan Hospital, Department of Emergency Medicine, Shanghai, China

Background and Aims: We have found that most patients with severe sepsis are accompanied with poly-serous cavity effusions in preliminary researches are still needed. This research aims to explore the pathogenesis of bloody serous cavity effusions in patients with severe sepsis and determine the blood concentration of VEGF, VEGFR, Ang, SICAM-1, SVCAM-1, Serpin1 and VEC adherin, together with hsCRP and PCT in patients with bloody/non-bloody effusions, healthy control and non-sepsis ICU patients.

Methods: The study enrolled 45 patients diagnosed with severe sepsis and underwent thoracentesis. At the same time, we collected 30 non-sepsis ICU admissions and 30 healthy volunteers. After peripheral blood serum separated, enzyme-linked immunosorbent assay (ELISA) was used to test the sepsis patients’ blood serum concentration of VEGF, VEGFR, Ang, SICAM, SVCAM, Serpin1 and VEC adherin, together with hsCRP and PCT, then controlled those indices of healthy individuals and non-sepsis ICU admissions with sepsis ICU admissions.

Results: The concentration of VEGF was undifferentiated between severe sepsis group and healthy volunteers. Compared with the concentration of VEGFR in healthy volunteers, it was dramatically higher in ICU non-sepsis group and the severe sepsis group, and the bloody effusion group rose more sharply.

Conclusions: The inflammatory reaction induced by sepsis infection in bloody effusion patients is more severe. On the basis of the physiological function together with the data from ELISA tests, we conclude that the vascular permeability in bloody effusion group is quite higher than in non-bloody group, then leading to exudation and bloody effusions.
INCIDENT AND ASSOCIATION FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNIT IN A UNIVERSITY HOSPITAL, MALAYSIA

M. KHAN1, Z. MOHAMED2, S. BINTI ALI3, R. BASRI4, N. SADDKI1, N. SUKMININGRUM5
1Universiti Sains Malaysia, Department of Dental public health, Kota Bharu, Malaysia,
2Universiti Sains Malaysia, Department of Medical Microbiology & Parasitology, Kota Bharu, Malaysia,
3Universiti Sains Malaysia, Department of Cardio anaesthesia and intensive care, Kota Bharu, Malaysia,
4Universiti Sains Malaysia, Department of Neuroscience, Kota Bharu, Malaysia, and
5Universiti Sains Malaysia, Department of Medical public health-School of dental sciences, Kota Bharu, Malaysia

Background and Aims: Ventilator-associate pneumonia is an important cause of nosocomial infections that are associated with high mortality and mortality rates, prolonged intensive care(ICU) stay and additional hospital cost. The objective of the study was to describe the incidence of VAP, mortality, association factors of VAP, and characteristics of VAP patients from all patients admitted to ICU of Hospital Universiti Sains Malaysia in year 2013.

Methods: We retrospectively reviewed 300 adult patients, who were admitted to Hospital USM in 2013. Patient medical records and information was retrieved from the record department and ETI microbiology result from microbiology department.

Results: There were 34.68% of patients developed VAP after 48 hours of mechanical ventilation. The mortality rate of VAP was 47.11%. Majority of them were male (72.11%). The mean duration of mechanical ventilation was 27.44 days. LOS in ICU was 28.03 days. The mean age of VAP patient was 52.43 years old. Altered consciousness (47.11%) were the most common cause of intubation. Hypertension (23.07%) and Diabetes mellitus (18.26%) were the most common comorbidities associated with VAP. Acinetobacter species (52.88%) is the most commonly cultured microorganism followed by Pseudomonas aeruginosa (36.63%) and Klebsiella pneumonia (39.42%). Patient with underlying malignancy (24.48%) and Diabetes mellitus (24.48%) had higher mortality of VAP.

Table 1: Comparison of demographic and associated risk factor between VAP and Non-VAP patient

| Risk Factor                 | VAP (%) | Non-VAP (%) |
|-----------------------------|---------|-------------|
| Age (years)                 | 52.43   | 42.77       |
| Cause                       | 47.11   | 56.63       |
| Severe sepsis               | 13.46%  | 12.72       |
| Duration of Mechanical Ventilation (days) | 27.44 | 14.06 |
| LOS ICU (days)             | 28.03   | 14.92       |
| Co-morbidities             | 18.26   | 12.75       |
| Diabetes mellitus          | 23.07   | 22.95       |
| Hypertension               | 52.88   | 52.68       |
| Diabetes mellitus          | 24.48   | 20.9        |

Conclusions: The incidence of VAP in ICU USM in 2013 was considerably high (34.68%) with mortality rate (47.11%). VAP is significantly associated with several factors. From our study, the majority of the microorganisms cultured in VAP patients is Gram-negative organisms. Hence, it can be concluded that most of the patients are having late onset of VAP.

ORAL PRESENTATION 19- RESPIRATORY NEUROBIOLOGY AND SLEEP: PATHOGENESIS IN PULMONARY MEDICINE

CARDIOVASCULAR AND METABOLIC COMORBIDITIES IN OBSTRUCTIVE SLEEP APNEA SYNDROME: DATA FROM 1576 ADULT JAPANESE PSG CASES.

A. MATSUO1, K. SONEHARA1, Y. WADA2, M. KOSAKA2, K. IKEGAWA2, N. KOBAYASHI3, T. HIRUCHI3, T. AGATSUMA2, A. USHIKI3, S. FURUYA2, S. KANDA2, M. OKADA2
1Shinshu General Hospital, Respiratory Medicine and Sleep Respiratory Center, Nagano, Japan, and Shinshu University School of Medicine, First Department of Internal Medicine, Matsumoto, Japan

Conclusions: Obstructive sleep apnea (OSA) has been associated with cardiovascular disease (CVD), hypertension (HT), and metabolic disorder. We investigated the prevalence and characteristics of adult OSA Japanese patients.

Methods: We retrospectively analyzed the data accrued in 1,576 patients who underwent the first time polysomnography (PSG) in our hospital from June 2001 to February 2014. They were 1,286 males and 290 females, the mean age of 55.5 ± 13.3 years, the mean body mass index (BMI) of 26.0 ± 4.3 kg/m², and the mean apnea-hypopnea index (AHI) of 38.4 ± 25.0. We examined the association between OSA and cardiovascular and metabolic comorbidities.

Results: 1,494 between 1,576 patients were diagnosed with OSA. The OSA patients had 39.1% with HT, 16.1% with diabetes mellitus (DM), 41.8% with hypertension (HT), 22.5% with liver dysfunction, and 8.7% with CVD. And the OSA patients treated with continuous positive airway pressure (CPAP) had 41.7% with HT, 17.7% with DM, 43.2% with HL, 22.9% with liver dysfunction, and 9.2% with CVD. On the other hand, the non-OSA patients had 23.1% with HT, 8.5% with DM, 28.0% with HL, 17.1% with liver dysfunction, and 0.1% with CVD.

Conclusions: The risk of cardiovascular and metabolic comorbidities in OSA patients was almost 2 ~ 8 times more than those of non-OSA patients. We suggested that the OSA patients with higher severity OSA tended with a higher rate of complications.
PREVALENCE OF OBSTRUCTIVE SLEEP APNEA (OSA) IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Y. WU, B. HE, Z. QIU, L. ZHOU, M. ZHU, Y. CHEN, Y. LUO
First Affiliated hospital of Guangzhou Medical University, State Key Laboratory of Respiratory Disease, Guangzhou, China

Background and Aims: Both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are common diseases. It has been hypothesized that coexisting OSA in COPD - "overlap syndrome" - has more severe oxygen desaturation when compared with that in either condition alone. The prevalence of overlap syndrome in patients with COPD who were screened from community is not known. The purpose of the present study was to investigate the prevalence of overlap syndrome in patients with COPD. We also observed whether hypoxia in patients with overlap syndrome is more severe than that in patients with COPD alone during sleep.

Methods: Fifty patients with COPD (male 49, female 1, FEV1 = 44.8 ± 13.1%) screened from Xining, a remote countryside of Guangdong, China were enrolled (mean ± SD of 69.6 ± 5.1 yrs, BMI = 21.1 ± 3.2 kg/m²). Full polysomnography (PSG) and ESS questionnaire were performed in all patients. Patients were then divided into two groups (overlap syndrome and pure COPD) based on apnea-hypopnea index (AHI).

Results: 31 of 50 COPD patients (62%) had OSA whose AHI ≥ 5 events/h. As expected that AHI and ODI in overlap group were significantly higher than pure COPD group (18.4 ± 14.0 vs 2.9 ± 1.4 for AHI, p < 0.001 and 8.3 ± 8.2 vs 2.8 ± 2.0 for ODI, p = 0.001). There was a significant difference in sleep stage between pure COPD and overlap syndrome (5.3 ± 6.4% vs 1.0 ± 1.7% for sleep stage 3, p = 0.05; 12.9 ± 8.2 events/h vs 24.0 ± 11.1 events/h for arousal index, p < 0.001). However, nocturnal mean oxygen saturation was similar between groups (94.6 ± 1.9% vs 95.1 ± 1.3%, p = 0.23).

Conclusions: There is a high prevalence of overlap syndrome in patients with COPD screened from community. Sleep quality was poorer in overlap group than pure COPD. The mean oxygen saturation during overnight study is similar between pure COPD and overlap syndrome. This project was funded by NSFC No. 81270123.

HABITUAL BEHAVIORS: ALCOHOL, SMOKING AND COFFEE INTAKE IN RELATION TO SEVERITY OF OBSTRUCTIVE SLEEP APNEA

M. M RAMANATHAN,1,2, R. ABDUL RAHMAN,1,2, D. MUNTHAM,3,5, N. CHIRAKALWASAN2,3
1Chest Clinic- Hospital Taiping, Medical Department Hospital Taiping, Taiping, Malaysia, 2Division of Pulmonary and Critical Care Medicine, Department of medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, 3Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, 4Respiratory unit, Hospital Sultanah Aminah Johor Bahru- Johor- Malaysia, Johor Bahru, Malaysia, and 5Section for Mathematics-, Faculty of Science and Technology- Rajamangala University of Technology Suvarnabhumi- Phra Nakhon Si Ayutthaya- Thailand, Bangkok, Thailand

Background and Aims: The most studied risk factors for obstructive sleep apnea (OSA) had been upper airway anatomical representation and body habitus. Studies on habitual risk factors for OSA that includes smoking, caffeine and alcohol intake are limited and mostly not adjusted for other risk factors. The relationship between all three habits and OSA has never been reported. This study is conducted to explore the link between all three habits to severity of OSA.

Methods: Five hundred and fourteen patients who were diagnosed with OSA from July 2014 till July 2015 at Excellence Center for Sleep Disorders at King Chulalongkorn Memorial Hospital, Bangkok, Thailand were included in this retrospective study.

Results: Two hundred and ninety-four patients (57.2%) had severe OSA as defined by respiratory disturbances index of more than 30. The odds ratio for developing severe OSA for 1 habitual risk factor, 2 habitual risk factors, and 3 habitual risk factors were 1.44 (95% CI 0.94-2.18; p = 0.091), 1.81 (95% CI 1.11-2.93; p = 0.017), and 2.75 (95% CI 1.37-5.52; p = 0.04), respectively. However when all these values were adjusted to the most important known risk factors for OSA; age, sex and BMI; the odds ratio for 1 habitual risk factor, 2 habitual risk factors, and 3 habitual risk factors dropped to 1.12 (95% CI 0.70-1.78; p = 0.643), 1.18 (95% CI 0.68-2.06; p = 0.553), and 1.65 (95% CI 0.75-3.60; p = 0.21); respectively.

Conclusions: This is the first report in the literature of combined habitual risk factors including smoking, alcohol and caffeine intake for developing OSA. Combination of more than 1 habitual behavior increased the risk of developing severe OSA. The risk did not persist after adjusted for age, sex and BMI. This finding suggested that clinical characteristics and anatomical factors may be more important than habitual behaviors in OSA development.

