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ORAL PRESENTATION – ASTHMA

O-A-001

PLUME TEMPERATURE AND FORCE OF FLUTICASONE PROPIONATE/FORMOTEROL pMDI COMPARED WITH FLUTICASONE PROPIONATE/SALMETEROL pMDI

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Background: Aerosol inhaler characteristics such as low plume temperature and high force may result in greater impaction of drug in the mouth and throat and reduced lung deposition.¹ This study compared plume temperature and force of two ICS/LABA combination products: fluticasone propionate/formoterol 125/5 µg (flutiform®, FP/FORM) and fluticasone propionate/salmeterol 125/50 µg (Seretide®, FP/SAL), delivered via metered-dose inhalers.

Methods: Inhalers were held in a fixed device and operated according to manufacturers' instructions. A thermal imaging video camera, operating at 30 frames per second, recorded plume temperature from the side of the device. The same test rig, with a copper disc attached to a sensitive load cell measured plume force over a range of distances 25 mm to 95 mm from the device.

Results: At 25 mm the FP/FORM plume was +6°C, while that of the FP/SAL plume was –38°C. The FP/SAL plume was colder over a longer distance. The force of the FP/SAL plume was greater than that of the FP/FORM device at all distances measured: mean force recorded for FP/SAL was 218.0 mN compared to 104.0 mN for FP/FORM.

Conclusion: The FP/SAL plume was considerably colder than the FP/FORM plume particularly over shorter distances. The FP/SAL plume was more forceful, approximately twice that of the FP/FORM device. These differences may be due to different types of HFA propellant with different boiling points, the excipients in each formulation, and actuator geometry. The plume characteristics of the FP/FORM device may facilitate lung deposition and lessen impaction in the throat.

Reference:1 Gabrio BJ. *Int J Pharm* 1999;186:3–12**Sponsor:** MUNDIPHARMA RESEARCH LTD

O-A-002

THERAPEUTIC EFFECTS OF HISTONE DEACETYLASE ENZYME 6 INHIBITORS (HDAC6I) IN A MURINE ASTHMA MODEL

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Background and Purpose: Airway inflammation, airway remodeling and airway hyperresponsiveness are major aspects of asthma pathology. Histone deacetylase inhibitors have a broad effects that demonstrate therapeutic effects in animal models of chronic inflammatory diseases. In this study, we investigated the effects of Tubastatin A Hcl, a selective HDAC6 inhibitor, on the development of chronic allergic airway disease mice with airway inflammation, airway remodeling and airway hyperresponsiveness.

Methods: Wild-type BALB/C mice were sensitized intraperitoneally three times with ovalbumin (OVA) and aluminum hydroxide gel (on weeks 0, 1, 2) and nebulized 1 week (early phase) or 8 weeks (prolonged phase). Ovalbumin-exposed mice were treated with Tubastatin A Hcl or vehicle control. Airway inflammation was assessed by bronchoalveolar lavage fluid cell counts and HE staining of lung tissue sections. Airway remodeling was assessed by Alcian blue-Periodic acid Schiff staining and Masson trichrome staining. Airway hyperresponsiveness was assessed by plethysmography measurement of airway resistance.

Results: Tubastatin A Hcl treatment relieved airway inflammation compared with vehicle treated mice ($P < 0.05$), but its effect was worse than dexamethasone treatment. However, Tubastatin A Hcl treatment reduced the thickening of airway smooth muscle ($P < 0.05$), the quantity of goblet cell ($P < 0.05$) and subepithelial collagen deposition ($P < 0.05$). Moreover, Tubastatin A Hcl treatment attenuated airway resistance ($P < 0.05$).

Conclusion: These results demonstrate that treatment with HDAC6 inhibitors can reduce airway inflammation, airway remodeling and airway hyperresponsiveness, suggesting that blockage of HDAC6 may be a useful treatment for bronchial asthma.

O-A-003

TRACHEOBRONCHIAL WALL VESSEL REMODELING AND ENDOTHELIAL CELL ACTIVATION IN A MURINE ASTHMA MODEL

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Background and Purpose: Vascular changes in asthma include increasing in vessel number/unit area and increasing in vessel activity: namely vasodilatation, leakage, and cell migration to target tissue. These changes will lead to airway wall thickening and reduced air flow. With these backgrounds in mind, we attempted to obtain in-depth information on microvascular network of bronchial walls and the phenotypes of their endothelial cells in a mouse model of asthma.

Methods: Male BALB/C mice were initially immunized intraperitoneally four times with ovalbumin (OVA) + aluminum hydroxide gel (on weeks 0, 4, 5, 7). Subsequently, the OVA inhalations were done everyday for 1 week (early phase) or 5 weeks (prolonged phase). Untreated mice were used for normal control subjects. The mice were perfused with FITC-dextran through the ascending aorta to probe tracheobronchial wall microvascular network. Tracheobronchial tissues were obtained and examined by light and laser confocal microscopy.

Results: We confirmed that the tracheobronchial walls underwent remodeling as indicated by epithelial cell metaplasia (mucin producing type), sub-epithelial edema, and inflammatory cell infiltration. Capillary networks increased and became dilated and endothelial cells proliferated as judged by Ki67 positivity in the early phase. Normal capillaries in the cartilage zone showed the phenotype of TM (previously shown) and CD31 positive, but not vWF, aSMA, or Desmin positive phenotype. Endothelial cell phenotypes changed into vWF, aSMA, and Desmin positive phenotype, suggesting a transformation into the phenotype of microvessels like venule or arteriole.

Conclusion: The vascular remodeling confirmed in the mouse model of asthma provides evidence that this model may be used for further studies to 1) analyse serum components of coagulation factors related, 2) identify key players in the bronchial microvascular remodeling, and 3) provide novel targets for therapeutic interventions.

O-A-004

O-A-005

OMALIZUMAB IMPROVES QUALITY OF LIFE AND ASTHMA CONTROL IN CHINESE PATIENTS WITH MODERATE-TO-SEVERE ASTHMA: A RANDOMIZED PHASE III STUDY

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Introduction: Omalizumab, an anti-IgE monoclonal antibody, has been found to be effective and safe in the treatment of patients of different ethnicities with moderate-to-severe allergic asthma. We report here the effect of omalizumab on the quality of life, asthma control and safety in Chinese patients with moderate to severe allergic asthma.

Methods: This was a randomized, double blind, parallel group, placebo controlled, phase III study to assess the quality of life, asthma control and safety of 24 weeks of omalizumab therapy in Chinese patients, aged 18–75 years, with moderate-to-severe persistent allergic asthma. Asthma Quality of Life Questionnaire (AQLQ) and Asthma Control Questionnaire (ACQ) scores were assessed at baseline and at week 24. Asthma exacerbation rates were also analysed.

Results: Among the 608 patients included in the full analysis set, at week 24 a higher proportion of patients treated with omalizumab (n = 306), vs. placebo (n = 302), achieved clinically relevant improvements in AQLQ (58.2% vs. 39.3% [analysed n = 182 vs. 178]; p < 0.001; change from baseline [Δ BL] = 0.51 vs. 0.10) and ACQ (49.5% vs. 35.5% [analysed n = 210 vs. 211]; p = 0.003; Δ BL = -0.51 vs. -0.34) scores. Although not powered to study differences in exacerbation rates (p = 0.097), exacerbations in winter months were less frequent in the omalizumab group vs. placebo (2 vs. 21). Adverse event and serious adverse event rates were comparable in both groups. One death from asthma exacerbation occurred in the omalizumab group.

Conclusions: Omalizumab improves quality of life and asthma control in Chinese patients with moderate-to-severe persistent allergic asthma with a good safety profile.

A NOVEL THROMBOXANE A2 RECEPTOR INHIBITOR, SERATRODAST SHOWS GREATER IMPROVEMENT IN PEAK EXPIRATORY FLOW, EXPECTORATION SCORE, SPUTUM EOSINOPHIL CATIONIC PROTEIN AND ALBUMIN LEVELS AS COMPARED TO MONTELUKAST IN A DOUBLE BLIND COMPARATIVE CLINICAL TRIAL

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Background: Thromboxane A2 (TXA2) has shown to play an important role in the pathogenesis of asthma. Various international guidelines recommend controller therapy for mild to moderate persistent asthma. Seratrodast, a specific TXA2 receptor antagonist, given orally, has demonstrated consistent benefit in controlling symptoms of asthma. Therefore, we designed a randomized, double blind, double dummy, multi-centre, parallel group study with non inferiority design to assess the efficacy, safety and tolerability of seratrodast versus montelukast, a leukotriene receptor antagonist, in controlling mild to moderate asthma in adult patients.

Methods: Patients (n = 205) with mild to moderate asthma continuing on the lowest dose of inhaled corticosteroid were recruited from 3 different centers across India. Patients were randomly assigned to receive either seratrodast 80 mg (n = 103) or montelukast 10 mg (n = 102) once daily for 28 days. The objective was to compare the treatments in terms of improvement from the baseline values, as per the changes in asthma symptom score (wheezing, shortness of breath, expectoration, cough and chest tightness), lung function parameters (PEF, FVC and FEV1), sputum and mucociliary parameters [fucose, eosinophil cationic protein (ECP) and albumin].

Results: Seratrodast and montelukast showed improvement in the clinical parameters of asthma as well as in the lung function tests and sputum parameters from baseline. Both the treatments significantly increased mean values of PEF, FVC and FEV1 from the baseline after a 4 week treatment but seratrodast produced significantly higher improvement in PEF (0.416 L/s, P < 0.05). Moreover, there was significantly higher reduction in expectoration score, sputum concentrations of ECP and albumin in seratrodast group (P < 0.05), signifying improvement in asthma condition. The two treatment groups had similar tolerability profiles. Mild increase in hepatic enzymes was seen in both the groups with no significant difference in incidence (n = 31 in montelukast and n = 37 in seratrodast group); no serious adverse events were reported during the study.

Conclusions: Seratrodast, a TXA2 receptor antagonist, was found to be better in the improvement of PEF, expectoration score, ECP and albumin level as compared to montelukast justifying preference of seratrodast as a controller medication in mild to moderate asthma.

Trial Registration: Clinical Trial Registry of India: CTRI/2013/03/003504 <http://ctri.nic.in/Clinicaltrials/rmaindet.php?trialid=3253&EncHid=28792.92343&modid=1&compid=19>

Key words: Thromboxane A2 receptor antagonist, asthma, seratrodast, montelukast, peak expiratory flow (PEF), eosinophil cationic protein (ECP), albumin.

O-A-006

MEDIAN MASS AERODYNAMIC DIAMETER (MMAD) AND FINE PARTICLE FRACTION (FPF): INFLUENCE ON LUNG DEPOSITION?

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Rationale: The influence of particle size on lung deposition (LD) and efficacy with inhaled drugs is increasingly discussed, yet the role of the FPF is often overlooked. FPF is the fraction of the total drug dose <5.0 µm; MMAD is the average size of particles constituting the dose which reach the impactor, excluding those that deposit in the 'throat'. This study investigated the influence of FPF and MMAD on LD using Functional Respiratory Imaging (FRI).

Methods: 3D airway models of 6 asthma patients (mean FEV1 83%) were included. Total lung (TLD), central (C) and peripheral (P) airway deposition of a monodisperse model aerosol with MMAD of 1.5–4.5 µm (geometric SD = 1.20) and FPF of 10–40% delivered by a pMDI were assessed with FRI (inhalation volume: 3 L; time: 3 s; actuation start of inhalation).

Results: TLD as % of nominal dose for each permutation of model aerosol are shown in the table.

MMAD (µm)	FPF (% of nominal dose)			
	40%	30%	20%	10%
1.5	34.05	25.54	17.03	8.51
3.0	32.47	24.35	16.23	8.12
4.5	33.58	25.18	16.78	8.39

The C/P ratio for MMAD of 1.5, 3.0 and 4.5 µm were 0.42, 0.69, and 1.39.

Conclusions: FPF had a large impact on TLD in vitro whereas MMAD had little effect, although MMAD had some influence on C and P deposition: both 1.5 and 3.0 µm MMAD profiles deposited mainly in P (C/P < 1.0); 4.5 µm aerosol deposited more in C airways (C/P > 1.0). Many inhaled respiratory drugs need to reach both P and C airways but the optimal delivery between these for different classes of drugs is less understood. These data highlight the importance of FPF on TLD; beneficial drug effects often attributed to small particle size may really be a consequence of high FPF. THIS STUDY WAS FUNDED BY MUNDIPHARMA.

O-A-008

ASTHMA SEVERITY AND PHENOTYPES ASSOCIATED WITH VOCAL CORD DYSFUNCTION

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Background and Aims: Vocal cord dysfunction (VCD) has been identified in up to 50% of patients with severe asthma (Low et al, AJRCCM 2011). It is not known if it is present in mild disease and if distinct phenotypes are associated with VCD.

Methods: We evaluated 57 patients with either mild to moderate non-refractory asthma (N = 31) or refractory asthma (N = 26). Dynamic 320 slice computerized tomography (CT) larynx was done and a validated algorithm was used to accurately measure vocal cord lateral diameter during inspiration and expiration. Excessive narrowing of the airways was diagnosed if a predetermined lower limit of normal was exceeded. The asthma groups were compared using semi-supervised cluster analysis to identify asthma phenotypes associated with laryngeal dysfunction.

Results: Overall vocal cord diameter was reduced below the lower limit of normal in 26 of 57 cases (46%). There was no relationship with refractory asthma: 12/26 (46%) versus non-refractory 14/31 (45%; p = 0.8). Laryngeal dysfunction was associated with increased age (P < 0.034) bronchodilator (BD) responses < 12% (P < 0.009) and difficult speech when breathless (p < 0.019). There were 3 unique phenotype clusters associated with VCD and determinants of cluster membership were:

1. age >40 years, female, bronchodilator response < 12%, difficulty speaking when breathless;
2. age >40 years, bronchodilator response < 12%, BMI > 30 kgs/m²;
3. female, bronchodilator response < 12%, BMI > 30 kgs/m².

Conclusion: Our results suggest that vocal cord movement is abnormal in a subgroup of patients with asthma, irrespective of severity. However, VCD may be associated with particular patient phenotypes and contribute to their overall symptomatic burden of disease.

O-A-009

STAT1/STAT6 PHOSPHORYLATION BALANCING OF CD4+ MEMORY T CELLS IN ASTHMA AND COPD

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Background: Memory T cells has the ability of initiating more effective immune response against antigen. It has been proved a large number of CD4+ memory T cells reside in human lung. We studied the phenotype and cell signalling pathway in CD4+ memory T cells in asthma and COPD and tried to find a new way help differentiating these two diseases.

Methods: 42 subjects were enrolled, which included 15 asthma, 15 COPD and 12 healthy control. CD4+ T cells were purified from blood and cultured under neutralizing, Th2, Th2 plus LPS, Th2 plus home dust mite conditions. On day 3, CD45RO expression was detected. On day 6, after PMA plus Inomycine stimulation, level of intracellular cytokines were measured. The freshly isolated PBMC on day 0 were stimulated by IL27 or IL4 to test STAT1 and STAT6 phosphorylation by flow. The STAT1 and STAT6 phosphorylation without cytokine stimulation were detected by western blot.

Results: The CD4+CD45RO+ T cells account for 49–59%, 40–46%, 30–35% in CD4+ T cell population in asthma, COPD and healthy control respectively. CD4+ memory T cells of Asthma released more IL5 and IL17 in Th2 plus home dust mite culture condition (3.5% vs 0.6%; 2.2% vs 1.2%) respectively, less IFN- γ in Th2 plus LPS culture condition (15.3% VS 22.5%) compared to healthy control. The cytokine profile of COPD was more like healthy control, with IL5, IL17, IFN- γ releasing (1.3% vs 0.6%; 1.7% vs 1.2%, 26% vs 22.5%) when comparing to healthy group. Small amount of IL10 was found, with no differences among 3 groups (0.9%, 0.5%, 0.7%). IL27-induced STAT1 phosphorylation and IL4-induced STAT6 phosphorylation were measured by flow cytometry, the ratios of STAT1-Py/STAT6-Py were 2.3, 1.17, 1.03 in asthma, COPD and healthy respectively. By western blot, the base phosphorylation of STAT1, STAT6 in asthma and COPD were detected, asthma was found to have a higher level of base STAT6-Py before IL4 induction.

Conclusions: There are more CD4+ memory T cells in the peripheral circulation system in asthma and COPD. The cytokine production profile of asthma was different from COPD, more Th2-type cytokine released. The balancing between STAT1-Py/STAT6-Py was prone to STAT1-Py in asthma, partially because of the relatively higher basic STAT6-Py before induction. We need more patients involved to prove this imbalance. These differences might be used to develop a new way to distinguish the hardly differentiated disease, especially late-onset asthma and asthma-COPD overlap syndrome.