OUTCOMES AND PROGNOSTIC FACTORS OF NON-HIV PATIENTS WITH PNEUMOCYSTIS JIROVECII PNEUMONIA AND CONCOMITANT CMV-DNA POSITIVE IN BALF: A RETROSPECTIVE COHORT STUDY

Q. YU,1 C. QUE,1 H. ZHAO,2 L. SU,1 P. JIA1
1Peking University First Hospital, Department of Respiratory and Critical Care Medicine, Bei Jing, China, and 2Peking University First Hospital, Department of Infectious Disease, Bei Jing, China

Background: Pneumocystis jirovecii pneumonia (PJP) and pulmonary cytomegalovirus(CMV) infection are both common opportunistic infections in immunocompromised patients, while their confection was less studied, especially in non-HIV patients. Our study aims to look for clinical characteristics of non-HIV patients with PJP coinfected with CMV, and analyze the prognostic implications of CMV-DNA in bronchoalveolar lavage fluid (BALF).

Methods: We conducted a retrospective study in patients who were diagnosed with PJP from 2009 to 2016. The patients were divided into two groups according to presence or absence of CMV-DNA in BALF. We compared demographics, clinical characteristics, and mortality in PJP patients with or without CMV-DNA positivity in BALF.

Results: We identified 70 non-HIV patients with PJP, in whom 54.3% (36/70) were CMV-DNA positive in BALF. There was no significant difference in mortality between patients with PJP with or without CMV-DNA positivity in BALF (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.02, p < 0.05). Patients with CMV-DNA presence in BALF were more likely to have more severe dyspnea, lower PaO2/FiO2, and more likely to have centrilobular nodules compared with those taking corticosteroids only (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.15). CMV-DNA was more common in BALF from patients taking both glucocorticoids and T-cell immunosuppressants compared with those taking corticosteroids only (p = 0.15).

Conclusions: Combined therapy with corticosteroids with other immuno-suppressants is a predisposing factor for CMV-DNA positivity in BALF in PJP patients.CMV pneumonia should be considered in non-HIV- PJP patients with severe hypoxemia when the chest CT revealed centrilobular nodules. Antiviral treatment should be promptly initiated in patients with high CMV-DNA loads in BALF because of their poorer prognosis.
Background and Aims: The incidence of NTM infections has been increasing worldwide. It has significant morbidity and mortality. Host factors such as genetic susceptibility, immune deficiency, lung diseases and environmental factors influence the development of NTM infection, treatment outcome and prognosis. Diagnosis of NTM pulmonary infection is difficult as its symptoms mimic the underlying lung diseases. Treatment of NTM lung disease is associated with poor compliance due to adverse drug events, prolonged course of treatment and poor treatment outcomes. Little is known on the profile of NTM and patients’ characteristics. We aimed to study the NTM profile, its clinical relevance and the characteristics of patients.

Methods: All hospitalised patients in whom NTM was isolated between January 2011 and December 2012 were studied. We analysed their demographics, smoking status, NTM species, source of specimens, and co-morbidities.

Results: 560 patients (62% male) with NTM isolation were identified. The median (IQR) age was 78 (55-74) years. 20% were current smokers. Majority (91%) of the NTM isolations were of pulmonary origin. M. abscessus (38.1%) was the commonest. Followed by M. fortuitum (16.6%), M. avium (15.4%), M. gordonae (7%), M. chelonae (1.6%), M. lentiflavum (1.5%), M. scrofulaceum (1.1%), M. haemophilum (0.8%), M. simiae (0.6%), M. szulgai (0.6%), and M. terrae (0.4%). Underlying lung diseases were common (29.3%), bronchiectasis, 15% COPD, 8.6% asthma, 3.6% pulmonary fibrosis. Other common co-morbidities were hypertension (31.3%), hyperlipidaemia (25.7%) and diabetes mellitus (17%). 11.6% of the patients had HIV infection and 5.7% had active cancer.

Conclusions: This study showed NTM infections to be common in elderly male patients. M. abscessus was the commonest among the 12 species identiﬁed in this cohort. More than half of patients had underlying lung condition. There is an urgent need to study the epidemiological trend, its specialisation, and the treatment of NTM infections.

DIRECT RECOGNITION OF CRYPTOCOCCAL CAPSULAR GLUCURONOXYLOMANNAN BY C-TYPE LECTIN RECEPTOR DECTIN-3 IS ESSENTIAL FOR HOST DEFENSE AGAINST CRYPTOCOCCUS NEOFORMANS

H.R. HUANG
Shanghai Pulmonary Hospital, Department of Respiratory and Critical Medicine, Shanghai, China

Background and Aims: Cryptococcus neoformans is an ubiquitous environmental yeast that can cause life-threatening pneumonia and meningitis both in immune-competent and immune-deficiency people. The polysaccharide capsule is considered to be the major virulence factor and pathogen-associated molecules of C. neoformans, which contains two major polysaccharides, glucuronoxylomannan (GXM) and galactoxylomannan (GalXM), accounting for 90%-95% and 5%-10% of the total polysaccharide mass, respectively. Dectin-3 is a novel pattern recognition receptor that can recognize α-mannans of C. albicans hyphae and trehalose 6, 6-dimycolate (TDM) of M. tuberculosis. Since class C-type lectin-like receptors such as TLR2 and TLR4 and members of C-type lectin-like receptors such as Dectin-1 and Dectin-2 did not play a role in recognition and host defense against cryptococcal infection, we wonder whether Dectin-3 can specifically recognize GXM and elicit protective immune activities.

Methods: In vitro, GXM was purified from the capsules of C. neoformans and used to stimulate Dectin-3-/- BMDMs and RAW264.7 cells over-expressing Dectin-3. NF-kB and ERK signal pathways were detected by western blot. IL-6, TNF-α, IL-1β and IL-12p40 amounts in cultures were measured with ELISA. CCL5, CXCL9, CXCL10 and CCL11 relative expressions were measured by QPCR. In vivo, live C. neoformans (1×10^5 or 1×10^6 cells) was inoculated into the trachea of each mouse and CFU of each lung and brain were counted.

Results: Dectin-3 can directly recognize GXM to activate NF-kB and ERK signal pathways, inducing chemokines (CCL5, CXCL9, CXCL10 and CXCL11) and pro-inflammatory cytokines (IL-6 and TNF-α) in innate immune cells. Dectin-3-deficient mice are more sensitive to pulmonary C. neoformans infections comparing to wild-type controls.

Conclusions: In this report, we proved that Dectin-3 is a direct receptor for cryptococcal capsular GXM. Furthermore, we demonstrate that Dectin-3 is an essential receptor for GXM-induced inflammatory responses through activating NF-κB and ERK pathways. Moreover, we have generated Dectin-3-deficient mice examined the roles of Dectin-3 in host defense against pulmonary Cryptococcus infection.

THE DIAGNOSTIC VALUE OF GALACTOMANNAN DETECTION IN INVASIVE PULMONARY ASPERGILLOSIS IN NON-NEUTROPENIC HOSTS

Y. LI, P. LIN, Y. ZHOU, S. SU, J. YE, C. CHEN
The First Affiliated Hospital of Wenzhou Medical University, the department of respiratory and critical medicine, Wenzhou, China

Background and Aims: To evaluate the value of galactomannan examination in serum and BALF in the diagnosis of IPA in non-neutropenic hosts.

Methods: We performed an observational retrospective cohort study from 2014 to 2015 in the department of pulmonary and critical care medicine of the First Affiliated Hospital of Wenzhou Medical University. Diagnostic criteria of IPA adapted from Blot and Bula according to their underlying diseases.

Results: 1372 non-neutropenic cases who were received serum GM examination, 96 cases received serum GM and BALF GM test in the same time. 65 cases were confirmed with IPA and accounted for 4.7%. The most common underlying disease is COPD and diabetes. The sensitivity, specificity, PPV and NPV was 37%, 94%, 22% and 97% respectively in serum GM. It was 88%, 52%, 28% and 95% respectively in BALF GM.

Conclusions: The sensitivity of GM test in serum in non-neutropenic hosts was low. It had a high negative predictive value. BALF GM has high sensitivity and low PPV. Combined serum and BALF GM can improve the diagnostic performance.
A CLINICAL REVIEW OF 34 CASES WITH PROGRESSIVE DISSEMINATED HISTOPLASMOSIS

J. MENG, X. LV
Xiangya Hospital of Central South University, Respiratory Medicine, Changsha, China

Background and Aims: Histoplasmosis is a rare mycosis, which is an epidemic disease occurred in several endemic areas, including the midwestern United States, Africa and most of Latin America. Cases of histoplasmosis are sporadic in China. Histoplasmosis is difficult to be diagnosed and the misdiagnosis rate of it is high.

Methods: The clinical data of 34 cases of histoplasmosis hospitalized in Xiangya Hospital of Central South University from 2003 to 2016 were analyzed retrospectively. The relevant literatures were reviewed roundly which were about histoplasmosis from 2001 to 2016 in Chinese mainland.

Results: Thirty-four patients were included in the study. All patients were pathogenic examination-proven, including 15 (44.1%) bone marrow smears, 14 (41.1%) lymph node biopsy, 3 (8.8%) lung tissue biopsy and 2 (5.9%) intestinal tissue biopsy. 22 (64.7%) were male, and mean age was 37 years. Eight (23.5%) patients had HIV infection. Organ involvement included lungs (52.9%), oral cavity (5.9%), intestinal (5.9%). Common clinical manifestations were fever (94.1%), weight loss (35.3%), anemia (67.6%), jaundice (5.9%), hepatomegaly and splenomegaly (55.9%), lymphadenopathy (70.6%), and skin rash (23.5%). Twenty-six (76.5%) patients’ chest radiography was abnormal. Twenty-one (61.7%) patients received amphotericin B therapy and 10 (29.4%) patients received itraconazole therapy. 13 (38.2%) patients achieved clinical cure and 14 (41.2%) patients were improved. 579 cases of histoplasmosis from literatures were collected in the study, with 214 (37.0%) cases occurred in Yunnan province, 69 (11.9%) cases in Hunan province and 67 (11.6%) cases in Hubei province.

Conclusions: Histoplasmosis is caused by H. capsulatum and can be diagnosed by bone marrow smears or histopathological examination. Antifungal therapy including amphotericin B and itraconazole are effective for histoplasmosis. Cases of histoplasmosis have a prominent geographical distribution in China.

CLINICAL ANALYSIS OF NINE PATIENTS WITH INVASIVE PULMONARY ASPERGILLOSIS IN CHILDREN

Z. FEIFEI1,2, T. YUHONG2
1Sichuan University, West China Medical School, Chengdu, China, and 2West China Second University Hospital of Sichuan University, Pediatrics, Chengdu, China

Background and Aims: To investigate diagnosis and treatment of invasive pulmonary aspergillosis (IPA) in children.

Methods: The risk factors, clinical manifestations, chest radiographic findings, microbiological and pathological evidence, treatment and prognosis were retrospectively reviewed in nine patients with proven or possible IPA from January 2004 to July 2016 in West China Second university Hospital, Sichuan University.

Results: Four cases had proven IPA, and 5 cases had possible IPA. Among the nine patients, five were male and four were female. The risk factors were found in seven cases. Cough, fever, moist rales were the most common manifestation, and only two cases had hemoptysis. The most common chest imaging is nodules and patchy shadow. Halo sign was found in three cases and air crescent sign was not been found. Pulmonary tuberculosis coexisted in three cases. Blood culture was negative in all patients. The positive rates of sputum and bronchoalveolar lavage fluid (BALF) were 22.22% and 44.44%, respectively. Lung biopsy was conducted in four cases, and the positive rate was 100%. Eight cases were treated with anti-fungal therapy (voriconazole, itraconazole, micafungin used alone), and only one case was treated with combination therapy (voriconazole and liposomal amphotericin B). Seven cases recovered, and two cases were still in treatment.

Conclusions: The clinical manifestations and imaging of IPA is nonspecific. Repeated sputum and BALF culture was the key point to clinical diagnosis. The patients in whom the anti-fungal therapy was initiated early had a good outcome.
RESULTS OF ACUTE EXACERBATION ASTHMA MANAGEMENT BASING ON THE USAGE OF PEDIATRIC ASTHMA SCORE (PAS) AT CHILDREN’S HOSPITAL NO.1 FROM OCTOBER, 2014 TO APRIL, 2015

H. HO
Ho Chi Minh, Vietnam

Background and Aims: - Primary objective: To evaluate the consequence of acute asthma exacerbation treatment by applying pediatric asthma score (PAS).
- Secondary objective: to determine
  + The average length of stay.
  + The proportion of asthma recurrence.
  + The average cost of treatment.
  + The factors relating to asthma patients who show bad response with treatment.

Methods: - Cross-sectional analysis.
- 261 cases were selected to satisfy with inclusion and exclusion criteria.
- Inclusion criteria: all of patients whose ages range from 2 to 15 years old admitted to the hospital with acute asthma exacerbation at Children’s Hospital 1 from October, 2014 to April, 2015.
- Exclusion criteria: patients with underlying diseases such as congenital heart diseases, abnormal respiratory tract, metabolism diseases, ...

Results: From October 2014 to April 2015, there were 261 cases admitted to hospital with acute asthma exacerbation at Children’s Hospital No.1. The average age was 4.2 years in which male and female proportion was 1.39 / 1. The average length of stay was 1.92 days. The length of stay of moderate and severe acute asthma attack was 1.7 days and 3.5 days, respectively. Besides, the average time alleviating the symptoms was 4.8 hours. In incompletely response asthma, some factors affect the process of treatment: co-infection pneumonia, the appropriate time of ipratropium bromide and intravenous hydrocortisone usage, over-use of antibiotics. The median cost of treatment was 399.680 Vietnam Dong (VND) while of the severe attack was 1.031.570 VND.

Table 1:

Conclusions: By basing on pediatric asthma score, the length of stay and average cost improve significantly. The inappropriate time of using ipratropium bromide and intravenous hydrocortisone, nonetheless, associated with the over-diagnosis of co-infection pneumonia and over-use of antibiotics affect badly the length of stay, the cost, and the response of treatment.

EARLY EFFECT OF MATERNAL MICROBIAL ENVIRONMENT ON T-REGULATORY CELLS IMMUNE RESPONSE IN CORD BLOOD OF OFFSPRING

J. LIU
the Second Hospital of Jilin University, Respiratory Medicine, Changchun, China

Background and Aims: To examine the amount and suppressive function of regulatory T cells in innate and adaptive immune response in cord blood from offspring of healthy mothers coming from the same area but with different level of microbial environment.

Methods: Cord blood mononuclear cells from 58 healthy neonates were isolated, and cultured with lipidA-TLR4 ligands, peptidoglycan (PPG)-TLR2 ligands and mitogen (phytohemagglutinin) stimulation for 3 days. And then the amount, specific genes expression and suppressive function of regulatory T cells, and production of cytokines were examined. The concentration of endotoxin in dust in bed of mothers was measured with the kinetic chromogenic Limulus Amebocyte Lysate (LAL) test.

Results: mother/neonate were divided into two groups depended on that the concentration of endotoxin in dust collected from bed of mothers was higher or lower than median. Cord blood from offspring of mothers with higher environmental endotoxin showed more PPG-induced regulatory T cells (CD4+CD25+Foxp3+T, \( P < 0.05 \)), increased IFN-\( \gamma \) and IL-9 secretion \( (P < 0.05) \). Furthermore, the suppressive capacity of regulatory T cells was increased in mitogen-induced division and proliferation of T effector cells in cord blood of offspring from mothers with higher environmental endotoxin \( (P < 0.05) \).

Conclusions: In offspring of mothers with higher microbial environment, the amount and suppressive function of regulatory T cells, and production of IFN-\( \gamma \) and IL-9 were increased at birth, which maybe potentially keep the offspring away from allergic diseases.
A PREFERABLE BIOMARKER INDICATING UNCONTROLLED STATE AND GLUCOCORTICOSTEROID RESPONSIVENESS

Background and Aims: To explore the clinical significances of plasma IL-8 in uncontrolled asthmatics as a biomarker so as to deepen understanding the knowledge of asthma phenotype and provide the basis for developing new targeting therapeutic agents.

Methods: A total of 246 uncontrolled asthma and 50 healthy control were enrolled in the outpatient clinic from October, 2015 to April, 2016. The clinical features including symptoms, atopic markers, FENO and spirometry values were collected. The levels of plasma IL-8, IL-6, TNF-α, IgE, SOD in peripheral blood were measured by ELISA method. The levels of plasma IL-8 were compared between the groups using different glucocorticosteroid administrative routine and their change was compared between well and poor glucocorticosteroid responsiveness asthmatics.

Results: Elevated plasma IL-8 was occurred in 58.13% of the uncontrolled asthma patients, which was more sensitive than other asthmatic biomarkers such as elevated FENO, blood eosinophils and serum IgE. The AUC area of plasma IL-8 level to indicating uncontrolled asthma state was 0.816 (95% Confidence Interval: 0.7605 To 0.8721, P < 0.0001), which was higher than FENO AUC area 0.711 (95% CI 0.640-0.865, P < 0.001),respectively while the cutoffs were 23.5 ppb and 44.5 ppb respectively, rendering sensitivities, specificities, PPV and NPV of 79.9%, 54.7%, 77.9%, 58.1% and 78.7%, 67.9%, 89.2%, and 48.7%, respectively. The cutoff of FeNO with specificity of 90% (FeNO90) for whole patients and patients with allergy and rhinitis were 59.5 ppb and 90.5 ppb, respectively, while FeNO90 decreased by 12 ppb every ten years.

Conclusions: The diagnostic value of FeNO varies and cut-off point should be adjusted in different asthmatic subpopulations. A cut-off point of FeNO with a specificity > 90% could decrease the false positive rate.
AN ASTHMATIC WITH MARKED BLOOD EOSINOPHILIA

S. TAN, A. TAKANO, K.L. LIM, K.L. TAN

Background and Aims: Peripheral blood eosinophilia is commonly seen in asthmatics but may be due to various other causes.

Methods: A 47 year old female non-smoker presented with cough and exertional dyspnea over 6 months. She was clinically diagnosed with asthma and was treated with high-dosed inhaled corticosteroids at another institution, but her symptoms persisted. Initial investigations showed markedly elevated peripheral blood eosinophilia (absolute eosinophils 9.38 x 10^9/L, differential count 56%). Previous records revealed similarly elevated eosinophil counts of up to 13.6%.

Results: Chest radiograph, autoimmune screen, spirometry and stool helminthic tests were normal. Chest computed tomography showed bilateral ground glass opacities in the upper lobes with no central bronchiectasis (Figure 1). Bronchoscopy was performed. Transbronchial lung biopsy and endobronchial biopsies showed prominent eosinophilic infiltrates in the bronchial wall and adjacent parenchyma (Figure 2). Bone marrow biopsy with cytogenetics showed normocellular marrow with increased eosinophils but no evidence of myeloproliferative or lymphomatous disorder. A diagnosis of chronic eosinophilic pneumonia (CEP) was made. She was started on oral steroids with dramatic improvement in eosinophil counts and resolution of symptoms.

Conclusions: Diagnosis of CEP involves clinical-radiological-pathological correlation and exclusion of other causes (parasitic, allergic, vasculitic, drugs and lymphoma). It is characterized by marked accumulation of eosinophils in the interstitium and alveoli of the lung. Patients often present with cough and dyspnea. Asthma typically precedes or accompanies in up to 50% of cases. A "photographic negative" opacity on chest imaging is seen in only one-fourth of patients. BAL and lung biopsy showing marked eosinophilia are characteristic of CEP.

Chronic eosinophilic pneumonia is a rare cause of markedly elevated peripheral eosinophilia. Along with other diagnoses, it should be suspected in asthmatics with poor response to therapy.

ORAL PRESENTATION 22 - CRITICAL CARE MEDICINE: BASIC SCIENCE KNOWLEDGE IN ICU

PRE-HOSPITAL ANTI-PLATELET THERAPY IS RELATED WITH ARDS: A META-ANALYSIS

W. JIN
First People’s Hospital of Hangzhou, respiratory medicine, Hangzhou, China

Background and Aims: Anti-platelet agents have the potential to play a role in the development of acute respiratory distress syndrome (ARDS). We conducted a meta-analysis to assess the effect of pre-hospital anti-platelet therapy (APT) in adults with ARDS.

Methods: We searched the PubMed, Web of Science, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. All human studies published in full text, abstract, or poster form were eligible for inclusion. We included prospectively or respectively cohort, case control trials or RCT. We included trials comparing the incidence of ARDS in patients with pre-hospital anti-platelet agents or not. The date of the most recent search was October 2015. Two authors independently assessed study risk of bias and extracted data. The primary outcome was ARDS morbidity, while secondary outcome was ICU or hospital mortality.

Results: We indentified 8 studies meeting the eligibility criteria (seven cohorts, one case control). Meta-analysis of 7 studies of 30291 patients showed that pre-hospital APT was associated with a decrease in the odds of ARDS compared with those without APT (OR 0.68, 95% CI 0.56 - 0.83, p = 0.0001). Of these studies, three calculated the ICU mortality, showing a 5.58% in the pre-hospital APT users and 5.66% in the nonusers (OR 0.84, 95% CI 0.63 - 1.11, p = 0.22, I^2 = 0%).

Conclusions: Clinical studies reviewed here have provided some evidence that pre-hospital APT significantly reduce ARDS rate, but not mortality in critically ill patients, compared to that in APT nonusers. The findings suggested an early use of anti-platelet agents would be beneficial in critical care patients at risk of ARDS.
INHIBITION OF PGES-1 REDUCES ACUTE LUNG INJURY IN MICE

M. GURUSAMY,1 S. NASSERI,1 A. AMBADE,1 H. LEE,1 A. PEKCEC,2 H. DOODS,2 D. WU1
1Chonbuk National University, BHN Convergence Technology, Jeonju, Republic of Korea, 2Boehringer Ingelheim Pharma GmbH & Co. KG G, CNS Diseases Research, Biberach, Germany, and 3Boehringer Ingelheim Pharma GmbH & Co. KG G, Global Department Research Beyond Borders, Biberach, Germany

Background and Aims: Prostaglandin E2 (PGE2) is a major proinflammatory mediator. Micronosal prostaglandin E synthase-1 (mPGES-1) is induced by proinflammatory stimuli and it catalyzes the terminal step in PGES production. mPGES-1 has recently emerged as a novel therapeutic target for inflammatory diseases. The aim of the present study was to evaluate the anti-inflammatory effects of a novel selective human mPGES-1 inhibitor (BI-1029539) in an experimental model of acute lung injury using knock-in mice that expressing human mPGES-1.

Methods: Acute lung injury was induced by intratracheal injection of lipopolysaccharide (LPS, 4 mg/kg) in male/female mice (8-10 week old). Thirty minutes later, mice were injected with vehicle, human mPGES-1 inhibitor (BI-1029539, 30 mg/kg, i.p.) or celecoxib (30 mg/kg, i.p.). At 6 hours following LPS administration, bronchoalveolar lavage was collected, and analyzed for inflammatory cell influx, total protein, IL-1β and TNF-α levels. Lung tissues were analyzed for myeloperoxidase activity, water content, and histology.

Results: Intratracheal LPS injection resulted in an excessive inflammatory cell infiltration in the lungs of vehicle-treated animals, compared to sham group. The number of total cellular infiltrates, neutrophils, and macrophages in the BALF were reduced by 80.7%, 93.6% and 67% respectively, in mice treated with BI-1029539, compared to 78.6%, 93.5 and 74% reduction in mice treated with celecoxib. Furthermore, lung vascular permeability, lung water content, myeloperoxidase activity, lung injury scores, total protein content, TNF-α, IL-1β and PGE2 levels in lavage fluid were significantly lower in mice treated with BI-1029539, compared to vehicle controls. However, the level of PGI2 was not reduced in BI-1029539 treated animals. In addition, COX-2, iNOS and ICAM expression were significantly lower in mice treated with BI-1029539, compared to 78.6%, 93.5 and 74% reduction in mice treated with celecoxib. These results demonstrated that corticosteroid mediated inflammatory responses were mainly dependent on NLRP3 inflamma- some signal pathway. Finally, we provided further insights by demonstrating that corticosteroid mediated NLRP3-inflammasome response by suppressing mitochondrial reactive oxygen species (ROS) generation in macrophages.