O-A-010

O-A-011

ADD-ON EFFECT OF TIOTROPIUM BROMIDE TO ICS/LABA COMBINATION INHALER FOR PERIPHERAL AIRWAYS AMONG PATIENTS WITH SEVERE UNCONTROLLED ASTHMA

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Background and Aim of Study: Recently, the evidence concerning clinical efficacy of Tiotropium Respimat (TIO) for bronchial asthma is accumulated. In Japan, clinical use of TIO is only allowed for COPD, not asthma yet, however, it is used for the uncontrolled severe asthmatics even with the treatment of GINA step 4 or 5 in daily clinical setting. The aim of this study is to investigate the clinical usefulness of TIO, especially its effect for peripheral airways, among severe asthmatics.

Methods: The subjects were severe asthmatics treated with TIO in addition to high doses of ICS/LABA combination inhaler for more than 6 months. The additional bronchodilator effect of TIO after the ICS/LABA inhalation in comparison with those of salbutamol were evaluated with forced oscillation technique Mostgraph-01 (Chest M.I., Co. Ltd, Tokyo, Japan). Asthma control test (ACT) score and fractional exhaled nitric oxide (FeNO) were examined simultaneously. The cases definitely overlapping with COPD were excluded from this study.

Results: Twenty-nine cases, male 13, female 16 were recruited. Mean age was 58.2 ± 14.5 years old and FEV_{1.0%} was $63.8 \pm 12.7\%$. Omalizumab was administered in 6 cases, and systemic corticosteroids in 7 cases. As an ICS/LABA, 14 cases used Salmeterol/Fluticasone 100/1000 $\mu\text{g}/\text{day}$, while Budesonide/Formoterol 1280/36 $\mu\text{g}/\text{day}$ 15 cases. Although ACT score and FeNO have not improved with 6 months treatment with TIO, only ACT question #2 (breathlessness) improved significantly from 2.68 ± 1.24 to 3.74 ± 1.02 ($p < 0.01$, paired-t test) Not only R5, R20 which represented respiratory system resistance, but also Fres, ALX, X5 which reflected respiratory reactance thereafter peripheral airway abnormality improved significantly 30 minutes after the inhalation of TIO even after the usual usage of ICS/LABA, while only R5 improved with salbutamol inhalation. $15.2 \pm 10.2\%$ improvement in R5 observed with the treatment with TIO was significantly higher than those with salbutamol ($7.8 \pm 11.2\%$, $p < 0.05$, paired-t test).

Conclusions: Additional bronchodilatation effect of Tiotropium bromide to ICS/LABA combination inhaler among patients with severe uncontrolled asthma, especially for the peripheral airways were strongly suggested.

IDENTIFICATION OF ATTITUDINAL CLUSTERS IN PATIENTS WITH ASTHMA: ANALYSIS FROM REALISE ASIA

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Background/Aim: Similar to the identification of clusters of patients in Europe based on survey of their attitudes towards asthma (REALISE), we sought to understand such attitudinal groups among Asian patients.

Methods: Online surveys were conducted among 2,467 adult patients with asthma across 8 countries in Asia. Using two-step approach, the respondents were segmented into groups, each containing patients who are similar in their attitudes, yet distinct from those in other groups.

Results: Five attitudinal clusters were uncovered:

- 1) 'Well-adjusted' (29%)
 - Generally cope well with their asthma
 - Asthma has minimal impact on their daily lives
 - Happy to go along with doctor's advice
 - No problem using their inhaler, reflecting carefree attitude and lower stress levels
- 2) 'Rejectors' (17%)
 - Refuse to accept asthma label
 - Yet to come to terms with emotional burden of living with asthma
 - Deprioritize their health despite some concerns about their asthma
 - High social consciousness about using inhaler
- 3) 'Lost' (14%)
 - High level of stress and anxiety about their asthma
 - Asthma has high impact on their daily lives
 - Avoid thinking about their health
 - High asthma information seeking frequency but do not know where to turn for answers
- 4) 'Endurers' (29%)
 - Accept their condition and that they do not have control over it
 - High acceptance of condition means they do not allow asthma to have a major impact on their daily life
 - Low level of confidence in managing their asthma
 - Less interested in seeking information than other uncontrolled patient types
- 5) 'Worriers' (11%)
 - Asthma is a constant worry on their mind
 - Accept their condition but live with a high level of stress and anxiety about their asthma
 - Exhibit high asthma information seeking frequency due to their concern

Based from GINA-defined control status, cluster 5 has the most number of uncontrolled patients (92%), followed by clusters 3 (79%) and 4 (74%). Meanwhile, clusters 1 and 2 have the most number of controlled patients (34 and 38% respectively). Cluster 3 has significantly higher number of days and nights when their activities are interrupted by asthma. Cluster 1 has the highest proportion of those who did not experience exacerbation in the last 12 months – no emergency visits (83%), no oral steroids (51%) and no antibiotics (42%) for asthma. In contrast, 95% of patients in cluster 5 had > 1 course of antibiotics for asthma-related problems in the past year.

Conclusion: Asian patients can be grouped into five clusters based on their concerns about their asthma and its management. The recognition of the clusters, offers an opportunity to customize management approaches for patients, and leverage on their attitudes to improve asthma control.

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O-A-012

EARLY EFFECT OF MATERNAL ALLERGIC ASTHMA ON T-REGULATORY CELLS IMMUNE RESPONSE IN CORD BLOOD OF OFFSPRINGS

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Objective: We examined the impairment of regulatory T cells in innate and adaptive immune response in cord blood from offspring of allergic asthmatic/healthy mothers.

Methods: Cord blood mononuclear cells from 126 healthy neonates (78 healthy mothers and 48 allergic asthmatic mothers) were isolated, and cultured with lipid A-TLR4 ligands, peptidoglycan (PPG)-TLR2 ligands and mitogen (phytohemagglutinin) stimulation for 3 days. And then the amount, specific genes expression, suppressive function and cytokines of regulatory T cells were examined.

Results: Cord blood from offspring of allergic asthmatic mothers showed PPG-induced fewer regulatory T cells (CD4+CD25+Foxp3+T, $P = 0.03$), lower IL-10 secretion ($P = 0.03$) and lower mRNA expression of associated markers (GITR, LAG3 and TGF- β , $P < 0.05$). Furthermore, the suppressive capacity of regulatory T cells was impaired in mitogen-induced division and proliferation of T effector cells in cord blood of offspring from allergic asthmatic mothers ($P = 0.05$). Meanwhile, the suppressive capacity of regulatory T cells to IL-13 production by effector cells was partially impaired ($P = 0.07$).

Conclusion: In offspring of allergic asthmatic mothers, regulatory T cells amount, specific gene expression, and suppressive function were impaired at birth, which maybe potentially contribute to the the susceptibility to allergic diseases.

O-A-013

DISCREPANCY BETWEEN PATIENT-PERCEPTION AND GUIDELINE-DEFINED ASTHMA CONTROL IN ASIA: A SURVEY OF OVER 2400 PATIENTS

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Background/Aim: A recent survey (REALISE) has revealed that patients in Europe perceive their asthma to be well-controlled despite the presence of symptoms. We report data from a similar survey of patients which assessed if such discrepancy is seen in Asia.

Methods: Online surveys were completed by patients (aged 18–50 years, >2 prescriptions for asthma in the past two years), recruited via validated consumer panels from 8 countries in Asia.

Results: A total of 2,467 patients participated, split across the following geographies: Mainland China (30%), Hong Kong (8%), Indonesia (7%), Korea (20%), Malaysia (6%), Philippines (6%), Singapore (8%), and Taiwan (12%). Mean age of respondents is 34 years, and relatively equal proportion of males (54%) and females (46%). While 89% consider their asthma to be well-controlled, only 18% can be classified as such according to GINA guidelines, the rest being partly controlled (32%) and uncontrolled (50%). In the past 7 days before completing the survey, 35% used their reliever inhaler > 3 times, 38% experienced symptoms > 3 days in a week, 64% had symptoms that interfere with normal activities, and 71% had night-time awakening due to asthma symptoms. In the past year, 33% have been hospitalized, 38% of the respondents had emergency visits, and 73% required oral steroids for worsening asthma. Despite symptoms and exacerbations, 82% do not consider their asthma as serious, 80% regard their state of health as similar as or better than other people their age, and 82% describe themselves as confident in managing their asthma. Interestingly, more than 2/3 of the respondents relate 'control' to managing attacks rather than absence or minimal symptoms. Patients' definitions of well-controlled asthma include: attacks are controllable with medical help, reduction of attacks within a time-frame, and prevention of attacks through lifestyle modification or alternative medicines (e.g. traditional Chinese medicines).

Conclusion: Patients consistently overestimate their own asthma to be controlled rather than what their clinical symptoms suggest. This discrepancy may be due to fundamental difference on how patients define 'control' which is currently geared towards management of exacerbation, instead of pre-defined level of symptom control. A shared understanding of such concepts between patients and physicians may help in achieving treatment goals in asthma care.

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O-A-014

PATTERNS OF HOSPITALIZATION AND HEALTHCARE UTILIZATION ACROSS ATTITUDINAL CLUSTERS: ANALYSIS FROM PATIENT SURVEY IN ASIA

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Background/Aim: Uncontrolled asthma is associated with higher utilization rates of healthcare services. REALISE, a recent survey in Europe has shown how patient attitudes towards asthma and its treatment impact on resource utilization. We present here the findings from a similar survey in 8 countries in Asia, focusing on hospitalization patterns in patients across the identified attitudinal clusters.

Methods: Previously reported analysis identified 5 attitudinal clusters from a multi-country online survey of 2,467 adult patients with asthma (age 18–50 years, ≥ 2 prescriptions for asthma in past two years). The 5 clusters are: 1. 'Well-adjusted' – high asthma control and most confident in managing it; 2. 'Rejector' – high control but refuse to accept the asthma label; 3. 'Lost' – low control and most socially conscious about asthma; 4. 'Endurers' – low control with low level of confidence in managing asthma, and; 5. 'Worriers' lowest control and high level of concern about their asthma.

Results: Cluster 1 had the highest proportion of patients who had not experienced asthma exacerbations in the past 12 months. Clusters 1 and 2 had the least proportion of emergency room visits for asthma (17% and 27% respectively), compared to the Clusters 3, 4, and 5 (58%, 47%, and 63% respectively). The same pattern is seen for overnight hospitalization as a result of asthma: 12%, 16%, 55%, 42%, and 62% for Clusters 1, 2, 3, 4, and 5 respectively. Mean number of times that patients in Cluster 5 were given antibiotics in the past 12 months because of asthma was 3.5x, compared to only 1.2x and 1.6x for those in Clusters 1 and 2.

Conclusion: The five attitudinal clusters have differing rates of hospitalization and health care utilization, which appears to be reflective of their level of control and attitudes towards their disease. Such insight can help health care professionals tailor a management approach for patients included in each of the clusters.

Disclosures/Acknowledgments: MUNDIPHARMA PTE LTD PROVIDED FUNDING FOR THE SURVEY. THE AUTHORS RECEIVED AN HONORARIUM FROM MUNDIPHARMA PTE LTD FOR THEIR PARTICIPATION IN REALISE ASIA WORKING GROUP MEETINGS AND DISCUSSIONS. G NEIRA IS AN EMPLOYEE OF MUNDIPHARMA PTE LTD. THE REALISE ASIA WORKING GROUP ACKNOWLEDGES PROFESSOR DAVID PRICE FOR HIS ADVICE ON THE SURVEY AND ANALYSIS OF RESULTS, AND RESEARCH PARTNERSHIP HEALTHCARE ASIA PTE LTD FOR SURVEY CONDUCT AND DATA ANALYSIS.

O-A-015

INCREASING LEVEL OF INTERLEUKIN-10, INTERLEUKIN-17 AND ACT SCORING IN ASTHMA BRONCHIAL PATIENT WITH VITAMIN D DEFICIENCY AFTER 2 MONTHS SUPPLEMENTATION OF 800 IU VITAMIN D

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Background: Vitamin D deficiency is hypothesized to play a role in increasing asthma incidence. Vitamin D as immunomodulator occurs through several mechanisms namely vitamin D on dendritic and T cell which promoting Treg in secreting IL-10. Recently study conducted by Lestari in 2013 stated that all patients with persistent asthma bronchial indicate vitamin D deficiency. The aim of this study is to prove the existence of vitamin D effects on interleukin-10, interleukin-17 serum levels and the score of ACT in asthma bronchial patient with vitamin D deficiency.

Method: In this pre and post design experimental study, 38 asthma bronchial patients with vitamin D deficiency who get standard therapy according to GINA 2012 in pulmonary outpatient clinic, Saiful Anwar Hospital, Malang, were given 800 IU of vitamin D supplementation for two months, then vitamin D plasma concentration, IL-10, IL-17 serum and ACT scoring were measured.

Result: After given 800 IU of vitamin D supplementation for two months, there were significant level increase either in vitamin D concentration ($p = 0.003$), IL-10 ($p = 0.004$), IL-17 ($p = 0.002$), or ACT scoring ($p < 0.001$). There is significant yet negative correlation ($p = 0.049$, $R = -0.321$) between vitamin D plasma and IL-10 level; no correlation between vitamin D and IL-17 level ($p = 0.074$, $R = -0.294$), as well as vitamin D concentration and ACT scoring ($p = 0.156$, $R = 0.235$).

Conclusion: Two months supplementation of 800 IU vitamin D in asthma bronchial patient with vitamin D deficiency can increase vitamin D plasma concentration, IL-10, IL-17 serum levels and ACT scoring. There is correlation between vitamin D plasma and IL-10 serum level, but no correlation among vitamin D plasma, IL-17 serum level, and ACT scoring.

O-A-016

PATIENT HANDLING STUDY OF FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE PRESSURIZED METERED-DOSE INHALER

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Background: All currently marketed inhaler devices are associated with handling errors in a significant proportion of patients, 1 with incorrect use of inhalers being associated with worse asthma control. Disappointingly, many patients fail to receive any adequate training in inhaler usage. This study investigated whether patients can be successfully trained to use the fluticasone propionate/formoterol fumarate pMDI (FP/FORM).

Methods: This was a randomized, open-label, two-period, crossover study to investigate whether patients with asthma or chronic obstructive pulmonary disease aged ≥ 12 years were able to use a placebo FP/FORM breath-actuated inhaler and a placebo FP/FORM pMDI. A trained nurse instructed patients in the correct use of each device (on separate days) prior to assessing handling technique according to 8 pre specified steps (for each device). Here we present the results for the pMDI.

Results and Conclusions: After training, 77% of patients (95% CI: 72.1, 81.8%, $N = 307$) completed all 8 steps correctly at the first assessed attempt. Considering only the 4 critical steps, the success rate was 82% (95% CI: 77.7, 86.5%) at the first attempt. Virtually all patients (99%) could be trained to complete all 8 steps correctly within 15 minutes, with the great majority (91%) achieving correct pMDI device usage by the second attempt. These results suggest that almost all patients can be trained to use the FP/FORM pMDI via a simple, quick and practical training regimen.

Sponsor: MUNDIPHARMA RESEARCH LTD

O-A-017

ASTHMA SELF MONITORING, BEHAVIOUR MODIFICATION AND MEDICATION COMPLIANCE IN COMPARISON TO PATIENTS WITH HYPERTENSION/HIGH CHOLESTEROL AND LINK TO ASTHMA HOSPITALIZATION PROFILE

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Aim: The aim of our study was to determine the prevalence and compliance of self monitoring and lifestyle modifications of patients with asthma versus hypertension/high cholesterol. Hospitalised asthma patient profile was assessed.

Methods: We conducted a study via questionnaire of self monitoring and lifestyle modifications of patients in a general respiratory medicine and renal clinic over a period of 2 months from May to July 2014.

Results: 98 out of 117 questionnaires were answered. Demographics: male 48% (n = 47), age (years): <21 (n = 9, 9.2%), 21–30 (n = 7, 7.1%), 31–40 (n = 21, 21.4%), 41–50 (n = 26, 26.5%), 51–70 (n = 28, 28.6%), 70 & above (n = 6, 6.1%) (1 non responder). Education level: primary (n = 4, 4.1%), secondary (n = 12, 12.2%), tertiary (n = 36, 36.7%), post-graduate (n = 41, 41.8%) (5 non responders). Race: Chinese (n = 29, 29.6%), Malay (n = 1, 1%), Indian (n = 11, 11.2%), Caucasian (n = 41, 41.8%), others (n = 14, 14.3%) (9 non-responders). Income: <\$20 000 (n = 13, 13.3%), \$20 000–\$50 000 (n = 11, 11.2%), \$50 000–\$100 000 (n = 16, 16.3%), >\$100 000 (n = 29, 29.6%), (29 non-responders).

Observations: Asthmatic group (n = 38), only 23.7% (n = 9) monitored their peak flow. 23.7% (n = 9) were compliant with their preventive inhalers. 73.7% (n = 28) practiced allergen avoidance (dust n = 17, pet n = 11, food n = 14). 13 (34.2%) were hospitalized for asthma of which 10 (76.9%) did not do home peak flow monitoring, 8 (61.5%) were non-compliant with their medication. All 13 (100%) practised allergen avoidance. In the hypertensive group, (n = 24), 66.7% (15) monitored their high blood pressure at home. 37.5% (9) were compliant with their blood pressure medication. 62.5% (15) changed their diet to low salt. In the high cholesterol group (n = 26), 30.8% (8) were compliant with medicines, 65.4% (17) changed their diet to low fat. All groups exercised: asthma 60.5%, hypertensive 54.2%, high cholesterol 57.7%.