Conclusions: Corticosteroid use inhibited LPS-induced lung inflammation and acute lung injury in the mouse through a mechanism involving reduced NLRP3’s inflammasome activation. Our findings suggested that corticosteroids may influence the inflammatory responses by inhibiting mitochondrial ROS to reduce damage, improve symptoms of ALI/ARDS.

OXYGEN SATURATION INDEX AS A SURROGATE OF PAO2/FIO2 IN ACUTE RESPIRATORY DISTRESS SYNDROME

C.B. KING KAY, P.G. MORAL
University of Santo Tomas Hospital, Section of Pulmonary and Critical Care, Manila, Philippines

Background and Aims: Acute Respiratory Distress Syndrome (ARDS) is diagnosed by the Berlin Definition: within one week of known clinical insult or newworsening respiratory symptoms; chest radiograph/computed tomography scan finding of bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules; respiratory failure not fully explained by cardiac failure or fluid overload, excluded by objective assessment; and oxygenation dysfunction classified as mild, moderate or severe based on PaO2/FIO2. Recently, Oxygenation Index (OI), another measure of oxygenation dysfunction, has been suggested as a more accurate means of determining respiratory failure severity compared to PaO2/FIO2, due to incorporation of Mean Airway Pressure (MAP). However, both PaO2/FIO2 and OI require arterial blood gas determination, which can be technically difficult and expensive. Pulse oximetry is an alternative, reliable, and inexpensive means of monitoring oxygenation dysfunction. Our objective was to determine the performance of Oxygen Saturation Index (OSI), as a surrogate of PaO2/FIO2, in the diagnosis of ARDS.

Methods: Review of patient records diagnosed with ARDS from January 2012 to December 2015 at the University of Santo Tomas Hospital was done. Simultaneous arterial blood gas, pulse oximetry and ventilator settingst were recorded during the first 1, 24, 48 and 72 hour of mechanical ventilation. PaO2/FIO2, OI and OSI were calculated. Descriptive statistics and two-way scatterplots were used to describe the correlation of PaO2/FIO2, OI and OSI. Linear modeling was used to derive predictive equation for PaO2/FIO2 using OSI, oxygen saturation (SpO2), respiratory rate (f) and MAP.

Results: Eighty five arterial blood gas, SpO2 and MAP values from 27 patients (mean age = 57; 55% males) were included. PaO2/FIO2 was inversely related to OI and OSI. OI and OSI were directly related. Predictive equation of PaO2/FIO2 = exp (3.33 + 0.03*SpO2–9.92*OSI−0.02 (f) + 0.06(MAP)) was derived (R2 = 61.4%).

Conclusions: OSI may be a noninvasive surrogate measure of oxygen dysfunction in patients with ARDS.
REFERENCE VALUES FOR SPIROMETRY IN KOREAN WORKING POPULATION WITH LMS METHODS

J.P. MYONG, 1 J. BUM-SEAK, 1, Y. HYOUNG-KYU2  
1Seoul St.Mary’s Hospital- College of Medicine- Catholic University of Korea, Occupational and Environmental Medicine, Seoul, Republic of Korea, and 2Yeouido St.Mary’s Hospital- College of Medicine- Catholic University of Korea, Internal Medicine, Seoul, Republic of Korea

Background and Aims: Spirometry is widely used to assess the lung function, to surveillance the worker’s lung condition, and diagnose respiratory diseases. The ERS Global Lung Function Initiative (GLI) Task Force recently released multi-ethnic spirometric reference equations derived using the LMS methods. With this methods a modeling of a spirometric indices from age-specific values for the lower limit of normal (LLN). In Korean Occupational Health and Safety Agency recommended to use the criteria LLN or lower spirometry for finding abnormal lung function among current working population those exposed to specified respiratory hazardous materials. However, KOSHA did not provided the reference of LLN for spirometry. Therefore, a suggestion for LLN of spirometry is important for physicians to make a decision for risky workers.

Methods: Spirometric data from healthy non-smokers (35,535 individuals aged 17–72 years, 29,303 males and 6,232 females) were collected from 7 centers across Korea (Korea Medical Institute, Specific Health Examination for Workers), and reference equations were derived using the LMS method. This method incorporates modeling skewness (lambda: L), mean (mu: M), and coefficient of variation (sigma: S), which are functions of sex, age, and height. In addition, the age-specific lower limits of normal (LLN) were calculated.

Results: The criteria LLN is as follows; LLN (5th percentile) = exp(ln(M) + ln(1-L-spline))+(S-spline)  
For FEV1 (L) among males:  
M = exp(-7.683639 + 1.902279ln(Height)-0.227864ln(Age) + M-spline)  
S = exp(-2.80781 + 0.17250ln(A) + S-spline)  
L = 1.05006  
For FEV1 (L) among females:  
M = exp(-7.756465 + 1.839661ln(Height)-0.166074ln(Age) + M-spline)  
S = exp(-2.43250 + 0.07968ln(A) + S-spline)  
L = 1.98765ln(A) + L-spline

In addition, other equation for FVC, FEV1/FVC were also calculated with LMS methods.

Conclusions: The new reference values faithfully reflect spirometric indices and provide an age-specific LLN for the 17–72-year age range, enabling improved lung health surveillance. This will provide proper LLN for workers in Korea. In the near future, a ethnic specific results for immigration workers should be followed.

SECOND-HAND SMOKER AS A RISK FACTOR OF CHRONIC BRONCHITIS IN HOUSEWIVES AGED 50–55 YEARS AT RURAL DISTRICT IN LAWANG, INDONESIA

R.A. NUGRAHA1, G. ANGGRIADI KSHA1, K. KOESANDRINI1,  
D. OCTAVIA1, N.S. PANENGGAK1, W. SUDIHardjo1,  
F.G. AQRINNA1, S. MUNIR2, D. NUSWANTORO3, S. PRAYITNO3  
1Faculty of Medicine - Universitas Airlangga, Medicine, Surabaya, Indonesia, 2National Institute of Health Human Resources Empowerment and Development, Research, Jakarta, Indonesia, and 3Faculty of Medicine - Universitas Airlangga, Public Health and Community Medicine, Surabaya, Indonesia

Background and Aims: At rural district in Lawang-Indonesia, more than half of housewives are second-hand smokers. Many studies proved a strong correlation between tobacco exposure among active smoker with incidence of chronic bronchitis and other respiratory diseases. However, to our knowledge, epidemiological evidence regarding the relationship between status of second-hand smoker and chronic bronchitis has not been summarized. Aim of this study was to understand relationship between status of second-hand smoker with chronic bronchitis in housewives aged 50–55 years at rural district in Randuagung Village, Lawang District, Indonesia.

Methods: Analytic observational study with cross-sectional design, using status of second-hand smoker as independent variable and chronic bronchitis as dependent variable. Population are housewives aged 50–55 years in Randuagung Village, Lawang District, Indonesia. From total of 2,972 housewives met inclusion criteria, we did a multistage cluster random sampling to get 663 subjects. Data were obtained by free-guided interview, questionnaire, and portable peak flow meter.

Results: From 663 subjects, 371 (55.95%) subjects were daily exposed to tobacco smoke for >10 years (second-hand smoker), and number of chronic bronchitis are 216 (34.12%) among total subjects. After adjusting some confounders, number of chronic bronchitis among second-hand smokers group were significantly higher (p < 0.001). Compared with non-exposed subjects, the PRs (95% CI) across second-hand smoker were 4.667 (3.057-6.585).

Conclusions: Status of second-hand smoker is one of the predictive factor for developing chronic bronchitis among housewives aged 50–55 years living in rural district. Further study is needed to prove the underlying mechanism.

Keywords: Chronic Bronchitis, Passive Smoker, Second-hand Smoker, Rural District
IMPACT OF AIR POLLUTION ON POPULATION HEALTH IN VIETNAM

C. NGO
Respiratory Center of Bach Mai Hospital, direction, Ha Noi, Vietnam

Background and Aims: Air pollution has become a major environmental health problem in Viet Nam. The rapid industrialization and socio-economic development are responsible for the progressive changes in the air pollution level. According to WHO, people living in low- and middle-income countries disproportionately experience the burden of outdoor air pollution with 88% (of the 3.7 million premature deaths) occurring in low- and middle-income countries, and the greatest burden in the WHO Western Pacific and South-East Asia regions.

Methods: We carried out a study for searches on the effect of ambient air pollution on population health in Viet Nam either in Pub Med or in non-indexed publications in vietnamese.

Results: A study of polycyclic aromatic hydrocarbons (PAHs) associated with particulate matter (TSP) in the ambient air in an urban area in Ho Chi Minh City (HCMC) was carried out from 2005 to 2006. The concentrations of 5- and 6-ring PAHs (BbF, BghiP, BaP, Fl, Py and Ch) were high in TSP samples in HCMC, accounting for 82% of total PAHs. These PAHs are known to be highly carcinogenic and mutagenic in humans. Another study conducted in HCMC with data collected from 2004 to 2007 revealed important information. Changes in levels of NO2 and PM10 were strongly associated with respiratory and cardiovascular diseases (CVD); whereas levels of SO2 were only moderately associated with respiratory and CVD hospital admissions and O3 concentration was not associated with any of them. For a 10 μg/m3 increase of each air pollutant, the risk of respiratory admissions increased from 0.7% to 8% while the risk of CVD admissions increased from 0.5% to 4%.

Conclusions: There were some studies in HCMC which showed that air pollution induced health problems but more studies should be conducted in order to persuade policy makers to introduce strong measures for reducing air pollution.

EVALUATE THE DEMANDS FOR SMOKING CESSATION SERVICES OF SMOKERS AT THE OUTPATIENT DEPARTMENT OF BACH MAI HOSPITAL

P. PHAN THU,1 C. NGO QUY,2 Q. VN VAN³, Q. PHAM LE²
1Hanoi, Vietnam, and 2Bach Mai Hospital, Respiratory centre, Hanoi, Vietnam

Background: Smoking is the leading cause of morbidity and mortality worldwide. Currently, Vietnam has not had many health facilities that provide support services for smoking cessation.

Objectives: 1. To describe smoking situation and smoking cessation of smokers at the outpatient department of Bach mai hospital; 2. To evaluate the demands of smokers for consulting services and smoking cessation.

Patients and methods: a cross-sectional descriptive prospective study, 275 smokers ≥ 18 yrs at the outpatient department of Bach mai hospital from 2008/07/2015 to 2012/12/2015.

Results: 47.6% of subjects start smoking at age of under 18; Only 31.6% of smokers think that smoking significantly costly; 62.5% of people have ever tried to quit smoking, of them 39.2% are successful; 81.3% of subjects believe that smoking helps control their weight and 58.2% of subjects said that waterpipe smoking is less harmful than tobacco; 24.7% would like to receive support from health workers; 17.5% would like to receive support from the drug; 61.6% would like to have the smoking cessation counseling via telephone; 88.3% wished to have consulting rooms for tobacco cessation at locals; 57.8% desired to be advised on the harms of smoking; The three most important contents that the subjects desired to be advised are the harms of smoking (57.8%), the methods for quitting smoking (53.1%) and how to overcome the discomforts of quitting (53.5%).

Conclusion: Desire to quit smoking and the demand of smokers for consulting services in smoking cessation is very high. Develop the counseling services for smoking cessation is very essential.
Results: The proportion of latent tuberculosis infection in naïve lung cancer patients

R. RAMDHANI, E. BURHAN, J. ZAINI
University of Indonesia, Pulmonology and Respiratory Medicine, East Jakarta, Indonesia

Background and Aims: Lung cancer and pulmonary tuberculosis (TB) are two major public health problems associated with significant morbidities and mortalities. The increased prevalence of active TB and latent TB reactivation in lung cancer patients and the negative effect of pulmonary TB in lung cancer prognosis underline the need for a thorough screening of lung cancer patients for latent TB infection (LTBI).

Methods: Newly diagnosed, treatment-naïve lung cancer patients were enrolled from a referral respiratory hospital in Jakarta. The presence of LTBI was determined by Quantiferon-TB Gold-in-Tube (QFT-GIT) after having Mycobacterium TB not detected result from Xpert MTB/RIF spu- tum test. Demographic characteristics and cancer-related factors associated with LTBI were investigated.

Results: There were 46 lung cancer patients enrolled, 28 (60%) men with mean of age 54.89 years old (31–74 years old). They had lung adenocarcinoma (34 patients, 74%) and most of them were at end stage (87% stage IV and 13% stage III) with WHO performance status (PS) 1 to 3 (24 % PS 1, 67% PS 2 and 9% PS 3). Comorbidities they had were COPD (3 patients), diabetes mellitus (2 patients), hypertension (4 patients), congestive heart failure (1 patient) and bronchial asthma (1 patient). QFT-GIT results were 6 (13%) LTBI, 28 (61%) non-LTBI and 12 (26%) indeterminate cases. The characteristics of LTBI patients were 67% men, two third were adenocarcinomas, 83% stage IV of lung cancer, 83% having WHO PS 2 and 3, 50% with underweight body mass index (BMI).

Conclusions: More than 10% of newly diagnosed lung cancer patients have LTBI. Most of them are men, adenocarcinoma, stage IV, having WHO PS 2–3, and half of them with underweight BMI.

Computerised tomography aortograms. With early treatment, prognosis is generally good. However, significant morbidity and mortality is associated with advanced age, thoracic location of aneurysm, and aortic rupture.

© 2016 Asian Pacific Society of Respirology
Respirology (2016) 21 (Suppl. 3), 3–213
**Radiological and Biochemical Characteristics of Smear Negative Culture Positive Pulmonary Tuberculosis in a Tertiary Center in Malaysia**

A.N. Musa, S.K. Othman, M.A. Mohd Zim, A.I. Ismail

Universiti Teknologi MARA, Faculty of Medicine, Sungai Buloh, Malaysia, and Gleneagles Medini Hospital, Respiratory Department, Johor Baharu, Malaysia

**Background and Aims:** The prevalence of smear negative pulmonary tuberculosis (PTB) is increasing in Malaysia yet its diagnosis often poses a great challenge. We aim to look at the common symptoms, radiological findings and biochemistry data that aid diagnosis of smear negative PTB.

**Methods:** This is a cross-sectional study of smear negative culture positive pulmonary tuberculosis patients diagnosed from BAL sample in patients who underwent bronchoscopy from January 2005 to December 2015 in our tertiary center in Malaysia.

**Results:** 124 patients were included in this study. Mean age was 47.1 ± 17.4 year. Majority were male (62.9%). The mean duration of symptoms onset prior to presentation was 86.2 ± 145.5 days and mean time to treatment was 56.8 ± 61.3 days.

Majority of patients presented with chronic cough (80.6%), loss of appetite and loss of weight (66.9%), prolonged fever (56.5%) and haemoptysis (29%). Risk factors include diabetes (26%), chronic kidney disease or end stage renal failure (11.3%), previous PTB (9.7%), immunosuppressive drugs (9.7%), HIV (7.3%), previous malignancy (5.6%), chronic lung diseases (5.6%), COPD (4.8%) and asthma (3.2%).

Chestx-ray findings were consolidation (79%), pleural effusion (21%), cavitation (14.4%), miliary TB (6.5%) and lung mass (4%). CT scan (done in 55.6% of patients) showed consolidation (41.9%), tree in buds (22.6%), cavitations (21.8%), pulmonary nodule (18.5%) and lung mass (6.6%). Biochemistry data showed raised ESR (27.3%, mean ESR 61.8 ± 33.6 mm/hour), anaemia (64.5%, mean haemoglobin 11.54 ± 2.24 g/dL with 35.5% were hypochromic microcytic anaemia), lymphopenia (50%, mean lymphocytes count 4.72 ± 9.21 x 10^9/L), neutrophilia (34.7%, mean neutrophil count 14.35 ± 20.98 x 10^9/L) and hypoalbuminaemia (52.5%, mean albumin 33.15 ± 7.32 g/L).

**Conclusions:** Patients with smear negative culture positive pulmonary tuberculosis often presents with chronic cough, are diabetic, have CXR and CT scan findings of consolidation with biochemistry data showing anaemia, lymphopenia and hypoalbuminaemia.

**Different Yield of TB Case Notification by Active Case Finding (ACF) in Operational Districts (OD) Where ACF Had Previously Implemented Versus Has Not Been Implemented**

S. Khann, N. Song, K. Tan

Family Health International 360, Tuberculosis, Phnom Penh, Cambodia, and National Center for Tuberculosis and Leprosy Control Program, Training, Phnom Penh, Cambodia

**Background and Aims:** ACF has been used extensively in a variety of settings for detecting TB, and this strategy has been demonstrably effective in reducing TB prevalence and incidence. Cambodia has done ACF in many ODs under TBREACH grant. The study aims to compare the different yield of TB case notification by ACF in ODs where ACF had previously implemented versus has not been implemented.

**Methods:** It is a retrospective cross sectional study which reviewing ACF data done from April to June 2016 in two ODs where ACF had previously implemented namely OD Sampov Meas in Pursat Province and OD Kampong Speu in Kg Speu province and one OD where no ACF has been implemented namely OD Bakan in Pursat province, Cambodia. ACF used a four-symptom screening and follow by Chest X-Ray (CXR) among positive symptoms. An abnormal CXR patient was collected one sputum sample for Xpert MTB/RIF testing. The team used CXR and Xpert result for diagnosing TB as per WHO TB case definition.

**Results:** VHSGs referred 1.8% (n = 13934) of population in the 3 ODs for diagnosing TB by ACF. Of those, 61.0% (n = 8500) got CXR, 26.7% rejected due to absence of TB symptoms and 12.3% were absence. Of populations taken CXR, we found 7.4% (n = 828) with TB. Among those TB cases, 36.0% (n = 226) were bacteriological positive TB. The above data shown, OD Sampov Meas and OD Kampong Speu found 7.6% (n = 504) with TB of 6607 TB suspects taken CXR comparing OD Bakan found 6.6% (n = 124) with TB of 1893 TB suspects taken CXR (P = 0.1223).

**Conclusions:** There was no statistically different between the proportion of TB notification cases in population where ACF has been done and has not been done in the past two years. A vigorous study design need to further evaluate if the ACF significantly contributed to the reduction incidence of TB case.
ORAL PRESENTATION 25 - TUBERCULOSIS: NEWS IN TUBERCULOSIS TREATMENT

THE CULTURE AND SENSITIVITY PATTERN OF MYCOBACTERIUM-TUBERCULOSIS IN CATEGORY-II PATIENTS OF REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAM(RNTCP) OF INDIA AND ITS INFLUENCE ON TREATMENT OUTCOME

S. MEHRA, S. HERAGANAHALLY, S. TRIPATHI, R. GARG, A. JAIN, R. PRASAD

Royal Darwin Hospital, Department of Respiratory medicine, Darwin, Australia, King George’s Medical University, Department of Pulmonary Medicine, Lucknow, India, King George’s Medical University, Department of Microbiology, Lucknow, India, and Era’s Lucknow Medical College and Hospital, Department of Pulmonary Medicine, Lucknow, India

Background and Aims: RNTCP uses short course anti-tubercular(ATT) chemotherapy given intermittently under direct observation (DOTS). Isoniazid (H), Rifampicin(R), Pyrazinamide(Z), Ethambutol(E) and Streptomycin(S) form part of Category-I (2H3R3Z3E3 + 4H3R3) and Category-II (2H3R3S3Z3E3 + 1H3R3Z3E3 + S5H5R5E5) regimen, which are recommended for treatment of new and previously treated tuberculosis patients respectively.

There is however concern regarding effectiveness of category-II (Retreatment) regimen especially in failure cases. Objective of this study was to know the prevalence and pattern of anti-tubercular drug resistance in category-II Tuberculosis(TB) patients and to measure effect of culture-sensitivity pattern and other factors on treatment outcome, further addressing the effectiveness of category-II regimen.

Methods: Normal 0 false false false EN-US JA X-NONE

All the patients registered under category-II at RNTCP center from August,2006 to july,2007 were included,demographics recorded and outcome observed prospectively.

Sputum sample was collected for culture-sensitivity mycobacterium-tuberculosis while starting treatment and at end of 3 months of treatment.

Acid-fast bacilli staining of sputum was done by Zeihl-Nelson’s Method, Culture by modified Lowenstein-Jensen’s medium and resistance testing was done by proportion method.

Results:

| Type of patient | Regimen |
|-----------------|---------|
| Category-I | All New Pulmonary Tuberculosis (Sputum smears-positive and negative) Extrapulmonary |
| Category-II | Relapse: TB patient declared cured who reports back and found sputum positive Treatment after default: Taken treatment for 1 month or more and then started for 3 more months and found sputum positive Failure: Sputum positive at 5 months or more after Category-I treatment |
| Others | 2H3R3S3Z3E3 + M6H6R6 |
| H-Isoniazid, R-Rifampicin, E-Ethambutol, Z-Pyrazinamide, S-Streptomycin |

Methods: Normal 0 false false false EN-US JA X-NONE

- All the patients registered under category-II at RNTCP center from August,2006 to july,2007 were included,demographics recorded and outcome observed prospectively.
- Sputum sample was collected for culture-sensitivity mycobacterium-tuberculosis while starting treatment and at end of 3 months of treatment.
- Acid-fast bacilli staining of sputum was done by Zeihl-Nelson’s Method, Culture by modified Lowenstein-Jensen’s medium and resistance testing was done by proportion method.

1. 65.5% of registered patients were pre-treatment susceptible to ATT or culture-negative
2. MDR-TB was observed in 10.3%,8.2% and 23% of relapse,treatment after default(TAD) and failure subcategories respectively.
3. Resistance to H,S,R,E,Z were 24.1%,17.2%,16.1%, 5.7% and 17.2% respectively
4. Emergence of resistance to Rifampicin was seen in 3.8%cases following category-II treatment.
5. Of the patients with known outcome,16% defaulted,13.3% failed treatment, 10.7% died, while 60% successfully completed treatment.
6. Failure rate was 7.7%, 9.5% and 55.6% for patients with susceptible, poly-drug resistance and MDR-TB respectively

Conclusions: 1. 10.4% of Category-II and 23% of failure subcategory patients respectively had MDR-TB
2. RNTCP retreatment regimen is adequate except for MDR-TB patients

© 2016 Asian Pacific Society of Respirology

Respirology (2016) 21 (Suppl. 3), 3–213
AN INTRIGUING CASE OF TUBERCULOUS PROSTATITIS WITH PLEURAL AND CEREBRAL INVOLVEMENT

N.Y. MOHD ESA, M. HANAFIAH, M. KOSHY, H. ABDULLAH, A.N. MUSA, M.F. ABDUL RANI, M.A. MOHD ZIM, A.I. ISMAIL
Universiti Teknologi MARA Uitm, Internal Medicine, Sungai Buloh, Malaysia

Background and Aims: About 10% of TB cases in Malaysia are classified as extra pulmonary TB. TB Prostatitis is very rare and has mainly been described in immunocompromised or elderly patients.

Methods: We describe a case of a young immunocompetent man who initially presented with respiratory signs followed by seizures and testicular swelling, and finally was diagnosed with TB Prostatitis.