Conclusion: Hospitalized asthmatics were non-compliant (61.5%) and did not monitor peak flow (76.9%). Overall, peak flow monitoring for asthmatics was low (23.7%). They practised mainly allergen avoidance (73.7%). In contrast, 66.7% of hypertensives practiced blood pressure monitoring. Compliance to medication was poor in all three groups [asthmatic (23.7%), hypertensive (37.5%) high cholesterol (30.8%)]. This was despite a high level of education of tertiary and above educated respondents (78.6%) and income level (45.9%) of \$50,000 and above. More resources and education should be provided to asthmatics and improved compliance regimes adopted.

O-A-018

ASSOCIATIONS OF ASTHMA CONTROL WITH SYSTEMIC INFLAMMATIONS

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Background: Asthma is a worldwide problem while in Indonesian country, asthma is one of top ten cause of morbidity and mortality. The inflammatory markers, high sensitivity C reactive protein (hs-CRP) known has a strong association with atherosclerosis and CVD risk in adults. Elevated levels of hs-CRP are now considered as an independent risk factor for CVD in adults. However, the potential interactions among asthma control and hs-CRP level have not been fully characterized in the adult asthma subject in Indonesia. In this study, we aimed to examine the associations of asthma control and systemic inflammation, using hs-CRP levels.

Objective: To determine the associations between asthma control and systemic inflammation using hs-CRP levels.

Methods: This was an observational study with cross-sectional approach in 48 subjects asthma aged 18–55 years old without diabetes, cardiovascular disease, hypertension and non smoker.

Results: Mean of hs-CRP levels were significantly higher in uncontrolled asthma than controlled asthma (4.23 ± 3.11 vs 0.92 ± 0.61 ; $p = 0.001$). The high hs-CRP levels were most found in uncontrolled asthma patients than asthma controlled. Subject obese with uncontrolled asthma have higher hs-CRP levels compared with subject obes with controlled asthma ($p = 0.026$). In subject non obese with asthma uncontrolled have also significantly high hs-CRP compared with non obese asthma controlled ($p = 0.005$). Hs-CRP level significantly higher in asthma uncontrolled both in obese and non-obese subject. Hs-CRP levels in asthma subject were not influenced by ages ($p = 1.000$), gender ($p = 0.822$), family history of asthma ($p = 0.117$), long duration of asthma ($p = 0.117$) and used of steroid. ($p = 0.358$).

Conclusion: Hs-CRP levels were significantly higher in asthma uncontrolled than asthma controlled both in obes and non obese subject.

O-A-019

LONG-TERM EFFICACY OF OMALIZUMAB IN PATIENTS WITH SEVERE ASTHMA

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Background: The efficacy of omalizumab, an anti-IgE antibody, has been studied in patients with severe bronchial asthma. It has been reported that omalizumab was unable to improve objective results; however, improvements were seen for subjective symptoms in asthmatic patients. The aim of this study is to evaluate the efficacy of omalizumab as a long-term disease therapy in severe and persistent asthmatic patients assessed by pulmonary function tests, AHQ scores, ACT scores, number of emergency visits and the dosage of methylprednisolone.

Methods: Omalizumab was administered subcutaneously every 2 or 4 weeks based on serum IgE levels and body weight in patients. Pulmonary function tests, AHQ, ACT, number of emergency visits and dosage of methylprednisolone during the 12-month period were compared with the previous year.

Results: Ten patients were enrolled. Treatment with omalizumab yielded no improves for lung function; however, the number of emergency visits (19.3 to 1.2 , $p = 0.020$) and dosage of methylprednisolone (871.5 mg to 119.0 mg, $p = 0.046$) showed significant reductions when compared to the previous year. AHQ and ACT at 16 weeks improved significantly compared to study baseline but after week 20, no significant improvement was noted. Four patients continued the treatment with omalizumab for four years. Omalizumab reduced the adverse events.

Conclusion: AHQ and ACT were considered useful in the assessment of subjective symptoms in asthmatic patients. Omalizumab significantly reduced the number of emergency visits and methylprednisolone usage. Long-term Omalizumab therapy is effective and offers the potential to reduce the rate of asthma exacerbations.

ORAL PRESENTATION – BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES

O-B-001

BRONCHOSCOPIC LIPIODOL-MARKING UTILIZING DIAGNOSTIC GUIDED-BRONCHOSCOPY TO FACILITATE MINIMAL SURGERY FOR SMALL PULMONARY NODULE

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Background: In minimal surgery, the identification of small pulmonary ground-glass opacity (GGO) lesion confirmed by high-resolution CT (HRCT) during the operation is important. It had been reported that the lesion that have diameters of <10 mm and that are >5 mm from the pleura was difficult to be detected. To facilitate marking procedure and to reduce its complications, we performed lipiodol-marking utilizing diagnostic guided-bronchoscopy before fluoroscopy-assisted minimal surgery for small GGO lesion.

Methods: All subjects were patients who were candidates for minimal surgery because they had small GGO lesion potentially difficult to see or palpate on the surface of pleura between November 2012 and May 2013. VB image and navigating pathway to induce a bronchoscope to the planned marked site was made from LungPoint software (Broncus Technologies, Inc., USA). We used a thin bronchoscope (P260F; Olympus, Japan), EBUS system (EU-ME1; Olympus, Japan) equipped with a 20-MHz mechanical radial-type probe (UM-S-20-17S, 20R; Olympus, Japan) and a guide sheath (GS) (K-201; Olympus, Japan). A bronchoscope was advanced to the bronchus as far as possible and radial-type EBUS probe (R-EBUS) was then inserted to the target. After visualization of the target by R-EBUS, the probe was removed, leaving a GS in place and lipiodol was injected to the target lesion via GS. All procedures were performed under C-arm-shaped fluoroscopy. We then evaluated the feasibility, safety, and efficacy of this technique.

Results: Our study included 2 patients (2 males). Each age was 64, 70 year old. Each lesion size was 11.1, 12.0 mm in the major axis. We succeeded in one case in which an injection tube was used, failed in the other case in which a micro catheter was used. CT-guided lipiodol-marking was performed in unsuccessful case. Pathologic studies revealed primary lung cancer in all lesions. Marking procedure was achieved without causing any complications in all cases. In patients undergoing minimal surgery, all lipiodol-marked sites were identified by intraoperative C-arm-shaped fluoroscopy and all lesions were resected.

Conclusions: This newly bronchoscopic lipiodol-marking could be a useful, safe, and inexpensive procedure for localizing small GGO lesion before fluoroscopy-assisted minimal surgery.

O-B-002

FLEXIBLE FIBRE-OPTIC BRONCHOSCOPY, OBESITY AND SLEEP DISORDERED BREATHING: PATIENTS' CHARACTERISTICS AND COMPLICATIONS IN 570 CASES

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Introduction: Fibre-optic bronchoscopy (FOB) is an essential diagnostic and therapeutic tool in Pulmonary Medicine. There are limited data on patients' characteristics including body mass index (BMI) and the presence of obstructive sleep apnoea (OSA) in relation to bronchoscopic complications.

Aim: To evaluate patients' characteristics, types of sedation, diagnostic yield and complications in FOB in a non-intensive care unit (ICU) setting.

Method: Retrospective chart review of consecutive patients undergoing FOB over a thirty-six month period in a tertiary care teaching hospital. Patients' characteristics, sedation details, endobronchial interventions, diagnostic outcome, and adverse events were reported.

Results: 596 patients underwent FOB from 1st January 2010 to 31st December 2012. Ten patients were excluded from analysis because FOB was performed in ICU. Sixteen patients had no information on weight and/or BMI, and were therefore excluded from analysis. 570 patients were analysed. 309 patients (54.2%) were male. The mean age was 61.5 ± 15.0 years. Thirty-seven patients (6.5%) had known OSA. The mean weight was 75.4 ± 18.0 kg. The mean BMI was 26.6 ± 5.7 kg/m². 156 patients (27.4%) had BMI ≥ 30. Forty-eight patients (8.4%) had BMI ≥ 35. 99.8% of patients received midazolam, the average dose was 3.6 mg (range 1–7 mg). 99.6% of patients received fentanyl, the average dose was 73.0 µg (range 25–100 µg). 10.7% of patients received propofol, the average dose was 51.3 mg (range 10–300 mg). Interventions including biopsies and brushings were performed in 39.6% of patients. The overall diagnostic yield was 53.9%, of which 17.4% were confirmed malignancies. 99.6% of FOB sedation were performed by trained nurse sedationists. 1.8% of FOB (10/570) were associated with adverse events, of which one patient had known OSA. The mean weight was 82.4 ± 20.3 kg. The mean BMI was 29.8 ± 7.4 kg/m². The overall mortality rate of our cohort was 0%. After adjusting for age and gender, there was a significant trend towards higher BMI associated with an increased risk of an adverse event (OR = 1.1; 95% CI = 1.0, 1.2; p = 0.05). OSA was not found to be significantly associated with adverse events (p = 0.9).

Conclusion: FOB appears to be a valuable diagnostic tool with a low rate of complications. Our chart review did not find a statistically significant association between OSA and adverse events in FOB. However, there was a significant trend towards higher BMI associated with an increased risk of adverse events.

O-B-003

FUNCTIONAL BRONCHOSCOPY IN THE MANAGEMENT OF AIRWAY STENOSIS DUE TO TRACHEOBRONCHIAL TUBERCULOSIS

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Background: The diagnosis and management of endobronchial tuberculosis (EBTB) can be challenging due to its nonspecific presentation. Current interventional bronchoscopic techniques are unable to manage EBTB because of the high rate of restenosis.

Objective: To assess the efficacy and complications of interventional bronchoscopic techniques in airway stenosis due to tracheobronchial tuberculosis.

Methods: Between February 2008 and November 2012, we performed interventional bronchoscopy on 33 cases. Of these, 19 patients received interventional bronchoscopy including: stent placement, laser photo resection, argon plasma coagulation (APC), balloon dilatation, stereoscopic bronchoscopy and endobronchial ultrasonography (EBUS).

Results: Seven patients underwent stent placement after balloon dilatation, while the debulking 12 patients underwent balloon dilatation only. In 3 patients, Dumon stents were placed after the patient had received APC treatment and mechanical debulking, using the bevel of a rigid bronchoscope. Dumon stents were successfully placed to reestablish patency of the central airway in patients. In 10 patients, stereoscopic bronchoscopy measured the diameter and cross-sectional area of the airway. EBUS images in 4 patients demonstrated the destruction of bronchial cartilage or the thickening of the bronchial wall.

Conclusion: Interventional bronchoscopy should be considered feasible for the management of tuberculosis tracheobronchial stenosis.

O-B-005

ENDOBROCHIAL ULTRASOUND ELASTOGRAPHY IN THE DIAGNOSIS OF MEDIASTINAL AND HILAR LYMPH NODES

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Background: Endobronchial ultrasound elastography is a new technique for describing the stiffness of tissue during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). The aims of this study were to evaluate the utility of EBUS elastography for mediastinal and hilar lymph nodes (LNs), and to compare the elastographic patterns of LNs with results from EBUS-TBNA.

Methods: Seventy-five LNs were evaluated. A convex probe EBUS was used with a new endoscopic ultrasound processor to assess elastographic patterns that were classified based on color distribution as follows:

Type 1, predominantly non-blue (green, yellow and red);

Type 2, part blue, part non-blue (green, yellow and red);

Type 3, predominantly blue.

The elastographic patterns were compared with the final pathologic results from EBUS-TBNA.

Results: On pathological evaluation of the LNs, 33 were benign and 42 were malignant. The LNs that were classified as Type 1 on EBUS elastography were benign in 24/24 (100%); for Type 2 LNs, 6/14 (46.9%) were benign and 8/14 (57.1%) were malignant; Type 3 LNs were benign in 2/37 (5.4%) and malignant in 35/37 (94.6%). In classifying Type 1 as "benign" and Type 3 as "malignant," the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy rate were 100%, 92.3%, 94.6%, 100% and 96.7%, respectively.

Conclusions: EBUS elastography of mediastinal and hilar LNs is a non-invasive technique that can be performed reliably and may be helpful in the prediction of nodal metastasis during EBUS-TBNA.

O-B-006

TALC POUDRAGE USING CATHETER THROUGH FLEXI-RIGID THORACOSCOPE UNDER LOCAL ANESTHESIA FOR MALIGNANT PLEURAL EFFUSIONS

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Background: Thoracoscopic talc poudrage is an established technique for the treatment of malignant pleural effusions. It has been performed with two ports under thoracoscopic visualization, one for thoracoscopy and another for talc insufflation. Recently, several investigators have reported the technique with a catheter which can be performed with a single port.

Aims and Objectives: The aim of this study was to investigate the feasibility, efficacy and safety of a single-port thoracoscopic talc poudrage using a catheter under local anesthesia for malignant pleural effusions.

Methods: Single-port talc poudrage was performed using a flexi-rigid thoracoscope and a catheter (Guide-Sheath; Olympus; Tokyo) under local anesthesia. Talc was administered to the pleural surface with a catheter, which was passed through the working channel of the thoracoscope. We retrospectively evaluated 26 patients with malignant pleural effusions treated by the procedure from Oct. 2010 to Dec. 2013, and compared with 16 previous patients who underwent thoracoscopic talc poudrage with two ports. We assessed the efficacy 30 days after pleurodesis. A chest radiograph showing pleural effusion occupying less than one third of the pleural space, and unnecessary additional drainage were judged to indicate successful pleurodesis.

Results: All patients could undergo the procedure and tolerated well. Twenty-six patients in the single-port group had lung cancer (n = 21), malignant mesothelioma (n = 1), esophageal cancer (n = 1), gastric cancer (n = 1), malignant lymphoma (n = 1) and peritoneal cancer (n = 1). Sixteen patients in the two-port group had lung cancer (n = 8), malignant mesothelioma (n = 2), gastric cancer (n = 1), malignant lymphoma (n = 1), pancreatic cancer (n = 1) and carcinoma of unknown origin (n = 3). The success rate of the single-port group and two-port group was 73.1% (19/26) and 75% (12/16), respectively. Adverse events over Grade 2 (CTCAE ver. 4.0) in the single-port group were fever 3.8% (1/26) and pain 50.0% (13/26), while those in the two-port group were fever 12.5% (2/16) and pain 100% (16/16). ARDS occurred in one patient in each group.

Conclusions: Thoracoscopic talc poudrage with a single port for the treatment of malignant pleural effusions is feasible, well-tolerated and equally effective as the two-port technique. The occurrence of ARDS should be monitored carefully.

ORAL PRESENTATION – CELL AND MOLECULAR BIOLOGY

O-C-001

ACTIVATION OF LYMPHOCYTES INDUCED BY RSV PERSISTENTLY INFECTED BRONCHIAL EPITHELIAL CELLS

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Respiratory syncytial virus (RSV) preferentially infects airway epithelial cells, which might be responsible for susceptibility to asthma but underlying mechanism is not clear. This study observed the activation of lymphocytes and drift of help T (Th) subsets induced by RSV infected human bronchial epithelial cells (HBECs) *in vitro*. HBECs were persistently infected with RSV. And lymphocytes isolated from human peripheral blood were co-cultured with RSV infected-HBECs. Four groups were set up, they were lymphocytes merely (Group L), lymphocytes interfered by RSV (Group RL), co-culture of lymphocytes with un-infected HBECs (Group HL), and co-culture of lymphocytes with infected HBECs (Group HRL). After co-cultured with HBECs for 24 hours, lymphocytes were collected and examined for cell cycle and apoptosis rate, and concentrations of IL-4, IFN- γ and IL-17 in supernatants from four groups were measured. Cell cycle analysis for lymphocytes showed a significant increase of S phase cells and decrease of G1 phase and higher apoptosis rate in Group HRL compared with other three groups. In group HRL, the levels of IL-4, IFN- γ and IL-17 in supernatant were also higher than other groups. For further study, lymphocytes were individually treated with supernatants from normal and RSV persistently infected HBECs for 24 h. We found that supernatant from RSV infected-HBECs could induce the differentiation of Th2 and Th17 subsets and suppress the differentiation of Treg subsets. Our results indicated that RSV persistently infected-HBECs can induce lymphocytes proliferation and apoptosis and enhance release of cytokines by lymphocytes. Even drift of the subsets might be caused by RSV infected HBECs.

O-C-002

MESENCHYMAL STEM CELL: DOES IT WORK IN AN EXPERIMENTAL MODEL WITH ACUTE RESPIRATORY DISTRESS SYNDROME?

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We hypothesized that bone marrow-derived mesenchymal stem cells (BM-MSCs) would have a possible role in the treatment of acute respiratory distress syndrome (ARDS). ARDS disease model was developed in Wistar albino male rats by intratracheal instillation of physiological saline solution. Anaesthetized and tracheotomized rats (n = 8) with ARDS were pressure-controlled ventilated. Isolated and characterized rat (r-) BM-MSCs were labeled with GFP gene, and introduced in the lungs of the ARDS rat model. After applying of MSCs, the life span of each rat was recorded. When rats died, their lung tissues were removed for histopathological examination. Also the tissue sections were analysed for GFP labeled rBM-MSCs and stained for vimentin, CK19, proinflammatory (MPO, IL-1 β , IL-6 and MIP-2) and anti-inflammatory [IL-1ra and prostaglandin E2 receptor (EP3)] cytokines. The histopathological signs of rat-model ARDS were similar to the acute phase of ARDS in humans. rBM-MSCs were observed to home in lung paranchyma. Although the infiltration of neutrophils slightly decreased in the interalveolar, peribronchial and perivascular area, a notable improvement was determined in the degree of haemorrhage, edema and hyaline membrane formation in rats treated with rBM-MSCs. Also decreased proinflammatory cytokines levels and increased the intensity of anti-inflammatory cytokines were established. Therefore, MSCs could promote alveolar epithelial repair by mediating of cytokines from a proinflammatory to an antiinflammatory response. As a novel therapeutic approach, mesenchymal stem cell treatment with intratracheal injection could be helpful in the management of critically ill patients with ARDS.

O-C-003

O-C-004

AN IN VITRO MODEL OF SICK BUILDING SYNDROME USING HUMAN BRONCHIAL EPITHELIAL CELLS

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Background and Aim of Study: Sick building syndrome (SBS) can be caused by indoor or outdoor air pollutants, for example, organophosphate insecticides and chemical contaminants from building materials. However, the mechanism underlying development of SBS has not been fully elucidated. We hypothesized that low doses of these chemicals may be harmless when airway is intact, but may enhance inflammation when airway is affected by other factors such as microorganisms.

Methods: A human bronchial epithelial cell line, BEAS2B cells were exposed to formaldehyde (1–10 μ M), or chlorpyrifos (0.285–570 μ M), or acetaldehyde (5–10,000 μ M), or toluene (0.1–1,000 μ M), or xylene (1–1,000 μ M) after poly I : C (10 μ g/ml) stimulation. Expression levels of IL-8 mRNA were measured by real-time RT-PCR. Using formaldehyde as a candidate air toxicant, we determined cell signalling pathways possibly involved in the response by Western blotting.

Results and Conclusion: Formaldehyde and chlorpyrifos after poly I : C stimulation significantly enhanced IL-8 mRNA expression. Phosphorylation of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal protein kinase (JNK) was enhanced in the cells exposed to formaldehyde after poly I : C stimulation, whereas p38 MAP kinase was unaffected. This in vitro model suggests that effects of formaldehyde and chlorpyrifos are small in normal conditions, but may enhance inflammatory response in pathological conditions via selective activation of inflammatory cell signalling molecules. It may provide insights into the pathogenesis of SBS.

THE ROLE OF THE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS IN LPS-INDUCED LUNG INJURY IN MICE

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Introduction: The receptor for advanced glycation end-products (RAGE) is a member of the immunoglobulin superfamily of cell-surface molecules. RAGE on macrophage binds to phosphatidylserine and involves in clearance of apoptotic cells. Clearance of apoptotic cells is necessary for resolution of inflammation. However, the role of RAGE in acute lung injury remains unknown.

Methods: We set up a LPS-induced lung injury model in wild-type and RAGE-deficient (RAGE^{-/-}) mice (8–12 weeks old). We compared the pathological changes of the lungs at 0 (baseline), 24, 72 h, and 1 week after intratracheal LPS administration. We performed a bronchoalveolar lavage (BAL) at 0 (baseline), 6, 24, 48, and 72 h after LPS administration, and examined the apoptotic cells recovered from the BAL fluid. We examined alveolar macrophage phagocytosis of apoptotic neutrophils in both wild-type and RAGE^{-/-} groups. In vitro study, intracellular TGF- β protein expression in peritoneum macrophages from wild-type and RAGE^{-/-} mice were examined by FACS when those cells phagocytose the apoptotic thymocytes.

Results: Histopathological study revealed that the similar degree of infiltration of the inflammatory cells was observed in the alveolar space of both mice at 24 and 72 h after LPS administration; however, there was a marked increase in the inflammatory cell infiltration within alveolar walls of RAGE^{-/-} lungs at 24 h. We also found that more severe emphysematous changes were observed in the lungs of RAGE^{-/-} mice than of wild-type mice at 1 week after LPS administration.

There was a rapid increase in inflammatory cells in BAL fluid from both mice at 2, 4, 6, and 24 h after LPS administration. The total number of the cells in BAL fluid in RAGE^{-/-} mice was substantially greater than that recovered from the wild-type mice at 2, 4, 6, and 24 h; and there was a statistically significant difference at 6 h between the two groups. We found that the increased number of inflammatory cells was largely attributable to the increase in apoptotic neutrophils in RAGE^{-/-} mice. We also observed defective clearance of apoptotic neutrophils in alveolar macrophages of RAGE^{-/-} mice after LPS administration. In vitro study, we found that intracellular TGF- β protein was increased in wild-type peritoneum macrophages when those cells phagocytose the apoptotic thymocytes. However, TGF- β protein was not increased in those of RAGE^{-/-} cells.

Conclusions: RAGE mediated the clearance of apoptotic neutrophils. RAGE may play an important role in apoptosis-associated inflammatory resolution of acute lung injury.

O-C-005

ROLE OF INTERFERON REGULATORY FACTOR 1 BASED ON NEXT GENERATION SEQUENCING IN MOUSE MODEL OF ACUTE RESPIRATORY DISTRESS SYNDROME

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Acute lung injury/acute respiratory distress syndrome (ARDS) is characterized by acute onset of pulmonary inflammation and disruption of alveolar barrier resulting in hypoxemia and devastating respiratory failure. Despite its high incidence and approximately 40% of mortality rate, current treatment for ARDS is limited to supportive care including mechanical ventilation with concomitant treatment or initiating factors such as surfactant or steroids. To elucidate the inflammatory pathways leading to ARDS, we compared and selected the significant genes through next generation sequencing (NGS) in lipopolysaccharide (LPS)-induced ARDS mouse model. After 24 hours of intratracheal LPS administration, neutrophil with increased myeloperoxidase activity were recruited and secretory IL-6/TNF α inflammatory cytokines were significantly increased in the lungs of mice.

In histological analysis, it showed remarkable inflammatory infiltrate by disruption of the lung alveolar – capillary membrane barrier, thickened interalveolar septal and patchy alveolitis. Expression of pro-inflammatory cytokines, myeloperoxidase (MPO) activity expressed by neutrophil and nitric oxide (NO) level were measured using with ELISA, MPO assay and Griess assay, respectively in bronchoalveolar lavage (BAL) fluid, lung homogenates and serum. After instillation of LPS, cytokines, MPO level and NO level were significantly increased compared with control. The mRNA levels of inflammatory cytokines were also increase. In NGS analysis, 661 genes were significantly up-regulated while 515 genes were down-regulated with fold change 2 over in the lungs of LPS-induced mice. Twenty four genes displayed distinctive expressions in LPS exposed mouse peritoneal macrophages and neutrophils using RT-PCR analysis. In this study, we focused transcriptional factor related acute inflammation and TLR-mediated signalling. Furthermore, we verified that interferon regulatory factor 1 (IRF 1), the transcription factor able to activate expression INF-beta, is significantly a critical signalling intermediator for endotoxin-induced ARDS using RT-PCR and western blotting. Taken together, we determined the pathophysiological intracellular pathway in ARDS model and this study could help development of therapy and drug screening for ARDS therapeutics.

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ORAL PRESENTATION – CLINICAL ALLERGY & IMMUNOLOGY

O-D-001

DYNAMIC CHANGE OF HOUSE DUST MITES AND ITS COMPONENTS – SIGE & SIGG4 IN SPECIFIC IMMUNOTHERAPY

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Objectives: Der p1 and Der p2 are two main components of house dust mite (Der p); the levels of IgE & IgG4 of Der p, Der p1 and Der p2 (3 allergens) may change dynamically during specific immunotherapy (SIT). This project aimed to compare the change of sIgE & sIgG4 before and after SIT, so as to evaluate the potential role of application of SIT in clinical diagnosis.

Methods: Serum immune indexes were analysed from 70 patients with rhinitis and asthma who had already had SIT of standardized Der p. The indicator included the level of sIgE & sIgG4 of 3 allergens in serum in three periods – before treatment (0W), 17 weeks after SIT (17W) and 57 weeks after SIT (57W). The dynamic change of sIgE & sIgG4 and correlation between each antibody before and after treatment were analysed.

Results: At 17W timepoint, the levels of sIgE of 3 allergens in serum increased continuously. However, at 57W, sIgE decreased significantly again, which resulted in no difference in sIgE with 0W. The level of sIgG4 of 3 allergens were observed and recorded in each of three periods, sIgG4 of 3 allergens increased significantly according to the process of treatment. The increasing of the range of level Der p IgG4 reached the maximum, followed by Der p1 and Der p2. There was also a correlation between sIgE and sIgG4 of Der p and Der p2 in the change of the range of increase (p < 0.05). In each of three periods, the level of sIgE and sIgG4 of 3 allergens in serum in children's group was higher than adults' group. With the process of SIT, sIgG4 of 3 allergens in rhinitis and asthma group was higher than it is in the rhinitis group.

Conclusions: The results showed that SIT is a dynamic immune process and Der p with its components sIgE & sIgG4 reflected the immune status in the immune process.

O-D-002

THE DYNAMIC CHANGE OF INFLAMMATORY CYTOKINES TREATED BY SPECIFIC IMMUNITY AND THE ANALYSIS OF THE DYNAMIC CHANGE OF HOUSE DUST MITES' COMPONENTS-IGE & IGG4

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Objectives: This project aimed to study the correlation between inflammatory cytokines and the dynamic change of sIgE and sIgG4 of house dust mites (Der p), Der p1 and Der p2 during specific immunotherapy (SIT).

Methods: Serum inflammatory cytokines and 3 allergens were analysed from 55 patients with asthma and/or rhinitis SIT in our hospital and Zhuhai People's Hospital. In three periods – before treatment (0W), 17 weeks after SIT (17W) and 57 weeks after SIT (57W), the level of eight kinds of inflammatory cytokines -IL-4, IL-5, IL-8, IL-10, IL-13, IL-17, IFN- γ and TNF- α 8 were detected; therefore, the dynamic change & correlation of house dust mites and its components-sIgE and sIgG4 of Der p1 and Der p2 were analysed.

Results: There was no significant difference in eight kinds of inflammatory cytokines before and after SIT. Before treatment, there was a correlation in level of IL-5 secreted by Th2, level of Der p-IgE, Der p-IgG4 and level of Der p2-IgG4. After 17W, there were correlations in IL-5 & Der p2-IgE and three kinds of allergens level of IgG4, IL-17 and IgG4 of three kinds of allergens, level of Der p2-IgE and IFN- γ secreted by Th1. After 57W, there were correlations in IL-5 and Der p-IgE, Der p1-IgE and Der p1-IgG4, level of IL-8 and level of IgG4. From 0-17W, there was positive correlation in the increasing range of house dust mites' components – sIgG4 of Der p1 & Der p2 and the D-value of IL-5 & IL-17 before and after treatment. Moreover, from 17 to 57 weeks, there was negative correlation in the increasing range of sIgG4 of Der p & Der p2 and the D-value of TNF- α before and after treatment.

Conclusions: SIT was a dynamic immune process and with the process of SIT, immune status of SIT was reflected by house dust mites and its main components- IgE & IgG4 of Der p1 & Der p2 in clinic detection.

O-D-003

TOBACCO SMOKE EXPOSURE ALTERS IMMUNE FUNCTIONS MEDIATED WITH DNA DAMAGE IN ALVEOLAR MACROPHAGE (AM)

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Introduction: Cigarette tobacco smoke is a risk factor for lung disease. Cigarette tobacco smoke is consisted from main-stream tobacco smoke (MTS) and side-stream tobacco smoke (STS). STS is released into the atmosphere, and impact lung health in non-smoker but not smoker. STS is inhaled into the lung by respiration and affect to alveolar macrophage (AM). AM is playing an important role of immune system in the lung. Therefore, it is important to investigate the effect of STS on immune system in the lung. In our previous study, we reported that MS induced DNA damage in AM associated with inhibition of immune function in AM. However, the effect of STS on AM is not yet fully demonstrated. In this study, we investigated the effect of STS on DNA damage and immune function in AM.

Materials and Methods: Mice were exposed to STS of 20 cigarettes/day during 10 days by using STS exposure auto-machine. Number of particles of 500 times diluted STS by air in one cigarette was measured by particle counter. Extract of water soluble side-stream cigarette smoke (WSTS) was obtained by which STS was bubbled in sterile distilled water and freeze-dried, and adjusted to final concentration of 1.25, 2.5, 5, 10 mg/ml with PBS. After STS exposure, AM were obtained by broncho-alveolar lavage (BAL). Dot plots, CD surface antigens and TLRs expressions of AM were analysed by FACS. Phagocytic activity was measured by FACS using FITC-labeled beads. DNA damage of AM was evaluated by comet assay.

Results: Particle concentration of STS was 60 mg/m³ from one cigarette. The number of AM was significantly increased in STS exposed mice compared with non-STS exposed mice. The cell size and intra-cellular structure of AM were changed in STS exposed mice. Phagocytic activity of AM was significantly inhibited in STS exposed mice. Expressions of CD11b, TLR-2, TLR-4 and CD14 on AM were significantly inhibited in STS exposed mice but not CD16. Tail moment of AM as indicator of DNA damage was significantly increased in STS exposed mice. Tail length of AM as indicator of DNA damage was significantly increased in STS exposed mice. DNA damage in AM was also induced by WSTS at dose dependent.

Conclusions: We investigated the effect of side-stream tobacco smoke (STS) on alveolar macrophage (AM). STS exposure caused the change of cell size and intracellular structure in AM. STS induced significantly increase of DNA damage in AM. DNA damage in AM was also significantly increased with WSTS. Expressions of CD11b, TLR-2, TLR-4 and CD14 in AM were decreased by STS, but not CD16. STS was a risk factor for DNA damage of AM and inhibited the immunological functions in AM mediated by DNA damage. These results suggest that changes of intracellular structure, inhibition of phagocytosis and TLR expression of AM by STS and induced-DNA damage of AM by STS may result in easily infection for bacteria or virus and carcinogenesis.

O-D-004

FENO COULD BE AN EFFECTIVE PREDICTOR FOR EOSINOPHILIC INFLAMMATION IN YOUNG ADULT PATIENTS WITH ALLERGIC RHINITIS

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Background: Fractional exhaled nitric oxide (FeNO) is an noninvasive biomark of airway eosinophilic inflammation and well tolerant. Nonasthmatic patients with allergic rhinitis showed eosinophilic inflammation in the lower airway might be in higher risk of developing asthma in the future. Detecting eosinophilic inflammation via induced sputum test might fail in these patients sometimes, as they can not always cough out enough amount of sputum for this test, especially in young adult patients.

Objective: Our study aims to investigate the significance of FeNO in detecting the eosinophilic inflammation in lower airway of nonasthmatic patients with allergic rhinitis.

Methods: A total of 196 young adult patients (18 to 22 years old) with isolated symptoms consistent to allergic rhinitis were included. Patients with other nasal or lung disease were strictly excluded. All patients went through series of tests, including FeNO, spirometry, methacholine challenge test, skin prick test, induced sputum test. Blood samples were taken for aeroallergen specific IgE test. All patients were divided into two groups, increase FeNO group and normal FeNO group, according to the cutoff FeNO value we set up via statistic analysis. Written consent was given to each patient.

Results: FeNO value > 25.5 ppb was a cutoff value to identify eosinophilic inflammation in the airway with sensitivity of 73.2% and specificity of 80%. However, we adopted 26 ppb as a cutoff value, as the machine could only show result in integer. The demographic characters and clinic state were comparable in both increase FeNO group (n = 69) and normal FeNO group (n = 127) (all P > 0.05). Sputum eosinophil count was higher in increase FeNO group (P < 0.01). The prevalence of sputum eosinophilia was significantly higher in increased FeNO group than that in normal FeNO group (59.42% Vs 12.60%, P < 0.01).

Conclusion: FeNO with a cutoff value of 26 ppb can be an effective predictor for eosinophilic inflammation in lower airway of young adult, nonasthmatic patients with allergic rhinitis. A further study with larger sample will be needed to confirm our result.

O-D-005

INDUCED PLURIPOTENT STEM CELLS REDUCES NEUTROPHILS CHEMOTAXIS VIA ACTIVATING GRK2 IN ENDOTOXIN-INDUCED ACUTE LUNG INJURY

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Objectives: Induced pluripotent stem (iPS) cells are novel stem cell populations, but the mechanism of iPS cells involving in acute lung injury (ALI) is not well known. We investigated the effect of iPS cells in moderating the neutrophils chemotaxis of endotoxin-induced ALI.