Results: A 44-year-old Malay man was referred to our chest clinic for further investigation of an incidental finding of right-sided pleural effusion. He was asymptomatic, and no history of contact with TB patients. Physical examination revealed decreased air entry and dullness to percussion over the right lower lung field. The initial TB work up were negative. The CXR revealed right-sided pleural effusion. CT Thorax showed minimal right pleural effusion and diffuse pleural thickening associated with sub-segmental atelectasis and consolidation in the right lower lobe. Bronchoscopy findings was normal and the results were negative for TB or malignancy. He was then readmitted with recurrent seizures and left testicular swelling. Scrotal examination revealed a palpable, non-tender, hard mass over the left testis measuring 1x2x1cm. The neurological examination was unremarkable. CT Brain demonstrated a non-specific small rim-enhancing lesion in the right parietal lobe. The CSF analysis was within normal limits. USG Testes showed a heterogeneous left epididymal lesion. His HIV status was negative, HBA1C: 5.6 and PSA levels was elevated. TRUS-guided biopsy revealed presence of AFB on ZN stain and granulomatous features. He was started on Akurit and subsequently, the testicular swelling resolved.

Conclusions: Tuberculosis can manifest in many forms, and a thorough history and physical examination is essential, especially in detecting rare forms of extra-pulmonary tuberculosis. In a country with high TB prevalence, whenever symptoms point to a pathology of the genitourinary system, TB prostatitis should be kept in mind even in immunocompetent young adults.

TREATMENT OUTCOMES OF CHILDHOOD TB PATIENTS IN FOUR TB HIGH BURDEN STATES OF MALAYSIA: RESULTS FROM A MULTICENTER RETROSPECTIVE COHORT STUDY

A. HAYAT
Universiti Sains Malaysia, Discipline of Clinical Pharmacy, Penang, Malaysia

Background and Aims: Aner Hayat Khan1, Syed Azhar Syed Sulaiman1, Abdul Razak Abdul Mutallif2, Mohamed Azmi Ahmad Hassali2, Nazleez Ahmad1, Omar Matteen1

Objective: The aim of the present study was to evaluate treatment outcomes and predictors of unsuccessful treatment outcome in children TB patients in four TB high burden states of Malaysia.

Methods: This was a retrospective cohort study conducted at 13 health care centers in four states of Malaysia i.e. Sabah, Sarawak, Selangor and Penang. All children TB patients (age < 15 years) enrolled for treatment at the study sites from January 1, 2006 to December 31, 2008 were included in the study. A purpose developed validated data collection form was used to extract the patients’ socio-demographic, clinical and microbiological data from their medical records. Patients were followed until treatment outcome was reported.

Results: During the study period a total of 8932 TB patients were enrolled for treatment at the study sites, of whom 206 (2.31%) were children. Majority of children TB patients were females (52.9%), and belonged to age group 6–10 years (42.7%). Pulmonary-TB accounted for 70.9% of childhood TB with 50% were sputum smear negative pulmonary-TB patients. One hundred and seventy eight patients (86.4%) were successfully treated (87 were cured and 91 completed treatment). Among 28 (13.6%) patients with unsuccessful treatment outcomes, 13 (6.3%) died, three (1.5%) failed treatment 9 (4.4%) defaulted and three transferred out (1.5%). In multivariate analysis the variables which had statistically significant associations with unsuccessful treatment outcomes were male gender (OR = 0.344, P = 0.029), age (8–10 years) (OR = 0.204, P = 0.007) presence of co-morbidity (OR = 2.871, P = 0.047).

Conclusions: The prevalence of childhood TB in the current study was comparable to the national estimates. The study sites reached the WHO target of treatment success. Special attention to the patients with identified risk factors can further improve treatment outcomes.

IMPLANTATION OF METALLIC STENT UNDER DIRECT VISUALIZATION OF FLEXIBLE BRONCHOSCOPE WITHOUT FLUOROSCOPIC GUIDANCE ON OROTRACHEAL INTUBATED PATIENTS

W. XU1, X. HAO,2, Z. GENG,2, H. MAHONG,3, L. FEIYAN,4, H. HUIPING5, W. TIEJUN6
1 Tongde Hospital of Zhejiang Province, Respiration Department, Hangzhou, China, 2The Second Affiliated Hospital of Zhejiang University School of Medicine, Respiration Department, Hangzhou, China, 3Tongde Hospital of Zhejiang Province, Intensive Care Unit, Hangzhou, China, and 4Tongde Hospital of Zhejiang Province, Endoscopy Department, Hangzhou, China

Background and Aims: Stent implantation has been used to liberate patients with severe airway stenosis and respiratory failure from mechanical ventilation; however, a rare clinical study is reported about metallic stent implantation via a flexible bronchoscope without using fluoroscopic guidance in ventilated patients. The present retrospective study aims to evaluate the feasibility, safety, efficacy, and complications of using a flexible bronchoscope without fluoroscopy to implant metallic stent in mechanically ventilated patients.

Methods: From January 2015 to April 2016, eight tracheobronchial metallic stents were implanted in six respiratory failure patients associated with central airway stenosis or fistula. First, a bronchoscope was inserted through an endotracheal tube into the trachea or bronchus, and a guide wire was placed into the stenosis site. The bronchoscope was reintroduced into the airway outside the endotracheal tube. Under bronchoscopic visualization, the delivery catheter was advanced over the guide wire to deploy the stent.

Results: These procedures were successfully performed in all patients, with three stents placed in the trachea and five stents in the main bronchus. The patients were all successfully liberated from mechanical ventilation. Five patients suffered from cough after the procedure. One patient, who received a covered metallic stent implantation in the left main bronchus, experienced increased mucus production. Granulation tissue formation was found in one patient. No patient presented with any stent migration or pneumothorax.

Conclusions: It is concluded that metallic stents can be safely implanted under the direct visualization of a bronchoscope without using fluoroscopic guidance in patients with respiratory failure to wean the patients from mechanical ventilation.

ORAL PRESENTATION 26 - BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES: ADVANCED ENDOBRONCHIAL THERAPY

APSR6-0047
Background and Aims: With the widespread use of computer tomography (CT) for imaging of the chest, as well as screening programs worldwide, there is an increasing need to obtain diagnosis of small pulmonary nodules and ground glass opacities (GGO). Electromagnetic navigation bronchoscopy (ENB) allows for the localization and biopsy of more peripheral pulmonary lesions with reported diagnostic yield of more than 65-70%. Radial EBUS and fluoroscopy is usually used to confirm successful navigation, however for very small and GGO lesions, these methodologies may not be useful. In this study we retrospectively reviewed our early experience with Hybrid (Hybbr) DynaCT and fluoroscopy to aid ENB localization and biopsy of lung lesions.

Methods: Since March 2015, 12 patients have undergone image guided ENB (IENB) in the Hybrid OR for diagnostic purpose with fluoroscopy and DynaCT real time guidance and confirmation of biopsy tool navigation to the target lesion. Pre-operative CT, intra-operative DynaCT imaging, diagnostic yield, complications and post-operative outcomes were reviewed.

Results: Lesion size ranged from 8 mm to 39 mm (Median 22 mm). Five were solid lesions. Five were mixed solid and GGO lesion and two were pure-GGO. Mean procedural time was 114 minutes (range 75-165 minutes). There was no post-operative pneumothorax, haemothorax, pulmonary haemorrhage or pneumonia. All patients were discharged on day 1 after the procedure. The diagnostic yield of IENB in our series was 63.3%. None of the patients required further diagnostic procedure before proceeding to definitive treatment.

Conclusions: The use of Hybrid OR IENB for diagnosis of pulmonary lesions is safe and feasible. The new approach may further improve diagnostic rate of ENB especially in smaller non-solid lesion and reduce complication rates. Further study is warranted to look into the potential benefit of Hybrid OR IENB.

A NOVEL, SIMPLE AND EFFICIENT TECHNIQUE OF AIRWAY Y-STENT DEPLOYMENT USING FLEXIBLE BRONCHOSCOPY IN MALIGNANT LESIONS AND TRACHEOESOPHAGEAL FISTULAE

S.L. GUO, O. GANGANAH, Y. LI
The First Affiliated Hospital of Chongqing Medical University, Department of Respiratory & Critical Care, Chongqing, China

Background and Aims: Self-expanding metallic Y-stents (SEMYs) are used in the treatment of central airway lesions and tracheoesophageal fistulae (TEF). The procedure is most commonly performed with 2 guide wires under rigid bronchoscopy and fluoroscopic guidance. A recent report described 6 cases of SEMYs placement using flexible bronchoscope where they reported difficulties, cross-kinking of guidewires and patients being unfairly uncomfortable. We, herein, describe our novel technique of SEMYs deployment using a flexible bronchoscope.

Methods: The patient was placed supine with extended neck under sedation. A mouth gag was placed. A 4.9 mm flexible bronchoscope was used for stenotic site or TEF identification and guidewire insertion. The guide wire was left in situ and the bronchoscope was reintroduced via the nostril for guidance. The delivery catheter was loaded on the guidewire. Due to its large size and weight it tended to make an ‘S-bend’ preventing advancement. By lifting the guidewire-delivery catheter assembly with an index finger, this angle is obliterated making advancement possible along a smooth curve. The flexible bronchoscope was advanced into the glottis for guidance. At the carina, the two bronchial limbs were released partially by opening the first luer-lock of the catheter and retracting the introducer sheath slightly. The two limbs were advanced until the stent bifurcation met the carina. The catheter’s second luer-lock was opened and the sheath was further retracted, deploying the tracheal limb. Then, the two threads were pulled deploying the two bronchial limbs.

Results: This procedure was successfully performed in 7 patients. Oxygen saturation was maintained above 88% throughout the procedure. The time taken was in the range of 7–25 mins. The mean time taken was 14.9 mins. There were no complications.

Conclusions: This technique can be performed safely in the bronchoscopic suite. It eliminates the need for fluoroscopy, general anesthesia, operation room and reduces the costs and the operation waiting time.

USE OF TRANSBRONCHOSCOPIC END-TIDAL CO2 DETECTION IN THE LOCATION OF THE PLEURAL AIR LEAKAGE IN INTRACTABLE PNEUMOTHORAX

Y. ZENG
Second Affiliated Hospital and Second Clinical Medical College of Fujian Medical, Pulmonary Medicine, Quanzhou, China

Background and Aims: Location of the leading bronchus to pleural fistula is the most important step of transbronchoscopic bronchial occlusion for the treatment of intractable pneumothorax. Balloon detection is the most commonly used technique but failed in some cases. The aim of this article is to determine 1) if bronchoscopic end-tidal CO2 (EICO2) measurement can identify the leading bronchus which is the source of persistent air leak, 2) To establish a methodology for EICO2 detection.

Methods: Twenty eight patients with intractable pneumothorax underwent bronchoscopy with 1) balloon occlusion identification (balloon detection) of the leading bronchus and 2) EICO2 determination at the orifices of multiple bronchi in the distal airway of the affected lung. The efficacy of these two methods of feeding bronchus identification was compared. The threshold end-tidal CO2 (T-EICO2) was determined.

Results: Bronchoscopic EICO2 determination identified 17 (60.7%) feeding bronchi. Balloon occlusion identified 18 (64.3%, P = 0.041) feeding bronchi and the combination of the two techniques 27 (96.4%). The average differences in EICO2 between the leading bronchus and the main carina, main bronchus, and non-leading bronchus were (in mmHg): 4.41 ± 1.99 (95% confidence interval: 3.55,3.97), 4.73 ± 2.10 (3.85,5.66) and 5.57 ± 2.53(4.46,6.69), respectively.

Conclusions: (1) end-tidal CO2 (EICO2) measurement is complementary to balloon detection of the leading bronchus. (2) Combination of the two is extremely effective in this identification. 3.5A threshold value of > 5 mmHg is optimal for this technique.

FACTORS AFFECTING DIAGNOSTIC BRONCHOSCOPY WITH RADIAL ENDOBRONCHIAL ULTRASOUND FOR PERIPHERAL PULMONARY LESIONS

Y. MATSUMOTO, T. IZUMO, T. NAKAI, T. TSUCHIDA
National Cancer Center Hospital, Department of Endoscopy- Respiratory Endoscopy Division, Tokyo, Japan

Background and Aims: Radial endobronchial ultrasound (R-EBUS) is known to be useful and recommended to use for diagnostic bronchoscopy for peripheral pulmonary lesions (PPLs). However, recent report showed the opposite result analyzing the registry-based clinical data. The author emphasizes that an evidence is composed of clinical research studies examined carefully selected and relatively small populations of patients. Conversely in our institution, most of the examination are operated by resident trainee under the direct supervision of bronchoscopic expert staff. Therefore, we aimed to clarify the factors affecting diagnostic bronchoscopy with R-EBUS for PPLs analyzing our huge daily clinical-based data.