Methods: Male C57BL/6 8–12 week-old mice were studied. Mouse iPS cells were delivered through the tail veins of mice 4 hours after intratracheal instillation of endotoxin. Lung histopathological findings, the neutrophils counts of peripheral blood and bronchoalveolar lavage fluid (BALF), bone marrow cells distribution, the expression of chemokine receptors and regulatory signalling pathway were analysed at the end of 24 hours.

Results: iPS cells significantly diminished the histopathological changes of ALI and the lung injury score in comparison with control-cell therapy with fibroblasts. There were also a significant reduction in the numbers and activity of neutrophils in the BALF, confirmed by immunostaining with Ly6G in the iPS cell-treated ALI mice. iPS cells therapy restored the changes of neutrophils counts in peripheral blood of ALI mice; however, the percentage of matured neutrophils in bone marrow were similar between iPS-treated and -untreated groups. iPS cells mediated a down-regulation of the chemotactic response to endotoxin (reducing CXCR2 expression on neutrophils of peripheral blood), which were also confirmed by *in vitro* migration assay. In addition, iPS cells enhanced the GRK2 expression on the surface of blood neutrophils in ALI. Treatment with conditioned medium of iPS cells showed the similar effects as iPS cells.

Conclusions: Intravenous delivery of iPS cells provides a beneficial effect to attenuate the neutrophils chemotaxis and lung accumulation in endotoxin-induced ALI, which in partly is mediated by an enhancement in GRK2 activity and reduction in CXCR2 expression.

O-D-006

EFFECTS OF FAMILIAL INHERITANCE ON REGULATION OF TH1/TH2 CYTOKINE EXPRESSION

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Objective: Different factors (individual characteristics, genetic factor, environmental factor and so on) play a critical position in allergic disease among children. By observing the expression of Th1/Th2 cytokines in children and their families, we can understand the effect on family inheritance on regulation of Th1/Th2 cytokines expression.

Methods: Selected 20 subjects (10 families), which includes positive and negative group with 10 cases in each one. Without a family history of atopy group, adult male 2 cases, female 3 cases, aged 31 ± 5 years old children, male 2 cases, female 3 cases, aged 4 ± 1 years old; have a family history of allergy: adult male 2 cases, female 3 cases, aged 32 ± 5 years old children, male 3 cases, female in 2, age 4 ± 1 years). Use flow cytometric detect subject's whole blood interleukin 4 (interleukin-4, IL-4) and interferon gamma (interferon- γ , IFN- γ).

Results

1) The whole blood of IL-4 results: The level of IL-4 were increased significantly of allergic patients compared with normal ($t = 2.401$, $P < 0.05$); IL-4 levels in family history of allergy group were significantly higher than those without family history ($t = 5.770$, $P < 0.05$); children with family history of allergies, whole blood level of IL-4 was significantly higher than children without family history of allergies, the difference was statistically significant ($t = 13.774$, $P < 0.01$).

2) The whole blood IFN- γ levels results: The level of IFN- γ in Allergic patients were significantly lower than the normal person, but the difference was not statistically significant ($t = -1.351$, $P > 0.05$); there were no significant differences in whole blood levels of IFN- γ between groups whether have a family history of allergy or not ($t = -0.105$, $P > 0.05$), but allergy group with family history IFN- γ levels were lower than controls; between the children with a family history of allergies, whole blood IFN- γ levels significantly lower than children without a family history of allergies, but the difference was not statistically significant ($t = 2.025$, $P > 0.05$).

3) In family history of allergy group, the whole blood of IFN- γ levels in adult were significantly lower than children, and the difference was statistically significant ($t = -4.110$, $P < 0.05$); on the other hand, without family history of allergy group, the whole blood level of IL-4 in adult was significantly higher than that in children, the difference was statistically significant ($t = 4.554$, $P < 0.05$).

Conclusions: Family history of allergy affects the balance of Th1/Th2 on children. On behalf of children with family history of allergy, Th2 perform relative advantage, whose cytokine IL-4 in TH2 cell function will be increased.

ORAL PRESENTATION – CLINICAL RESPIRATORY MEDICINE

O-E-001

FACTORS ASSOCIATED WITH RADIOLOGIC PROGRESSION OF NON-CYSTIC FIBROSIS BRONCHIECTASIS DURING LONG TERM FOLLOW UP

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Background: Non-cystic fibrosis (CF) bronchiectasis is a chronic airway inflammatory disease and shows diverse clinical courses. Though some patients remain stable, some undergo radiologic progression. The purpose of present study was to find out factors influencing radiologic progression of non-CF bronchiectasis.

Method: The medical records of non-CF bronchiectasis patients, who were followed up with CT scan for more than at least 5 years, were retrospectively reviewed. All CT scan images were reevaluated and radiologic severity of bronchiectasis was determined by Bhalla score. The association between the baseline Bhalla score and the clinical, laboratory, microbiological and pulmonary functional test (PFT) parameters were analysed. We also evaluate the association between the changes of Bhalla scores during study period and other variables shown above.

Results: Total 155 stable adult non-CF bronchiectasis patients (mean age, 67.1 years, male 45.2 %) were included. The mean follow up time was 7.11 ± 1.42 (5–10) years. Baseline Bhalla score was 9.52 ± 3.14 (4–19). The baseline Bhalla score was significantly associated with body mass index (BMI), white blood cell (WBC) count, c-reactive protein (CRP), albumin, initial PFT parameters, isolation of *P. aeruginosa* and bacterial colonization. Bhalla score did not change in 87 (56.1%), improved in 12 (7.7%), and progressed in 56 (36.1%). The mean change of Bhalla score during follow up was 0.55 ± 1.14 (–2 to 5). The Bhalla score change was significantly correlated with age ($p = .038$), BMI ($p = .022$), the isolation of *P. aeruginosa* ($p = .02$), and nontuberculous mycobacterium (NTM) ($p < 0.01$). The Bhalla score change was also significantly combined with the change of PFT parameters such as FVC ($p = .030$), FEV1 ($p = <.01$), PEF ($p = <.01$), DLCO ($p = .025$). The number of lung segments involved by bronchiectasis, which is a component of nine Bhalla scoring system parameters, was highly correlated with total Bhalla score (RR 0.681; CI 0.70 to 1.29; $p = <.01$).

Conclusion: The radiologic progression occurred in significant portion of non-CF bronchiectasis patients, and was associated with age, BMI, isolation of *P. aeruginosa*, isolation of NTM, and change of PFT parameters.

O-E-002

THROMBOEMBOLIC EVENTS IN MALIGNANT PLEURAL MESOTHELIOMA

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Aim: Thromboembolic events are higher in patients with cancer compared to general population. Malignant pleural mesothelioma (MPM) also increases the risk of thromboembolic events. In this retrospective study we aimed to determine the rate of thromboembolic events in patients with MPM.

Methods: The study included 178 patients (106 males/72 females) who were histopathologically diagnosed as MPM during the last 6 years. The files of the patients were evaluated retrospectively. The demographic data, clinical, radiological, pathological findings, applied therapies, and the thromboembolic events were noted.

Results: The study included 178 patients (106 males, 72 females) with a mean age of 58.7 ± 11.8 years (min: 31 – max: 83). VATS-pleural biopsy was the most common way of diagnosis with a ratio of 58.4%. The histopathological diagnosis was epithelial in 97 (54.5%), biphasic in 31 (17.4%), sarcomatous in 4 (2.2%), and unidentified in 46 (25.8%) patients.

Disease stages were: Stage 1 ($n = 14$, 7.9%), Stage 2/ $n = 75$, 42.1%), Stage 3 ($n = 57$, 32%), and Stage 4 ($n = 32$, 18%). The applied therapies were chemotherapy in 109 (61.2%), multimodality therapy 14 (7.9%), and supportive therapy in 41 (23%) patients. Pleurodesis was performed in 94 (52.8%) patients. In total, 14 (7.9%) thromboembolic events were identified: 6 (3.4%) pulmonary thromboembolism, 6 (3.4%) deep venous thrombosis (4 lower and 2 upper extremity thrombosis), and 2 (1.1%) myocardial infarctions. Five events (35.7%) were diagnosed before the diagnosis (median 10 months), 1 (7.2%) event simultaneously with the diagnosis, and 8 (57.1%) events after the diagnosis of MPM (median 2.5 months).

Conclusion: The rate of thromboembolic events was found 7.9%. Despite being a retrospective observational study, this result demonstrated the high incidence of thromboembolic events in patients with MPM.

O-E-003

IMPACT OF ANCILLIARY FINDINGS IN PATIENTS WITH SUSPECTED PULMONARY EMBOLISMBERGIC A¹, CUKIC V², LINDQVIST A³, MINIATI M⁴, BAJC M⁵

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Introduction: Ventilation/perfusion tomography (V/P SPECT) is the recommended method for and follow-up of pulmonary embolism (PE). Symptoms and signs of PE are nonspecific and often similar to those of other cardiopulmonary diseases. An imaging method is needed to clarify clinical diagnosis. With V/P SPECT it is possible to recognize other pathologies in addition to PE, such as pneumonia, chronic obstructive pulmonary disease (COPD), left heart failure (LHF) and tumour. The objective of this study was to identify how frequently other cardiopulmonary pathological findings are among patients with suspected PE as shown by V/P SPECT and to assess the clinical consequences of these findings after one month.

Material and Method: Three hundred thirty one consecutive patients with clinically suspected PE were examined and classified with V/P SPECT. Patients were followed up clinically by means of other laboratory tests.

Results: Eighty patients (24.2 %) had a normal ventilation and perfusion SPECT and no clinical consequences of cardiopulmonary pathology appeared. PE was identified in 103 (31.1 %) patients: all were treated with anticoagulants. Twenty-six of them had additional findings. Typical signs of pneumonia were shown in 93 (28.9 %): 88 had acute pneumonia and 5 were followed up for a chronic post-inflammatory state. Patterns with different degrees of COPD were present in 49 patients (14.8 %): all were obstructive on spirometry and were treated for obstruction. Sign of LHF was observed in 15 (4.53 %) patients: in 10 patients the acute LHF diagnosis was established clinically and they improved with therapy. Another 5 patients were classified as having a chronic cardiopulmonary disease. Furthermore, in 17 patients (5.13 %) the V/P pattern was suggestive of a tumour: clinical outcomes were 7 lung tumours, 1 empyema, 1 sarcoidosis. Two patients remained unclassified, 4 refused further diagnostics and 2 were lost in follow up.

Conclusion: This study shows high prevalence of other cardiopulmonary diseases among patients with a clinical suspicion of PE. All of them may be identified by V/P SPECT. V/P SPECT ancillary findings can clarify patients' symptoms and might have impact on treatment.

O-E-004

PREPARATION AND CHARACTERIZATION OF CONTROLLED RELEASE MICROSPHERES FOR MANAGEMENT OF PULMONARY HYPERTENSIONSAIGAL A^{1,3}, HENG ST¹, NG WK^{1,3}, TAN RBH^{2,3}, CHAN SY¹

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Objective: To develop a controlled release system, whereby drug would be suitably encapsulated and released consistently and continuously over a prolonged period of time to reduce the frequency of dose administration to manage pulmonary hypertension.

Methods: To formulate microspheres for controlled release, chitosan was chosen as the release modifier and nifedipine as the model drug.

Microspheres were formulated by spray drying technique to obtain particles suitable for inhalation. After optimizing the spray drying conditions, particles were characterized for their physical properties like particle size, morphology, flow properties and surface area. The drug release from the microspheres was determined followed by examination of the particle interior by FIB and aerosol profile using the MSLI. To determine the toxic effect of chitosan on the lung cells, cytotoxicity assay was performed on chitosan for 48 h.

Results: The particle size and morphology was found to be suitable for inhalation particles with acceptable flow properties. The large surface area allows for lesser friction and better flow of the microspheres. Drug release was considerably reduced in the microspheres with only 60% drug release after 8 h. FIB images show that the particles have a hollow interior and a "golf ball" surface resulting in good aerosol performance. Impinger study shows that ~70% of the microsphere sample deposits in the later stages of the MSLI indicating very good aerosol profile. Lastly the cytotoxicity study suggests that chitosan is nontoxic to the lung cells as the cell viability remains close to 100% even after 48 h of exposure.

Conclusion: Nifedipine loaded microsphere formulation significantly reduced the release rate of the drug. Particle size was well controlled, with most particles having spherical morphology, low density and acceptable flowability. Large surface area, hollow interior and "golf ball" surface ensured good aerosolization performance, with high FPF values. The slow release chitosan microspheres provide a patient friendly alternative to the current regimens which require frequent dosing.

O-E-005

PREGNANCY DOESN'T ALWAYS CAUSE DETERIORATION OF LYMPHANGIOLEIOMYOMATOSIS

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Backgrounds: Lymphangiomyomatosis (LAM) is a rare cystic lung disease that is found primarily in women of childbearing age. It has been suspected that pregnancy in LAM is associated with an increased risk of accelerating disease course thereafter. However, no objective data on the comparison of the decline rates of pulmonary function before and after pregnancy has existed.

Purpose: To evaluate the effect of pregnancy on disease progression LAM, we conducted an observational study of LAM patients who experienced pregnancy after the establishment of the diagnosis of LAM.

Methods: From 2001 to 2013, we had ten LAM patients who experienced pregnancy after its diagnosis. To determine the effect of pregnancy on the disease activity, we retrospectively reviewed pulmonary function data before pregnancy as well as those after delivery and then the decline rates were assessed by mixed linear effect model. The complications during pregnancy and chest CT findings were investigated. The concentration in serum of both VEGF-D and soluble form of VEGF receptor 3 (sVEGFR-3) were determined.

Results: All patients were nulliparous and sporadic disease. Ten patients became pregnant 13 times in total: twice in three patients and once in seven. None of the patients had miscarriage or abortion. Seven (88%) in eight patients who had a history of pneumothorax before pregnancy had experienced a total of 13 episodes of its recurrence during pregnancy; eight were relieved only by rest, but five were managed with thoracic drainage. Meanwhile, pneumothorax was not identified in patients without its history. The decline rates of FEV1 before pregnancy and after delivery showed no significant difference, -136 and -104 ml/yr, respectively ($p = 0.655$), suggesting that pregnancy didn't accelerate disease course. In addition, serum VEGF-D levels decreased during pregnancy as compared with baseline (before pregnancy) (768 vs. 1.850 pg/ml, $p = 0.053$), but returned to the baseline level after delivery ($p < 0.001$). In contrast, serum sVEGFR-3 concentration reciprocally increased during pregnancy from baseline (63.8 vs. 7.7 ng/ml, $p < 0.001$) and reverted after delivery ($p < 0.001$). In one patient who has no decrease in serum VEGF-D during pregnancy, DLco showed a substantial decrease after delivery.

Conclusion: Our study suggests that pregnancy in LAM is not always a risk of deterioration of pulmonary function, but the recurrence of pneumothorax should be aware in patients with its past history. The monitoring of serum VEGF-D levels may be useful for predicting the postpartum exacerbation.

O-E-006

FREQUENCY OF PULMONARY MEDICINE CONSULTATION IN HYPERBARIC MEDICINE CLINIC

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Background: Hyperbaric Oxygen Therapy (HBOT) is based on administration of 100% oxygen to the patients in a pressurized chamber. With this treatment, partial pressure of oxygen in the blood and body tissues is increased. Major urgent HBOT indications are CO poisoning, decompression sickness, and sudden vision/hearing loss. Routine indications are non-healing wounds, osteomyelitis, and radionecrosis. Patients will receive HBOT should be evaluated for spontaneous pneumothorax, pneumothorax, recent pulmonary infections, pleural empyema, tumours, severe emphysema and COPD. For this purpose, patient are underwent physical check, laboratory testing and radiological investigations. Pulmonary medicine specialist consultation is required in these indications for patients. The aim of our study is to demonstrate the prevalence of pulmonary medicine clinic consultation for HBOT in our hospital.

Method: A multi-place HBOT chamber is used in our hospital. Patients are evaluated by Aerospace Medicine specialist and the necessary follow-up and treatments are planned. Study data were created by scanning patient records of HBOT clinic. Calculations and tables were prepared by using the Microsoft Excel program.

Results: 355 patients were treated in our clinic and included in the study between dates June 2013-July 2014. 47 of these patients (13.24%) were consulted to pulmonary medicine specialist. 28 (7.89%) of the patients as low risk, 17 (4.79%) of the patients as intermediate-risk and 2 (0.56%) patients were assessed as high risk for HBOT.

Conclusion: Patients who were assessed as high risk for HBOT were not accepted to the HBOT and were provided medical and surgical treatments. Patients, who had intermediate/low-risk for HBOT, were informed about their disease and possible complications in HBOT. HBOT acceptance decision was made by aerospace medicine specialist and the patient together. In order to minimize the complications of Chest Diseases in administration of HBOT coordination with pulmonary medicine clinic is considered to be an appropriate approach.

O-E-007

A MULTI-DISCIPLINARY SURVEY ON ATTITUDES AND PERCEPTIONS ON ADULT OUTPATIENT TRACHEOSTOMY CARE IN THE PHILIPPINE GENERAL HOSPITAL

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Background: Tracheostomy is an old and commonly performed surgical procedure among critically ill patients for a variety of reasons. Upon discharge, a multidisciplinary approach to post-tracheostomy care is recommended.