Methods: Consecutive patients who underwent bronchoscopy with R-EBUS for PPLs from April 2012 to September 2014 were collected. Of these, the cases with definite diagnoses were enrolled in this study. All bronchoscopies were performed under X-ray fluoroscopy guidance under conscious sedation. The clinical and imaging factors likely to affect the diagnostic outcome were analyzed using chi-square and multivariate logistic regression test.

Results: We analyzed total 1,007 cases, and the diagnostic yield was 73.1%. As a pre-examination information, positive bronchus sign, X-ray visible, and the nearest bronchial generation 6 or less were the significant factors affected the diagnostic success in the multivariate analysis (p < 0.001, p = 0.001, p = 0.043, respectively). On the other hand, as during an examination information, the obtained R-EBUS findings (within, adjacent to, or invisible) significantly affected the diagnostic yield (90.7%, 59.8%, 10.6%, respectively; p < 0.001). Besides, the multivariate analysis showed multiple factors complicatedly affected the accessibility confirmed by R-EBUS; bronchus sign, X-ray visibility, lesion size, lesion location, with virtual bronchoscopy, and using needle (p < 0.001, p < 0.001, p < 0.001, p < 0.01, respectively). There were no complications.

Conclusions: Positive bronchus sign and X-ray visible are considered to be important positive factors in diagnostic bronchoscopy for PPLs.
Background and Aims: Endobronchial ultrasound (EBUS) is a minimally invasive procedure allowing visualization and sampling of structures at a 2–5 cm depth within the airway wall, lung and mediastinum at real-time. Studies show that EBUS morphology of lymph nodes could predict benign histology with a size of <10 mm, triangular shape and the presence of a central vessel. Patients with isolated mediastinal lymphadenopathy may be asymptomatic, but commonly present with cough, dyspnea, weight loss and fever. Correlating the patients’ clinical profile and EBUS lymph morphology to benign histology may reduce the number of nodes required for sampling and the need for further invasive investigation.

The aim of the study is to determine the association of patients’ clinical profile and lymph node morphology on EBUS as predictors of benign disease.

Methods: This was a retrospective observational study. The patients’ demographic characteristics, symptoms, risk factors, family history, as well as lymph node size, shape, margins, echogenic pattern, presence or absence of a central vessel and central necrosis on EBUS were obtained. These features were correlated to benign lymph node histology.

Results: There were 24 patients in the study. 14 had malignant histology and 7 were classified as benign due to the presence of Mycobacterium tuberculosis in cultures or clinical or radiologic findings consistent with benign disease in a 12-month follow-up. The mean age was 61 years ± 13.4. There was a significant correlation for fever (p = 0.027), previous pulmonary tuberculosis (PTB) (p = 0.0002), family history of PTB and tuberculous pleurisy (23/35), parapneumonic pleural effusion (1/35). When 48.7 kilo-Pascals (kPa) was set as the cut-off of diagnosis of MPE. The UE diagnosis was compared with de histology and lymph node morphology on EBUS as predictors of benign disease.

Conclusions: There are different lymph node morphologies predictive of a benign histology when compared to other studies perhaps due to the small sample size in the study. The significant correlation for fever, previous PTB and family history of PTB could be explained by the high prevalence of tuberculosis in the country.

ORAL PRESENTATION 27 - CLINICAL RESPIRATORY MEDICINE: PULMONARY DISEASE: MANAGEMENT IN THE FUTURE

PLEURAL ULTRASONIC ELASTOGRAPHY IN THE DIAGNOSIS OF MALIGNANT PLEURAL EFFUSION

G. Hou1, B. Jian,2, Y. Yin3, Q. Wang1, J. Kang1

The First Hospital of China Medical University, Respiratory medicine, Shenyang, China, and 2The First hospital of China Medical University, Ultrasound, Shenyang, China

Background and Aims: Thoracic ultrasound (TUS) is useful in differentiating malignant pleural effusion (MPE) from benign pleural effusion. While ultrasonic elastography (UE) has been shown to be valuable in the diagnosis of thyroid and breast cancers, its use in the diagnosis of malignant pleural disease has not been assessed. Here a study was performed to assess the accuracy of UE of pleura in differentiating MPE from benign pleural diseases.

Methods: Sixty one consecutive patients with suspected MPE were undertaken TUS and UE (ShearWave™ Elastography, Supersonic Imagine, France) performed by two operators. Receiver operating characteristic curve of elasticity value (EV) was built to confirm the cut-off of diagnosis of MPE. Definitive diagnosis of MPE was based on histology, and benign pleural effusion was based on negative histology and follow-up over 12 months. The UE diagnosis was compared with definitive diagnosis.

Results: Malignant diagnoses included lung cancer (19/26), malignant mesothelioma (3/26) and breast cancer (1/26). Benign diagnoses included tuberculous pleuritis (23/35), parapneumonic pleural effusion (5/35), bacterial empyema (2/35), cardiac failure (2/35) and rheumatoid arthritis (1/35). When 48.7 kilo-Pascals (kPa) was set as the cut-off of mean EV or 60.05 kPa was set as the cut-off of maximum EV (sensitivity 80.8%, specificity 80%, positive predictive value 75%, negative predictive value 84.8%; Area under curve was 0.780 and 0.792 separately). The tuberculous pleuritis and empyema was the main reason for false positivity of UE in diagnosis of MPE.

Conclusions: Pleural ultrasonic elastography is a valuable and effective technique in differentiating MPE from benign pleural effusion and may become an important adjunct in diagnostic methods.
LATANOPROST EYE DROP INCREASES COUGH SENSITIVITY BY DECREASING THRESHOLD OF VAGAL SENSORY NERVES

N. BENJATIKUL,1 S. JIRIYASIN,2 N. PAKAPROT,2 K. MANEECHOTESUWAN,2 T. OGA,1 K. SOONTRAPA,1
1Faculty of Medicine Siriraj Hospital- Mahidol University, Pharmacology, Bangkok, Thailand, 2Faculty of Medicine Siriraj Hospital- Mahidol University, Physiology, Bangkok, Thailand, 2Faculty of Medicine Siriraj Hospital- Mahidol University, Internal Medicine, Bangkok, Thailand, and 4Graduate School of Medicine- Kyoto University, Respiratory Care and Sleep Control Medicine, Kyoto, Japan

Background and Aims: The PGF₂α analogue, latanoprost, as topical eye drop is increasingly chosen for treatment of open-angle glaucoma. However, treatment with latanoprost can make patient cough more easily and lead to discontinuation of the drug. We confirmed this adverse effect using an animal model of cough. We also demonstrated latanoprost decreases threshold of action potential (AP) of vagus nerve involved in cough reflex.

Methods: Conscious guinea pigs were individually placed in a chamber. Various doses of citric acid (0.03, 0.1, 0.3, 1 M) were delivered via a nebulizer for 10 minutes to induce cough in them. The number of coughs was counted during this period by observing a typical postural change of guinea pigs, splaying of the front legs, forward stretching of the head and neck, and open mouth. We then treated them with latanoprost eye drop via either intraocular, intranasal, or intraperitoneal routes 10 minutes before cough induction. Besides, vagus nerves of guinea pigs were resected including nodose ganglia and caudally attached tracheobronchi. We used Krebs-Henseleit solution as physiologic solution. Placed in modified nerve chamber, each resected nerve was used in electrophysiologic experiment measuring the AP threshold. We stimulated nerve by electric current, equivalent to cough stimulator, and found the nerve threshold (mV). Then the nerve was treated by various doses of latanoprost (10, 30, 100 mcM) dissolved in Krebs-Henseleit solution and was re-stimulated by current again.

Results: Intracellular-treated group showed a significant increase in the number of coughs compared with the controls (p < 0.05). Comparing intranasally- and intraperitoneally-treated groups, the number of coughs significantly increased in the former (p < 0.05). Additionally, the treated resected vagus nerves showed significant decrease in threshold potential compared with the controls (p < 0.05).

Conclusions: This study indicated latanoprost increases the cough sensitivity by topical effect, such as via vagal sensory nerve ending distribute along airway, not by systemic effect.

STANDARDIZATION WITH COMPUTER PROTOCOLS IS NECESSARY TO ASSURE REPLICABLE INTERPRETATIONS OF PULMONARY FUNCTION TESTS (PFT)

A. MORRIS,1 O. LINARES2, M. HEGEWALD1
1University of Utah, Internal Medicine Pulmonary/Critical Care Division, Salt Lake City, USA, and 2Intermountain Healthcare, Pulmonary/Critical Care, Murray, USA

Background and Aims: PFT interpretation in developed and developing countries is variable and associated with unwarranted variation. As a result, miscategorizations of patients occur and inappropriately influence both diagnoses and management of patients with pulmonary disorders. Miscategorizations also occur because of the high frequency of technical performance errors and of clinician interpretation errors. Non-replicable clinical decision methods rely on clinician judgment to fill the logic gaps in commonly used protocols and guidelines. It is clear that detailed computer protocol replicable clinician decision methods can be exported across cultures and across medical disciplines. These methods can translate research results to clinical practice, achieving clinician compliance rates of 95% with protocol instructions. They standardize clinician decisions and behavior, while retaining personalized patient care instructions. We have used a detailed computer protocol to interpret PFTs according to ATS/ERS guidelines for thousands of patients during the past 3.5 years. FEV1/FVC ratio depends on different prediction and interpretation strategies that use different variables (Figure 1, GLI12:Global Lung Initiative 2012. GOLD:Global Initiative for Chronic Obstruction Lung Disease), NHANESIII:National Health and Nutrition Examination Survey III). We aimed to quantify the NHANESIII and GLI12 spiromgram prediction differences in a clinical population.

Methods: We used the detailed computer protocol to interpret PFTs according to ATS-1984 and the ATS/ERS-2005 spiromgram interpretations. We compared NHANESIII and GLI12 reference equation spiromgram results in patients with restriction based on plethysmographic TLC measurement (shaded boxes in Figure 1).

Results: We categorized PFT result differences between NHANESIII and GLI12 reference equations (Figure 2a, b).

Conclusions: Standardized PFT interpretations allow scientifically rigorous comparisons that lead to credible clinical conclusions. A systematic use of such protocols could standardize and improve the diagnosis and categorization of patients with respiratory disease in the Asian Pacific region.
Background and Aims: Roflumilast, a phosphodiesterase-4 inhibitor, is recommended by clinical guideline, is always be used in combination with at least one long-acting bronchodilator in patients with stable chronic obstructive pulmonary disease (COPD). However, there are few evidences about whether the combination of roflumilast and long-acting bronchodilators is safer and more effective than long-acting bronchodilators alone in preventing COPD exacerbation. The purpose of this paper was to investigate the effect and safety of roflumilast combined with long-acting bronchodilators on moderate-to-severe stable COPD patients.

Methods: Several databases including PubMed, Embase, Google Scholar and the Cochrane Central Register of Controlled Trials were adopted in Nov,2015, so as to identify relevant randomized controlled trials (RCT). Studies indicated that the patients in the experimental group had to have received roflumilast and concomitant treatment with long-acting bronchodilators, the patients in the control group had to have received placebo and concomitant treatment with long-acting bronchodilators. The relative risks (RRs) and 95% confidence intervals (CIs) were calculated.

Results: Six trials involving 5746 patients accorded with the inclusion criteria. Roflumilast combined with long-acting bronchodilators could lead to significant reduction in exacerbation of COPD (RR, 0.77; 95% CI, 0.69 to 0.86; P < 0.00001, I² = 0%). According to the subgroup analysis, the test for subgroup difference between roflumilast combined with long-acting bronchodilators and roflumilast combined with ICS and long-acting bronchodilators showed no significance. Compared with the exclusive use of long-acting bronchodilators, roflumilast combined with long-acting bronchodilators could cause some adverse events such as: back pains, headache, diarrhea, nausea, weight loss, insomnia and decreased appetite.