Objectives: The study aims to determine and compare the attitudes, opinions, and perceptions of surgeons, otorhinolaryngologists, general internists, and family physicians training in a tertiary hospital regarding adult outpatient tracheostomy care and eventual decannulation.

Methodology: An 11-question discipline-specific questionnaire was distributed. Frequency tables were used to describe the different responses. A Chi-square-test was used to determine significant differences in the responses of the different disciplines.

Results: 106 responses were obtained at the end of the study period (39 general internists, 34 general surgeons, 21 otorhinolaryngologists, 12 family physicians). 33% of general surgeons and 29% of otorhinolaryngologists claim that they perform tracheostomy follow-up care themselves, but 60% of surgeons and 62% of otorhinolaryngologists expect the primary care provider to jointly perform it with them. 74% of internists and 55% of family physicians report that they have not received any form of training on routine tracheostomy care. 56% of internists and 45% of family physicians feel very uncomfortable in handling outpatient tracheostomy care, but 36% of internists and 67% of family physicians would perform some tracheostomy care and would only refer to a surgeon for further recommendations. 85% of general surgeons, 85% of otorhinolaryngologists, 92% of general internists, and 100% of family physicians believe that the surgeon is the most qualified to perform outpatient tracheostomy care, while 55.2% of general surgeons, 70% of otorhinolaryngologists, 58% of general internists, 30% of family physicians believe that the surgeon should primarily take charge.

Conclusions: Majority of surgeons perform outpatient tracheostomy follow-up care, but also expect the primary care physicians to jointly co-manage. Unfortunately, majority of primary physicians are not trained to do so. Majority feel uncomfortable doing it, and would rather refer to the surgeons. Surgeons and primary physicians agree that the surgeon is the most qualified to perform outpatient tracheostomy care and should be the service to primarily provide it.

ORAL PRESENTATION – CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

O-F-001

LONG ACTING BETA 2 AGONIST INHIBITS CIGARETTE SMOKE-INDUCED AIRWAY INFLAMMATION AND REMODELING THROUGH CAMP PATHWAY

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Background and Aim of Study: Long acting β_2 -adrenergic receptor agonist (LABA) remains the principal pharmaceutical management for chronic obstructive pulmonary disease (COPD) patients. However, the role of LABA in the management of cigarette smoker-induced airway inflammation and remodeling in COPD remains unclear. We hypothesize that LABA may inhibit cigarette smoke extract (CSE)-induced IL-8 release in human bronchial epithelial cells and collagen production in lung fibroblasts via cyclic AMP (cAMP) and protein kinase A (PKA) pathway. Moreover, LABA could attenuate cigarette smoke-induced airway inflammation and remodeling in a mouse model.

Methods: Human primary bronchial epithelial cells (PBEC) were stimulated by CSE, and IL-8 and cAMP were measured. Indacaterol, a LABA, was applied to investigate the inhibitory effect on CSE-induced IL-8 production. Specific adenylyl cyclase (AC) inhibitor and PKA inhibitor were added to determine IL-8 production after pretreatment with indacaterol. Collagen production from fibroblasts and cell proliferation were also measured. In the mouse model of cigarette smoke-induced airway inflammation and remodeling, inflammatory cells, mediators in the airways and parenchyma were assessed. Indacaterol was applied intraperitoneally after cigarette smoke stimulation.

Results: CSE significantly induced IL-8 production in PBEC. The IL-8 production was significantly inhibited by indacaterol which increased intracellular level of cAMP. Specific inhibitors for AC and PKA both suppressed inhibitory effect of indacaterol on IL-8 production. In the mouse model, a significant increase of inflammatory cells, chemoattractant protein-1, macrophage inflammatory protein-2 and total protein were observed in the bronchoalveolar lavage fluid (BALF) as well as peribronchial inflammatory cell infiltration and collagen production after four weeks cigarette smoke exposure. All these actions were significantly blocked by treatment with indacaterol.

Conclusion: Indacaterol can inhibit cigarette smoke-induced airway inflammation and remodeling through cAMP pathway.

O-F-002

METHYLATION STATUS OF PERFORIN GENE PROMOTER IN CD4+ T LYMPHOCYTES OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: It is widely accepted that methylation-sensitive perforin gene promoter are hypomethylated in CD4+ T cells from patients with active lupus and subacute cutaneous lupus erythematosus, but whether this is the case in chronic obstructive pulmonary disease (COPD), also regarded as one of autoimmune diseases, is not clear yet. This study aimed at investigating the role of hypomethylation of perforin gene promoter in CD4+ T cells from peripheral blood of COPD patients.

Methods: The peripheral blood CD4+ T lymphocytes of 8 patients with acute exacerbations of COPD and 8 healthy controls were separated with a magnetic cells sorting system (MACS), and genomic DNA and RNA was extracted from the isolated cells. The methylation level of perforin gene promoter in peripheral blood CD4+ T lymphocytes was determined using bisulfite sequencing. Expression of perforin was investigated using RT-PCR.

Results: The methylation levels in perforin gene promoter region of CD4+ T lymphocytes of patients with COPD were significantly lower than those in the control group, while the expression levels of perforin gene were relatively higher and the differences were statistically significant (all $P < 0.05$).

Conclusions: Hypomethylation in perforin gene promoter region of CD4+ T lymphocytes may induce increased expression of perforin gene, which plays an important role in the pathogenesis of COPD.

O-F-004

VITAMIN D INHIBITS EXPRESSION AND ACTIVITY OF MATRIX METALLOPROTEINASE (MMP) IN HUMAN LUNG FIBROBLASTS (HFL-1) CELLS

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Background: Low levels of serum vitamin D is associated with several lung diseases. Production and activation of matrix metalloproteinases (MMPs), including MMP-2 and MMP-9, by human lung fibroblasts in response to the stimulation of inflammatory cytokines may play an important role in the pathogenesis of emphysema. The aim of the current study therefore is to investigate if vitamin D modulates expression and activation of MMP-2 and MMP-9 in human lung fibroblasts (HFL-1) cells.

Methods: HFL-1 cells were cast into three-dimensional collagen gels and stimulated with or without IL-1 β in the presence or absence of 100 nM 25-hydroxyvitamin D (25(OH)D) or 1,25-dihydroxyvitamin D (1,25-(OH) $_2$ D) for 48 hours. Trypsin was then added into the culture medium in order to activate MMPs. Expression of tissue inhibitor of metalloproteinase (TIMP-1, TIMP-2) measured by Enzyme-linked immunosorbent assay (ELISA). Expression of MMP-9 mRNA and TIMP-1, TIMP-2 mRNA was quantified by real time RT-PCR.

Results: IL-1 β significantly stimulated MMP-9 production and mRNA expression. Trypsin converted latent MMP-9 into its active form (82 kDa) within 24 hours (100%), and this conversion was significantly inhibited by 25(OH)D (100 nM) and 1,25(OH) $_2$ D (100 nM). Expression of MMP-9 mRNA was also significantly inhibited by 25(OH)D and 1,25(OH) $_2$ D. Consistently, vitamin D, 25(OH)D and 1,25(OH) $_2$ D significantly inhibited collagen degradation by IL-1 β +trypsin as determined by hydroxyproline.

Conclusion: Vitamin D, 25(OH)D and 1,25(OH) $_2$ D play a role in regulating human lung fibroblast functions in wound repair and tissue remodeling through not only inhibiting IL-1 β stimulated MMP-9 production and conversion to its active form but also inhibiting IL-1 β inhibition on TIMP-1 and TIMP-2 production.

IMPACT OF EXTRAPULMONARY COMORBIDITIES ON QUALITY OF LIFE IN MALE PATIENT WITH STABLE COPD

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Objective: To study the impact of comorbidities on the quality of life in the male patient with stable chronic obstructive pulmonary disease (COPD).

Methods: 86 male COPD patients in stable conditions were recruited from Department of Respiratory Medicine in Beijing Chao-yang Hospital from March 2013 to January 2014. Measurements included lung function, body composition by bioelectrical impedance analysis, and bone stiffness by quantitative ultrasound, depression by hospital anxiety and depression scale (HAD-D). In COPD patients, the symptoms were assessed by COPD Assess Test (CAT) and Modified British Medical Research Council (mMRC) respectively. Extrapulmonary comorbidities were also recorded, such as coronary heart disease, hypertension, and diabetes.

Results: According to the number of comorbidities, the number of patient not having comorbidity is 16, with the number of comorbidity adding, the patients, number is 38, 26 and 6 respectively, while the grade of CAT is 14.25 \pm 7.11, 14.00 \pm 7.90, 14.96 \pm 6.70 and 25.67 \pm 7.06, separately.

Conclusions: Extrapulmonary comorbidities have notable impact on the quality of life in the male patient with stable COPD, the quality of life deteriorated as the number of comorbidities increased.

O-F-006

MILD TO MODERATE AIRFLOW OBSTRUCTION IS NOT DIRECTLY ASSOCIATED WITH CORONARY ARTERIOSCLEROSIS BUT IS ASSOCIATED WITH THE ELEVATION OF SERUM CREATININE LEVELS

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Background: Chronic obstructive pulmonary disease (COPD) is thought to be associated with arteriosclerosis and its related disorders such as coronary artery disease. Nonetheless, COPD, arteriosclerosis, and coronary artery disease involve overlapping risk factors; therefore, evidence of a direct effect is still lacking.

Subjects and Methods: A retrospective study of the association between COPD and cardiovascular risk factors was conducted on 214 patients who underwent respiratory function testing and a computed tomography scan of coronary arteries.

Results: Subjects included 58 patients with COPD and 156 patients without COPD. Of the patients with COPD, 38 had Global Initiative for Obstructive Lung Disease (GOLD) Grade I COPD, and 20 had GOLD Grade II COPD. All COPD patients analysed had mild to moderate COPD. Intergroup comparison of patients with COPD and those without COPD revealed no significant differences in coronary artery stenosis or the coronary artery calcium score, but serum creatinine levels were significantly elevated in patients with COPD ($p = 0.02$). Independent variables were selected for multivariate analysis using forward selection based on the likelihood ratio test. This analysis indicated that an obstructive defect significantly correlated with an elevated serum creatinine level ($p = 0.046$). In addition, there was a significant simple correlation between a decrease in the log-transformed predicted FEV $_1$ and an elevated serum creatinine level ($r = -0.186$, $p = 0.006$).

Conclusion: There was no apparent correlation between mild to moderate airflow obstruction and the extent of coronary artery stenosis or coronary artery calcification. However, mild to moderate airflow obstruction was significantly correlated with elevated serum creatinine levels and could thus be associated with future cardiovascular events.

O-F-007

MIR-146A PLAYS PATHOGENIC ROLE IN ABNORMAL INFLAMMATORY RESPONSE OF A MURINE COPD MODEL

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Background: Cigarette smoking is the most important cause of chronic obstructive pulmonary disease (COPD), but the mechanisms of pathogenesis are incompletely defined. We have previously reported that senescence marker protein-30 knockout (SMP30-KO) mice are proper animal models of senile lung and can be useful for investigating cigarette smoke-induced pulmonary emphysema. Moreover, we have already shown that a specific microRNA, miR-146a, plays a pathogenic role in the abnormal inflammatory response in COPD.

Methods: Four-months-old and vitamin C-controlled SMP30 knockout mice were given miR-146a inhibitor on day 1 and 8 intranasally during exposure to either diluted cigarette smoke or fresh air for 2 weeks. Total RNAs were extracted from the lungs followed by histologic evaluation of pulmonary emphysema. The bronchoalveolar lavage fluid (BALF) was pooled and total cell counts, cell populations and prostaglandin E $_2$ (PGE $_2$) levels in each BALF specimen were determined. Cyclooxygenase-2 (COX-2) and interleukin-6 expressions in the lungs were evaluated by qPCR.

Results: MiR-146a levels in the lungs was revealed to reach a peak after 2-week exposure of cigarette smoke and to be significantly higher in vitamin C-lacked mice. Total cell and lymphocyte numbers were increased in the BALF of both miR-146a inhibitor and smoke exposed mice. PGE $_2$ production and COX-2 expression were also increased significantly higher by exposure to both miR-146a inhibitor and cigarette smoke.

Conclusion: miR-146a appears to play a pathogenic role in the abnormal inflammatory response in a cigarette smoke-exposed murine model of COPD.

O-F-008

EVALUATING DRUG UTILIZATION PATTERN AND DIRECT COST OF CRITICAL CARE MANAGEMENT IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN MANGALORE, INDIA

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Background and Objectives: COPD comprises an important health issue in developing countries resulting in health threats, financial burden on patients and an immense strain on hospital services. This study aims to evaluate the clinical picture, outcomes, drug utilization pattern and cost of intensive care management associated with COPD admissions in a tertiary care centre in India.

Methodology: We followed a retrospective cohort design comprising of COPD inpatients admitted from Jan 2013 to Apr 2014. Patient case records and hospital billing details were reviewed and demographic details, clinical profile and outcomes were evaluated. WHO prescribing indicators were used to assess the prescription pattern. Patient expenses were allocated into four cost blocks (clinical care services, consumables, staff charges and others). Multivariate logistic regression analysis was performed to identify predictors for treatment cost.

Results: Study included 426 COPD inpatients; 72.76% were males and 27.24 % females with mean age of 66.65 years. Prevalence of COPD was 27.19 cases per 1,000 hospitalizations. ICU admissions were required in 8.45% (n = 36). The in-hospital mortality rate was 7.7%. Patients were hospitalized for a median of 4 days (IQR 3–8). Mean number of drugs prescribed per patient was 8.38 (95% CI: 6.71–10.04). Comorbidities observed included Diabetes Mellitus (20.21%), Hypertension (18.02%) and Coronary artery disease (15%). Frequently encountered prescriptions pertaining to COPD included Corticosteroids (36%), Methylxanthines (33.31%), Short acting beta agonist (25.33%) and miscellaneous (8.37%). Other commonly utilized drug groups include Antibiotics (26.04%), Proton pump inhibitors (20.4%), Loop diuretics (10.3%), NSAIDs (5.6%) etc. Among antibiotics Cephalosporins (41.86%) were the most prescribed. Dosage forms encountered in the ICU were Injectables (Median 6 injectable per patient, IQR 3–8) followed by Oral Medications & Inhalational Dosage Forms. Budesonide (62.5%) and Salbutamol (25%) were the frequently prescribed Respules. Correlation between Polypharmacy and Hospital Stay (R 0.79, p < 0.005) were observed. Cost of critical care treatment per patient is IQR 42633.10 (~\$713.41) (IQR 25173.48–77052.42). Major determinants of total cost were Clinical care services (46.92%) and Consumables (28.42%). The average economic burden for drugs were significantly higher in non survivors than survivors (p < 0.005).

Conclusion: Comorbidities, Polypharmacy, Duration of hospitalization and Injectable dosage forms were significant factors affecting the total treatment cost. This study helps in identifying certain lacunae in prescribing pattern, there is need for updating existing treatment protocols for rational drug usage and cost reduction in COPD patients.

O-F-009

EOSINOPENIA AS A MARKER OF OUTCOME IN ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a common cause of hospitalization and mortality. Recent studies showed usefulness of eosinopenia in predicting outcome in ICU patients. This study examined the association of eosinopenia with outcome in AECOPD.

Methods: Patients who were admitted because of AECOPD were divided into two cohort's patients with eosinopenia and without eosinopenia on the base of admission day CBC. Duration of hospitalization, need of mechanical ventilation, and mortality in hospital, re-hospitalization, or death within 30 days after discharge were compared in these two cohorts. Eosinopenia was defined as eosinophil count less than 40/mm³ prospectively.

Results: Among 100 patients with AECOPD, 44 patients were eosinopenic and 56 not. Duration of hospitalization in patients with eosinopenia was 12.38 ± 9.85 days and in patients without eosinopenia were 7.35 ± 5.68 days (p value: 0.001). In the group with eosinopenia 16 patients (36%) and in the other group seven patients (12%) needed mechanical ventilation (p value: 0.005). In hospital mortality rate among eosinopenic and non-eosinopenic patients was 12/44 (37.5%) vs. 4/56 (7.6%) respectively with p value: 0.006. Of all 100 patient with AECOPD 16 died in hospital, 12 (27.27%) in eosinopenic and 4 (7.6%) without eosinopenia (p = 0.006) Mean eosinophil count in patients who died in hospital (n = 16) was 44.00 cell/ml, while in survivors (n = 84) was 107.41 cell/ml (p value of 0.022).

Conclusion: There was a significant relationship between eosinopenia and outcome in the patients admitted because of the AECOPD. We considered eosinopenia could be a useful, easy-to-measure and inexpensive biomarker to predict the prognosis of the patients.