Conclusions: Roflumilast combined with long-acting bronchodilators is a better option for moderate-to-severe COPD patients than exclusive use of long-acting bronchodilators in reducing exacerbation. However, Roflumilast combined with long-acting bronchodilators can cause some adverse effects. Clinical workers should consider well enough of the benefits and adverse events caused by roflumilast combined with long-acting bronchodilators.
ORAL PRESENTATION 28: LUNG CANCER: UNDERSTAND BASIC AND CLINICAL

IMPACT OF LENT SCORE ON MALIGNANT PLEURAL EFFUSIONS DUE TO LUNG CANCER

S. TAY, S. ONG, P. LEE
National University Health System, Division of Respiratory and Critical Care Medicine, Singapore, Singapore

Background and Aims: LENT score, a composite of pleural fluid lactate dehydrogenase, Eastern Cooperative Oncology Group Performance Score (ECOG-PS), neutrophil-to-lymphocyte ratio and tumour type, demonstrated superiority over ECOG-PS in prognosticating survival of patients with malignant pleural effusions (MPE). Median survivals of low, moderate and high-risk categories were 319, 130 and 44 days respectively. We determined if LENT was predictive of survival in lung cancer-related MPEs where epidermal growth factor receptor (EGFR) mutations were prevalent.

Methods: Consecutive patients (n = 68) with MPEs and data on demographics, tumor type, EGFR mutation status and LENT score were analysed. All were followed till death for survival computation.

Results: Median age was 70 years, 35 (51.5%) were males, 47 (69%) were due to lung cancers. Most common histological subtype was lung adenocarcinoma (n = 45, 65%) which were analysed for EGFR mutations; 21/45 (47%) were positive, 20 (95%) received tyrosine kinase inhibitors (TKI) while the rest received conventional chemotherapy. Majority were moderate-risk as categorised by LENT (Table 1).

Median survival in low, moderate and high-risk categories were 631, 171 and 98 days respectively (p = 0.047). In the LENT moderate-risk group where heterogeneity was apparent, lung adenocarcinoma showed survival advantage over other cancers (195 vs 67 days, p = 0.005) and EGFR mutation played an important role (EGFR-positive 414 vs EGFR-negative 161 days, p = 0.027) (Fig.1).

Conclusions: LENT underestimates survival of patients with lung cancer-related MPE where EGFR mutations are prevalent. Robust prognostication strategies incorporating cancer molecular signatures should be the way forward in the era of personalised therapy.

Table 1: LENT score risk categories

| Category                  | Low risk, n (%) | Moderate risk, n (%) | High risk, n (%) |
|---------------------------|-----------------|----------------------|-----------------|
| Mesothelioma              | 4 (5.9)         | 54 (79.4)            | 9 (13.2)        |
| Haematological malignancy | 1 (1.5)         |                      |                 |
| Lung adenocarcinoma       | 37 (54.4)       |                      |                 |
| EGFR positive             | 16              |                      |                 |
| EGFR negative             | 21              |                      |                 |
| Squamous carcinoma        | 1 (1.5)         |                      |                 |
| Small cell carcinoma      | 1 (1.5)         |                      |                 |
| Mesothelioma              | 1 (1.5)         |                      |                 |
| Others                    | 14 (20.5)       |                      |                 |
| Breast carcinoma          | 4               |                      |                 |
| Gastric carcinoma         | 2               |                      |                 |
| Ovarian carcinoma         | 2               |                      |                 |
| Renal cell carcinoma      | 2               |                      |                 |
| Colorectal carcinoma      | 1               |                      |                 |
| Thymic carcinoma          | 1               |                      |                 |
| Unknown primary           | 1               |                      |                 |

Median survival in low, moderate and high-risk categories were 631, 171 and 98 days respectively (p = 0.016) which were longer than reported. There was no survival difference between lung cancer-related MPE and other cancers (184 vs 103 days, p = 0.834). Patients with EGFR-positive lung adenocarcinomas survived longer than EGFR-negative counterparts (234 vs 136 days, p = 0.047). In the LENT moderate-risk group where heterogeneity was apparent, lung adenocarcinoma showed survival advantage over other cancers (195 vs 67 days, p = 0.005) and EGFR mutation played an important role (EGFR-positive 414 vs EGFR-negative 161 days, p = 0.027) (Fig.1).

Conclusions: LENT underestimates survival of patients with lung cancer-related MPE where EGFR mutations are prevalent. Robust prognostication strategies incorporating cancer molecular signatures should be the way forward in the era of personalised therapy.

Figure 1: Survival of moderate-risk lung adenocarcinoma stratified by EGFR status

PREOPERATIVE NUTRITIONAL CONDITION AS A PROGNOSTIC FACTOR FOR LUNG CANCER IN ELDERLY PATIENTS

I. WATANABE, N. KANAUCHI, H. WATANABE
Nihonkai General Hospital, General Thoracic Surgery, sakata, Japan

Background and Aims: This study aimed to assess the prognostic factors, especially the preoperative nutritional condition as estimated with the prognostic nutritional index (PNI), after surgical treatment of patients aged 75 years or older with primary lung cancer. PNI is scored based on laboratory data of albumin and lymphocyte count.

Methods: From July 2008 to December 2014, 137 elderly patients who had undergone curative operations at our hospital were enrolled. There were 74 men and 63 women with a median age of 79 years (range 75–88 years). Operative procedures were lobectomy in 90 (65%), segmentectomy in 24 (17%), and wedge resection in 23 (17%). Histological types were adenocarcinoma in 104 (76%) and non-adenocarcinoma in 33 (24%). Postoperative stage was I in 112 (82%) and, over II in 25 (18%). One hundred fifteen (84%) had a PNI high score (≥45) and 22 (16%) had a low score. We retrospectively analyzed the association between PNI and the following clinical factors: Charlson Comorbidity Index (CCI), operation approach and procedures, node dissection, histological types, postoperative complications, and c-stage, and p-stage.

Results: The 5-year overall survival rate was 57% and the cancer specific survival was 70%. Among patients who died within 5-years, the death rate due to other diseases was 31%. Univariate analysis were observed for identified sex (p = 0.002), PNI (p = 0.012), c-stage (p = 0.001), histological types (p = 0.001), and p-stage (p ≤ < 0.001) as prognostic factors. Multivariate analysis were observed found that PNI (HR 2.46, p = 0.038) and p-stage (HR 3.99, p = 0.001) were independent prognostic factors in elderly lung cancer patients who had undergone curative operations.

Conclusions: Our analysis revealed that PNI and p-stage were independent prognostic factors in elderly patients with primary lung cancer. Therefore, PNI might be a useful factor for prognostication in elderly lung cancer patients.
Background and Aims: Epidermal Growth Factor Receptor (EGFR) mutation testing is mandatory for all new non small cell lung carcinoma (NSCLC) patients prior to prescription of EGFR Tyrosine Kinase Inhibitors (TKI). Treatment of TKI are given to patients with test results showing TKI sensitizing mutations in exon 18 (codon G719S), exon 19 (insertions/deletions), and exon 21 (codons L858R, L861Q). Good response may last for a year until disease becomes TKI resistant due to emergence of tumor clones harboring EGFR T790M mutation in exon 20 of EGFR gene. Extent of pre-existing T790M in TKI naïve patients are not yet known.

Methods: Consecutive patients undergoing EGFR testing (September 2015-April 2016) ordered by three physicians JZ, SLA, and AH were extracted from electronic database of ISO15189 accredited central laboratory. Tumor contents and adenocarcinoma histology were verified by pathologist GW and HH. Four exons of EGFR were tested using a combination of PCR High Resolution Melting, fragment sizing, and direct DNA sequencing.

Results: One hundred and fourteen patients were identified. Most cytological specimens were obtained using bronchoscopy (31%) followed by TTN (Transthoracal Needle Aspiration) (29%), and Pleura smear (17%). Overall, EGFR mutation rate was 31%, which included T790M mutation rate (13%). About half of T790M mutations were found together with TKI sensitizing mutations. The incidence of T790M was more often in women (13%) than men (9%). T790M also tend to coexist with substitution mutations in exon 18 (9.6% vs 77.2% P = 0.026). In addition, we revealed that the inhibition of Jak2 or STAT3 activity could also suppressed HPF-induced A549 migration and invasion in vitro.

Conclusions: Our results identify T790M as a novel inhibitor of CAFs-triggered NSCLC migration and invasion. To explore the effects of J201, a novel sulfated oligosaccharide, on CAFs-triggered NSCLC migration and invasion.

Methods: NSCLC cells A549 were cocultured with human pulmonary fibroblast (HPF). The impacts of J201 on HPF-induced tumor motility were investigated using transwell migration and invasion assays. The effects of J201 on intracellular Jak2-STAT3 signalling of cocultured A549 were examined via immunoblotting.

Results: Conditional medium of coculture promoted the migration and invasion of A549 cells in vitro, which were inhibited by J201 in a dose-dependent manner (0, 25, 100 μg/mL). Cocultured A549 exhibited elevated expression of phosphorylated Jak2 and STAT3, and elevated secretion of matrix metalloproteinase (MMP)-9, which were reversed by J201 dose-dependently (10, 50, 200 μg/mL). In addition, we revealed that the inhibition of Jak2 or STAT3 activity could also suppressed HPF-induced A549 migration and invasion in vitro.

Conclusions: Our results identify J201 as a novel inhibitor of CAFs-induced tumor migration and invasion in human NSCLC, possibly through inactivating the Jak2-STAT3 signal pathway. We suggest that J201 may serve as a useful antimitastatic agent.

Background and Aims: Afatinib (AFA), second-generation epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs), have overall extended the survival rates for patients (pts) with non-small-cell lung cancer (NSCLC) harboring a positive EGFR gene mutation. On the other hand, severe adverse effects, such as diarrhea, frequently occur when compared to 1st generation EGFR-TKIs, and many pts are required to implement a dose reduction or a drug withdrawal. Since the objective predictive index for adverse effects by AFA haven’t been established, we prospectively examined the relationship between plasma AFA concentration and the severity of adverse events.

Methods: NSCLC pts, with consent, had been enrolled from July 2014 to March 2015 at Iwate Medical University Hospital. The study measured the serum AFA trough plasma concentration via a high performance liquid chromatography mass spectograph on the 1st, 3rd, 8th, and 14th day after medication (47.0 ± 9.5 vs 24.4 ± 0.1 ng/mL, P = 0.017). Renal function (estimated glomerular filtration rate) was also indicated to be significantly lower before administration (58.0 ± 9.6 vs 77.2 ± 9.0 ml/min, P = 0.026).

Conclusions: High AFA concentration was associated with AFA adverse effects in this study.

**Background and Aims:** Recent evidence suggests that cancer-associated fibroblasts (CAFs) could facilitate tumor migration and invasion in non-small cell lung cancer (NSCLC). The present study was aimed to investigate the effects of J201 on the in vitro motility and invasion of NSCLC A549 cells cocultured with human pulmonary fibroblasts (HPFs). The study investigated the effects of J201 on the migration and invasion of A549 cells in vitro, and the impact of J201 on the expression of phosphorylated Jak2 and STAT3, and the secretion of matrix metalloproteinase (MMP)-9. The research also evaluated the effects of J201 on the proliferation and migration of A549 cells in vitro.

**Methods:** NSCLC cells A549 were cocultured with human pulmonary fibroblasts (HPFs). The study examined the effects of J201 on the migration and invasion of A549 cells in vitro, and the expression of phosphorylated Jak2 and STAT3, and the secretion of matrix metalloproteinase (MMP)-9. The study also investigated the effects of J201 on the proliferation of A549 cells.

**Results:** The study found that J201 significantly inhibited the migration and invasion of A549 cells, and reduced the expression of phosphorylated Jak2 and STAT3, and the secretion of MMP-9. In addition, J201 significantly inhibited the proliferation of A549 cells.

**Conclusions:** The study identified J201 as a novel inhibitor of CAFs-induced tumor migration and invasion in human NSCLC, possibly through inactivating the Jak2-STAT3 signal pathway. The study suggests that J201 may serve as a useful antimitastatic agent.