O-F-010

DECREASE OF INTERLEUKIN 6 SERUM LEVEL, IMPROVEMENT OF SGRQ AND DEPRESSION COMORBIDITY IN COPD PATIENT POPULATION TREATED WITH MEDICAL REHABILITATION

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Background: Depression is a major comorbidity in Chronic Obstructive Pulmonary Disease (COPD) patients. The prevalence is 10–42%, associated with a decline in health status and increased mortality. There are limited research on medical rehabilitation therapies associated with systemic effects of COPD, primarily in the areas of depression manifestation. Depression is assessed by the markers of inflammation in the blood. The purpose of this study is to proof the influence of medical rehabilitation programs in improving the level of depression, quality of life, and decreasing the level of interleukin 6 (IL-6), as well as to change COPD progression.

Method: This clinical study used quasi-experimental method to assess depression in COPD – 15 patients were in the control group, and 15 performed medical rehabilitation for 8 weeks, with blood samples taken to measure the levels of IL-6. Also, all patients performed St George's Respiratory Questionnaire for COPD patients (SGRQ-C) and Beck Depression Inventory (BDI) measurement, at baseline, the end of 2nd and 3rd month.

Results: After medical rehabilitation intervention for 8 months, there are differences in the levels of depression (p = 0.003) between the control vs intervention. There was a COPD progression change after the administration of medical rehabilitation in the COPD population. There were significant decrease in the levels of IL-6 among COPD population with depression, after the intervention (p = 0.001). Medical rehabilitation had an impact in the parameter of SGRQ-C (p = 0.036).

Conclusion: Medical rehabilitation can improve depression level in COPD population, and lower IL-6 level resulting in improvement in the patient's quality of life.

O-F-011

O-F-013

MEF50/MEF25 AND RV/TLC% CORRELATE WITH HRCT PHENOTYPES OF COPD

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Background: Heterogeneity of clinical presentation of chronic obstructive pulmonary disease (COPD) attributes to different pathological basis. As we know, high-resolution computed tomography (HRCT) may reflect the pathologic basis of COPD indirectly by evaluating the small airway inflammation and emphysema. The aim was to explore the relationship between spirometric parameters and HRCT findings.

Methods: 63 patients with COPD were enrolled the study with spirometry evaluated, who comprised three groups based on different phenotypes of HRCT, i.e. phenotype A (absence of emphysema, with minimal evidence of emphysema with or without bronchial wall thickening), phenotype E (emphysema without bronchial wall thickening), and phenotype M (emphysema with bronchial wall thickening). The relationship between spirometric parameters and HRCT findings was analysed.

Results: The values of FEV1/FVC%, FEV1% and MEF50% were significantly higher in phenotype A ($p < 0.05$), RV/TLC% was higher in phenotype E ($p < 0.05$). Those with MEF50/MEF25 >4.0 were more prevalence in phenotype A than in phenotype E and M (OR = 2.214, $p < 0.05$). Meanwhile, the occurrence of RV/TLC% $>40\%$ were higher in phenotype E than phenotype A and M (OR = 3.906, $p < 0.05$). ROC analysis showed that the cutoff value of MEF50/MEF25 for identifying phenotype A was 2.5, with sensitivity 66.7% and specificity 92.9%. The cutoff value of RV/TLC% for identifying phenotype E was 57.4%, with sensitivity 75.0% and specificity 79.1%.

Conclusion: The MEF50/MEF25 and RV/TLC% correlate with HRCT phenotypes.

O-F-012

A SUMMARY OF THE DIFFICULTIES IN DIAGNOSIS AND TREATMENT OF ELDERLY PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim: Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory disease in elderly patients, as the increase of age the incidence will increase gradually. In most cases, due to the limitations of atypical clinical symptoms, lung function and other tests, the diagnosis of many elderly patients with COPD is difficult and these patients can not receive timely treatment, result to exacerbations, increased mortality. Meanwhile elderly COPD patients are often combined with respiratory failure, coronary heart disease, kidney damage and other complications, which seriously impact the patient's outcomes and prognosis. Therefore, it is seriously important to investigate the characteristic of diagnosis and treatment in elderly COPD patients. We collected the elderly patients with COPD in our department for January 01, 2013 to April 31, 2014, and made a summary of the difficulties in diagnosis and problems in treatment in these patients.

Material: 134 cases were included. Basic information (including education, family, etc) and clinical data (including awareness, weight, respiratory manifestation, non-respiratory manifestation, etc) were included. Lung function, drug treatment and adjuvant therapy were recorded.

Results: All patients were moderate to severe COPD, aged from 70–98 years old. The main difficulties of diagnosis were atypical symptoms (32.1%), improper lung function standard for elderly patients (45.8%), unable to finish lung function test (28.3%), mixed up with asthma (10.5%). The particularities of treatment of elderly COPD patients were non elderly-specific drugs (35.0%), difficulty in inhalation device (22.7%) and deficiencies in comprehensive intervention (50.6%).

Discussion: Due to specificity of aging, the atypia of clinical manifestations and the limitations of tests and drugs for elderly COPD patients, we will inevitably face the obstacles in diagnosis and treatment of elderly COPD patients and it is unsuitable to use Global initiative for chronic obstructive lung disease (GLOD) to deal with these patient. Therefore, in order to improve the diagnosis and prognosis of elderly patients with COPD, we should develop an appropriate and specific standard for diagnosis, and apply integrated and particular interventions for treatment of elderly patients.

CLINICAL IMPACT OF COMBINED VIRAL AND BACTERIAL INFECTION IN COPD PATIENTS WITH COMMUNITY-ONSET PNEUMONIA

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Background: Chronic Obstructive Pulmonary Disease (COPD) is one of the most frequent comorbid conditions and a risk factor for developing pneumonia. Some authors reported that combined viral and bacterial increased the severity of CAP and COPD exacerbations. We hypothesize coinfection increase the severity of community-onset pneumonia (COP) in COPD patients.

Method: This study was performed as a sub-analysis of registry sponsored by Adult Pneumonia Study Group Japan (APSG-J). We included 75 COPD patients with COP in Kameda Medical Center from Feb 2012 to Jan 2013. Multiplex polymerase chain reaction for 12 viruses was performed in all patients. We analysed severity and clinical outcomes of patients with co-infection and with bacterial infection alone. The etiology was considered definitive if one of the following criteria was met: 1) Blood cultures, or pleural fluid cultures yielding a bacterial pathogen. 2) Significant quantitative culture growth from bronchoscopic respiratory samples. 3) Positive urinary antigen for *L. pneumophila* type 1 or *S. pneumoniae*. An etiologic diagnosis was considered to be presumptive if a validated sputum sample yielded one or more bacterial strains. Patients with definitive or presumptive causes were regarded as having etiologic diagnosis. A viral etiology was deemed probable if virus was detected in respiratory secretions by isolation or PCR.

Result: Of the 75 COPD patients with COP, an etiologic diagnosis was made in 34 (45.3%). 19 patients were diagnosed as having pneumonia with bacterial infection alone and 15 were diagnosed as pneumonia with co-infection. The likelihood of having a score corresponding to CURB-65 class III to V was higher in patients with co-infection than in those with a bacterial pathogen alone. (OR 5.74, 95% CI 1.01–44.17; $p = 0.030$). 30-day death was seen in 1 (6.7%) with co-infection and in none with bacterial infection alone ($p = 0.441$).

Conclusion: The likelihood of having a score corresponding to CURB-65 class III to V was higher in patient with co-infection. This suggests that co-infection increase the severity of community-onset pneumonia (COP) in COPD patient.

O-F-014

HIGHER CIRCULATING IL-13 IN BIOMASS-RELATED COPD COMPARED TO SMOKERS WITH OR WITHOUT COPD

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Background: Interleukin 13 is a protein cytokine predominantly secreted by Th2 cells and implicated in inflammation of allergic origin. Its role in non-allergic inflammatory conditions such as COPD is not well established.

Objectives: To elucidate the role of circulating interleukin 13 (IL-13) in patients with COPD due to smoking and biomass exposure and to compare it with non-COPD smokers.

Methods: 225 subjects with COPD and a history of smoking or having a history of chronic biomass exposure were recruited from the Department of Pulmonary Medicine, All India Institute of Medical Sciences, Delhi. They were categorized into three groups with 75 subjects in each: group I – smokers with COPD; group II – smokers without COPD, and group III – COPD due to biomass exposure. Detailed history including smoking status and dyspnea by modified medical research council (MMRC) was recorded. Lung function and was assessed by spirometry as per ATS/ERS recommendation. Serum IL-13 levels were estimated by ELISA technique using kits from Diaclone (France) as per the manufacturer's instructions.

Results: Mean age was highest in group I (60.72 ± 10.04). Males predominated (93.33% & 94.67%) in groups I and II respectively, whereas group III entirely comprised of females. Groups I and II had almost equal smoking indices whereas group III had history of biomass exposure. Median dyspnoea grading was 2, 0 and 3 in groups I, II and III respectively. Smokers with COPD had significantly poorer lung function compared to biomass exposed COPD subjects (%pred FEV1 42.8 ± 20.42 vs 51.02 ± 20.26 p value = 0.02). Serum IL-13 was significantly elevated in biomass – related COPD compared to the other two groups [median (range) of serum IL-13 levels were 0 (0–208.11), 3.43 (0–278.24) and 5.1 (0.23–238.03) in the three groups respectively]. However, IL-13 showed no correlation with %pred FEV1 [Pearson's correlation coefficient (r) = 0.2635 (Group I), -0.0989 (group II) and -0.0061 (group III)].

Conclusion: COPD due to biomass exposure was associated with higher levels of circulating IL-13 compared to smoking related COPD and was independent of lung functions. This may have useful implications for anti-cytokine therapy for COPD in the future.

O-F-016

TNF- α RELATIONSHIP ON AIR FLOW RESISTANCE MECHANISM OF COPD

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Background: Chronic Obstructive Pulmonary Disease (COPD) is a disease that has the characteristic of airway limitation that is not fully reversible, progressive chronic inflammation caused due to exposure to toxic particles or gases occurring in a long time with the main symptoms of shortness of breath, cough, and sputum production. TNF- α is an inflammatory cytokine that can affect the working of macrophages, neutrophils, increased adhesion molecules on the endothelial wall, inducing growth factor, and affect fibroblast, where the higher levels of TNF- α , the greater inflammatory process that occurs, continuous and persistent will result in damage and worsening of airway obstruction in COPD and heavier air flow resistance. Examination of airway inflammatory cells using the method of sputum induction as a valid, non-invasive and can be used as a guideline to determine the airway inflammatory cells.

Methods: This is a cross-sectional observational analytic study using consecutive sampling design that was conducted at Dr. Soetomo Hospital, Surabaya. The total of 38 COPD patients which is not exacerbate.

Result: In this study obtained mean levels of TNF- α was 88.01 ± 40.12 pg/ml. The results in this study was not a significant association between TNF- α levels of sputum induction on air flow resistance mechanism of COPD or decrease in FEV1 % predicted ($r = 0.178$; $p > 0.05$). In this study also test the relationship Pearsons (parametric test) between levels of TNF- α induced sputum and pulmonary function (FEV1, FEV1 % predicted, FVC, FVC % predicted and FEV1/FVC) none showed statistically significant correlation with the levels of TNF- α induced sputum study subject, as well as data analysis by category of severity of mild, moderate, and severe, whether using the test and multivariate relationship, the results remained statistically not significant, although not statistically significant in all lung function parameters measured, continued to show a trend or tendency relationship is consistent with the theory, the levels of TNF- α has a negative trend with parameters of pulmonary function and has a positive trend towards the severity of COPD.

Conclusion: On this research there is no relationship between levels of TNF- α sputum induction with mechanism obstructive air flow COPD which is not exacerbations. Examination of TNF- α the sputum induction could not be used for see obstructive air flow in COPD

O-F-017

O-F-019

THE EFFICACY AND SAFETY OF INHALED UMECLIDINIUM BROMIDE/VILANTEROL IN ASIAN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim: The combination of the long-acting muscarinic antagonist umeclidinium (UMEC) with the long-acting β -agonist vilanterol (VI) is approved as maintenance treatment for chronic obstructive pulmonary disease (COPD) in the US and EU. We evaluated the efficacy and safety of two UMEC/VI doses in Northeast Asian patients with symptomatic moderate-to-severe COPD.

Methods: This was a 24-week, double-blind, placebo-controlled, parallel-group study. Patients were randomized 1:1:1 to UMEC/VI 62.5/25 (delivering 55/22 mcg), UMEC/VI 125/25 (delivering 113/22 mcg), or placebo (N = 580 [intent-to-treat]). Treatments were administered once daily (morning) via ELLIPTA™ dry powder inhaler. The primary endpoint was trough forced expiratory volume in one second (FEV1) at Week 24. Secondary endpoints were transition dyspnea index (TDI) focal score at Week 24 and weighted mean (WM) FEV1 over 0–6 hours post-dose at Day 1. Other endpoints included trough FEV1 and TDI focal score at other time-points, rescue medication use, and St George's Respiratory Questionnaire score. Safety measures included adverse events (AEs), vital signs, electrocardiograms (ECG), and clinical laboratory evaluations.

Results: Both UMEC/VI doses produced statistically significant and clinically-meaningful improvements vs placebo in trough FEV1 least squares (LS) mean change from baseline at Week 24 (UMEC/VI 62.5/25 = 0.151 L [95% confidence interval {CI}: 0.110–0.191], $p < 0.001$; UMEC/VI 125/25 = 0.216 L [95% CI: 0.175–0.257], $p < 0.001$). For TDI score, UMEC/VI 62.5/25 and UMEC/VI 125/25 produced statistically significant improvements vs placebo of 0.7 units (95% CI: 0.1–1.2, $p = 0.016$) and 0.9 units (95% CI: 0.3–1.4, $p = 0.002$), proximate to the minimal clinically important difference of 1 unit. Both UMEC/VI doses provided statistically significant improvements vs placebo in 0–6 hour WM FEV1 LS mean change from baseline at Day 1 (UMEC/VI 62.5/25 = 0.160 L [95% CI: 0.139–0.181], $p < 0.001$; UMEC/VI 125/25 = 0.182 L [95% CI: 0.161–0.203], $p < 0.001$). The overall incidence of on treatment AEs was consistent across treatments (placebo: 39%; UMEC/VI 62.5/25: 34%; UMEC/VI 125/25: 34%). The most common AEs were nasopharyngitis (9% in each group), upper respiratory tract infection (6–10%), COPD (2–5%), and cough (2–3%). No notable active-treatment-related changes in vital signs, ECGs, or clinical laboratory parameters were observed. Two deaths occurred during the study (UMEC/VI 62.5/25, $n = 1$ [drowning; not considered treatment-related]; UMEC/VI 125/25, $n = 1$ [acute respiratory failure, COPD, pneumonia, and septic shock; considered treatment-related]).

Conclusion: Both UMEC/VI 62.5/25 and UMEC/VI 125/25 improved lung function vs placebo. Safety and tolerability profiles were consistent across treatments.

O-F-018

CLINICAL SIGNIFICANCE OF INTERLEUKIN (IL)-33 IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Interleukin (IL)-33 is recently identified member of the IL-1 family and promote a variety of actions from a number of different cell types. However, little is known regarding the significance of IL-33 in patients with COPD.

Method: Plasma was obtained from stable COPD patients in Korean Obstructive Lung Disease (KOLD) cohort ($n = 354$). Plasma from patients with acute exacerbation was obtained in Seoul and Yeouido St Mary's Hospital ($n = 56$). IL-33 was measured by ELISA method.

Result: The level of IL-33 is significantly higher in patients with acute exacerbation compared with stable patients. In the analysis of stable patients, IL-33 level was significantly correlated with CT emphysema index, SGRQ, and exacerbation/year score. Significant negative correlation was noted between IL-33 level and BMI, FEV1 (%). In the multivariate analysis, IL-33 was a significant factors associated with acute exacerbation ($P < 0.05$).

Conclusion: There was significant difference in the level of IL-33 between stable and exacerbation COPD. There was significant correlation between the level of IL-33 and number of exacerbation. IL-33 was significant factor for affecting the number of exacerbation.

NUMBER OF PACK YEAR SMOKED DECREASES THE DISTANCE TRAVELLED IN 6MWT

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Smoking is the most important risk factor involved in pathogenesis of COPD. Quantification of the risk due to smoking has done in form of pack per year (1). We investigate effect of increase quantity of risk factor (pack years) on the exercise capacity [distance travelled in 6 minute walk test (6MWT)] in patients with COPD.

Methods: We evaluated 50 patients of COPD and classify them in 4 groups according to number of pack year smoked. Group-1 (0 pack years, the non-smokers), group-2 (1–10 pack years), group-3 (11–20 pack years), and group-4 (>20 pack years). We excluded group-1 from our study as some of non-smokers had other risk factors like exposure to biomass fuel etc, which were difficult to quantify. All the patients included in the study were asked to perform 6 minute walk test and distance travelled in 6 minutes was recorded. Obtained data was analysed statically.

Results: In our study we found that mean value of distance travelled in 6 minute for group-2 was 138.75 meters (with standard deviation of ± 22.45), for group-3 it was 106.81 meters (with standard deviation of ± 38.5) and in case of group-4 it was 85.64 (with standard deviation of ± 49.39). Number of pack per year has significant negative correlation with distance travelled in 6 minute walk test (f -value 4.164, p -value 0.025).

Conclusion: As the numbers of pack per year increases distance travelled in 6 minute walk test decreases.

Reference:

1 Cigarette Calculator – American Cancer Society www.cancer.org > Stay Healthy > Tools and Calculators > Calculators

O-F-020

THE DIAGNOSTIC VALUE OF MACAO PREDICTIVE VALUES IN CHRONIC OBSTRUCTIVE LUNG DISEASE OF ADVANCED AGE BY IMPULSE OSCILLOMETRY

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Objective: To investigate the clinical value of Macao predictive values by impulse oscillometry (IOS) in the chronic obstructive lung disease patients (COPD) of advanced age.

Methods: We measured lung impedance with IOS in the healthy advanced age ($n = 168$), and the patients with COPD of advanced age ($n = 281$) and related these parameters with spirometry and compared the parameters calculated by Macao predictive equations with Lechtenboerger equations.

Results: There was a significantly increase in respiratory impedance (Zrs), respiratory resistance at 5 Hz (R5), R5-R20, resonant frequency (Fres) in the COPD group compared to those in the healthy group. Reactance at 5 Hz (X5) in the COPD group was significantly lower than that in the healthy group. Zrs, R5, R5-R20 and Fres were negatively correlated with parameters (FEV1/FVC%, FEV1/Pre%) of spirometry, while X5 were positively correlated with them. Compared ROC areas under the curve, Zrs(A/P2), R5(A/P2) is each larger than Zrs(A/P1) and Zrs(A), R5(A/P1). X5(P2-A) is larger than X5(P1-A) in male group, is as same as in female group. In two groups, when Zrs (A/P2)% is larger than 130, R5(A/P2)% is larger than 130, X5(P2-A) is larger than 0.1, Fres is larger than 15 in male, 20 in female, their each Youden's index is the highest.

Conclusion: There are good correlations between spirometry and respiratory impedance measured by IOS in the diagnosis of COPD. Macao predictive equations have higher sensitivity and specificity for diagnosing COPD of advanced age.

O-F-021

HYDROGEN SULFIDE ATTENUATES AIRWAY INFLAMMATION IN RATS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Chronic airway inflammation is a characteristic feature of chronic obstructive pulmonary disease (COPD). Hydrogen sulfide (H₂S) can reduce the secretion of inflammatory cytokines. Recent studies have demonstrated that H₂S was associated with the development of COPD and its severity. However, the underlying mechanisms of H₂S in the pathogenesis of COPD have not been fully elucidated. In the present study, we studied the effects of H₂S on a rat model of COPD and explored the potential mechanisms. Forty male Wistar rats were randomly divided into four groups (10 rats for each group): control group, COPD group, COPD+NaHS group and COPD+PPG group. Rats were challenged with cigarette smoke exposure and lipopolysaccharide (LPS) to induce a rat model of COPD for eight weeks. Rats in the COPD+NaHS group or COPD+PPG group were injected intraperitoneally with a H₂S donor NaHS or a cystathionine-γ-lyase (CSE) inhibitor DL-propargylglycine (PPG), respectively. Pulmonary function, lung histopathology, the levels of H₂S, TNF-α and IL-8 in serum, the expression of CSE and phosphorylation of NF-κB p65 in lung tissue were measured. We found that rats in the COPD group had typical impaired pulmonary function and lung histopathology, reduced H₂S and elevated TNF-α, IL-8 in serum, decreased CSE expression and increased NF-κB p65 phosphorylation in lung tissue as compared with the control group. Treatment with NaHS prevented the development of COPD and reduced inflammatory markers TNF-α, IL-8 and NF-κB p65 phosphorylation as compared with the COPD group. Whereas inhibition of CSE activity by PPG exacerbated the development of COPD and enhanced inflammatory markers TNF-α, IL-8 and NF-κB p65 phosphorylation as compared with the COPD group. In conclusion, our findings indicated that H₂S could attenuate the development of COPD, which was possibly mediated by reducing inflammatory cytokines TNF-α, IL-8 via suppressing NF-κB signalling pathway.

O-F-023

RISK FACTORS FOR DISCONTINUATION OF ROFLUMILAST IN COPD PATIENTS

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Introduction: Roflumilast is PDE4 inhibitor, which can decrease exacerbation in patients with COPD. However, adverse effect is a major barrier to use medication. However, little is known regarding the risk factors for discontinuation of roflumilast in COPD patients.

Method: Patients who administered roflumilast in Seoul St Mary's Hospital during December 2012 and June 2014 were enrolled. During the study period, 157 patients administered roflumilast. Male constituted 93.0% of the study population, and mean age was 70.1 ± 9.9 (mean ± SD). Mean post bronchodilator FVC (%), FEV1 (%), and FEV1/FVC (%) were 77.2 ± 20.6, 46.4 ± 16.4, and 43.2 ± 13.8. Among them, 53 (33.8%) patients discontinued roflumilast because of adverse effect. In univariate analysis, never smoker was significantly higher in patients who discontinued roflumilast (15.4% vs 5.1%). BMI was significantly lower in patients who discontinued roflumilast (21.0 vs 22.7). In multivariate analysis, low BMI and never smoker were both significant factors for discontinuation of roflumilast. Odd ratio of BMI (1 unit decrease) was 1.14 (95% CI: 1.03–1.27, P = 0.011) and never smoker was 3.66 (1.09–12.29, P = 0.036).

Conclusion: Never smoker and low BMI were significant factors for discontinuation of roflumilast in patients with COPD.

ORAL PRESENTATION – CRITICAL CARE MEDICINE

O-G-001

DIFFERENCE IN OUTCOMES BETWEEN SENIOR PHYSICIAN AND MEDICINE RESIDENT LED CODE BLUES

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Introduction: Despite advances, survival after inpatient cardiac arrest remains poor, averaging 18%. The University of California, San Diego (UCSD) has developed a robust quality improvement-based training program that focuses on a simplified cardiopulmonary arrest (CPA) resuscitation algorithm and the use of advanced technology. Training is focused on the code blue nurse, respiratory therapist and senior medicine resident code leader. With the increased emphasis on duty hours and oversight, more code blues are led by fellows and attending physician. We hypothesize that medicine resident-run code blue outcomes are not inferior to those run by senior physicians.

Methods: A retrospective study of code blues at our academic hospital system was performed from July 2005 until June 2013. A comprehensive database of all inpatient resuscitative events is maintained at these institutions, including demographic, clinical, and outcomes data. Arrests are stratified by primary etiology of arrest using a priori criteria. All first in-patient cardiac arrests, defined as defibrillation and/or chest compressions, were included. Patients with an active "do not resuscitate" order were excluded. Medicine resident-led code blues were compared to all other code blues. Etiology of arrest (pulseless electrical activity/asystole or ventricular fibrillation/pulseless ventricular tachycardia), time of day, return of spontaneous circulation (ROSC), and outcome were all compared.

Results: A total of 631 inpatient CPA were included. While absolute number of CPA is increasing over time, the rate of CPA/1000 patient discharges is decreasing. With that, the proportion of code blues run by non-medicine residents is increasing. Two hundred fifty-four CPA resuscitations were run by medicine residents with an overall ROSC of 76.6% and 37.4 % survival to discharge. Of 377 inpatient CPA run by non-medicine residents, ROSC occurred 64.9% of the time and survival to discharge was 29.8%. Resuscitations led by medicine residents were more likely to occur at night.

Conclusion: Outcomes for medicine resident-led resuscitation of inpatient CPA are not inferior to those run by senior physicians. As more CPA resuscitations are led by senior physicians, focused training may continue to improve outcomes.

O-F-022

DIFFERENCES BETWEEN CAT AND MMRC IN KOREAN COPD PATIENTS

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Background: The GOLD consensus uses symptoms to categorize patients according to disease severity and guide treatment. COPD Assessment Test (CAT) and modified Medical Research Council (mMRC) are both used to evaluate the symptoms.

Purpose: To examine the discrepancy between CAT and mMRC in patients with COPD.

Methods: Patients were recruited from 50 centers in Korea, as part of the Korean COPD Study Group (KOCOSS) cohort.

Results: Total 882 patients with COPD were eligible for analysis. Age was 71.1 ± 7.8 (mean ± SD) and 90.8% were male. Post bronchodilator FVC, FEV1, and FEV1/FVC were 81.7 ± 17.6%, 55.7 ± 16.7%, and 49.0 ± 12.0%. Mean CAT, mMRC, and SGRQ-c score was 15.6 ± 7.8, 1.6 ± 1.0, and 35.0 ± 19.7. There was significant correlation between CAT and mMRC (R = 0.49, P < 0.01), SGRQ-c and mMRC (R = 0.57, P < 0.01), and CAT and SGRQ-c (R = 0.74, P < 0.01). However, mMRC was less than 2 in 53.3% of patients while CAT was less than 10 in only 23.3% of patients. By using ROC curve, CAT score 15 (Sensitivity: 0.70, Specificity: 0.66, AUC: 0.74 (0.71–0.77, 95% CI)) and SGRQ-c 31.3 (Sensitivity: 0.72, Specificity: 0.74, AUC: 0.79 (0.76–0.82, 95% CI)) were compatible with mMRC 2.

Conclusion: Although there was correlation between CAT and mMRC, discrepancy between two scores was noted. Further study regarding CAT and mMRC in patients with COPD is needed.

O-G-002

EVALUATION OF IMPACT OF PROTECTIVE OVER-SHOES ON FLOOR CONTAMINATION OF ICUS. IS THE PRACTICE A PARADIGM?

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The practice of using protective over-shoes before entering the intensive care units (ICU) is enforced in some ICUs with the assumption that it lowers the incidence of bacterial floor colonization. It is also assumed that it may lower the chances of infections caused due to failures in decontamination and aseptic techniques. The studies carried out in ICUs across the world have been contradictory.

Aim: To find the efficacy of protective over-shoes on bacterial floor colonization in ICU. This study carried out in the ICUs of Imam Khomeini hospital a tertiary care centre in Urmia, Iran. The study was divided into two phases of two weeks each, phase I with and phase II without use of protective over-shoes. Samples were taken at 4 different sites in ICUs. Floor samples were taken at 0700, 1300, and 1900 hours. The difference between the two phases (with & without over-shoes) was statistically not significant (p value > 0.05) for *Pseudomonas*, *Sataphilocooci*, *E coli*, and *Clebsilla* colonizations.

Conclusion: Over-shoes are not necessary in ICUs and has no significant impact on reduction in ICU floor contamination. Wearing over-shoes is only a paradigm. On the other hand wearing and putting off of over-shoes may cause contamination of hand and may increase infection rate.

O-G-004

ENDOTRACHEAL TUBE CUFF (ETT CUFF) PRESSURE OF PATIENTS ADMITTED AT THE INTENSIVE CARE UNITS (ICU) OF THE PHILIPPINE GENERAL HOSPITAL (THE PGH ETT CUFF STUDY)

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Introduction: In the Philippines, the incidence of hospital-acquired pneumonia, including ventilator-associated pneumonia (VAP), is 6 per 1000 admissions with mortality rate of 42.4%. Aside from antimicrobial therapy, modifiable risk factors for HAP are obvious targets for improved management and one of these include maintaining an optimal endotracheal cuff pressure. Studies show that 20 cmH₂O is the minimal ETT cuff pressure recommended to prevent aspiration and VAP. Inflation of endotracheal cuff pressures >30 cmH₂O is thought to contribute to mucosal ischemia and subsequent laryngeal injury.

Method: A descriptive observational study of 62 intubated patients admitted at the ICUs of PGH was done. The ETT cuff pressure is measured upon admission at the ICU to determine if it is within the recommended level (20–30 cmH₂O) for safety. Descriptive statistics and correlation analysis were performed.

Results: Only 16.1% (10 of 62) of measured cuff pressure were within the recommended level of 20 to 30 cmH₂O. More than half (56.5%; 35 of 62) fell below 20 cmH₂O while 27.4% (17 of 62) were above 30 cmH₂O.

Conclusion: Majority (56.5%) of ETT cuff pressures were underinflated (below 20 cmH₂O) while 27.4% were overinflated (above 30 cmH₂O). Only 16.1% (10 of 62) of measured cuff pressure were within the recommended level of 20 to 30 cmH₂O. The routine measurement and adjustment of ETT cuff pressure by a cuff manometer should be recommended. Patient safety should be prioritized.

O-G-005

INITIAL END-TIDAL CARBON DIOXIDE AS A PROGNOSTIC INDICATOR FOR INPATIENT PEA ARREST

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Introduction: During cardiopulmonary resuscitation (CPR), end tidal carbon dioxide (PetCO₂) is used to assess the quality of compressions, return of spontaneous circulation (ROSC), and the utility of continued resuscitative efforts. For out-of-hospital cardiac arrest, the first measured etCO₂ correlates with the etiology of arrest, as well as likelihood of ROSC and survival. Previous data from our institution documented a relationship between PetCO₂ and outcome for ventricular fibrillation arrest. This has not been explored for pulseless electrical activity (PEA) arrest in the inpatient setting.

Hypothesis: Initial PetCO₂ values of patients during inpatient PEA cardiopulmonary arrest predict ROSC and survival to discharge.

Methods: This study was performed in two urban, academic inpatient hospitals. Patients were enrolled from July 2009–July 2013. A comprehensive database of all inpatient resuscitative events is maintained at these institutions, including demographic, clinical, and outcomes data. Arrests are stratified by primary etiology of arrest using a priori criteria. Inpatients with PEA arrest for whom recorded PetCO₂ was available were included in the analysis. Capnography data obtained after ROSC and/or more than 10 minutes after initiation of CPR were excluded. Multivariable logistic regression was used to explore the association between initial PetCO₂ >20 mmHg and both ROSC and survival-to-discharge.

Results: A total of 50 patients with PEA arrest and pre-ROSC capnography were analysed. CPR continued an average of 11.8 minutes after initial PetCO₂ was recorded confirming absence of ROSC at time of measurement. Initial PetCO₂ was higher in patients with versus without eventual ROSC (25.3 ± 14.4 mmHg versus 13.4 ± 6.9 mmHg, $p = 0.003$). After adjusting for age, gender, and arrest location (ICU versus non-ICU), initial PetCO₂ >20 mmHg was associated with increased likelihood of ROSC (adjusted OR 4.8, 95% CI 1.2–19.2, $p = 0.028$). Initial PetCO₂ was not significantly associated with survival-to-discharge ($p = 0.251$).

Conclusions: Initial PetCO₂ >20 mmHg during CPR was associated with ROSC but not survival-to-discharge among inpatient PEA arrest victims. This analysis is limited by relatively small sample size.

O-G-003

EVALUATION OF THROMBOCYTOPENIA AND ITS TREND AS A MARKER OF MORTALITY IN MEDICAL INTENSIVE CARE UNIT PATIENTS

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Background and Objectives: Recent study shows thrombocytopenia (TP) is associated with poor outcome in patients with pneumonia, burn, and H1N1 influenza. To determine impact of cheap and easy available platelets count, its trend and TP on mortality among medical intensive care unit patients.

Methods: TP was defined as a platelet count of $<150,000/\text{mm}^3$. In this study, 300 patients who admitted to ICU because internal disease evaluated for platelets count on admission day CBC and following days CBC for presence of TP. Platelets count trend evaluated with repeated measurement test by SPSS.

Results: The prevalence of TP was as 131 (43.7%) totally 60% vs. 34% in died and survived patients respectively ($p < 0.001$ and risk ratio 3.07 CI 1.88–5.006). Mean platelets count on admission day and all four of following days CBC were lower in died patients than survived patients (p value < 0.001). Following days CBCs showed increase in trend of platelet count in survived and decrease in non-survived patients.

Conclusion: TP is a common in medical patients in ICU. TP by itself as well as its decreasing trend over time are predictor of mortality in ICU. It is a cheap and easy available marker for mortality in medical ICU patients.

O-G-006

OUTCOMES OF EARLY SEDATION VERSUS NO SEDATION AMONG MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS: A PROSPECTIVE COMPARATIVE STUDY

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Background: Mechanical ventilation is associated with significant patient pain and anxiety. Studies recommend that ventilated patients be given adequate comfort using sedation. The use of sedation among mechanically ventilated critically ill patients is not a common practice in our local setting. This study aims to ascertain if there are significant differences in outcomes of early sedation versus no sedation in mechanically ventilated patients.

Methods: This is a prospective longitudinal cohort comparative study of mechanically ventilated medical and surgical patients admitted at the ICU and ventilated for at least 24 hours. We recorded administration of sedative agents, use of restraints, time to extubation, failure of extubation, self-extubation, reintubation post-extubation, ICU and hospital length of stay and in-hospital mortality. Categorical variables were compared using a 2 × 2 Fischer Exact test while rates among the two groups were juxtaposed using Z test of difference in proportion.

Results: We enrolled a total of 56 patients (18 in the sedated group; 38 in the no sedation group). Restraints were used by 44.4% of the sedated patients and 26.3% of the no sedation group ($p = 0.225$). There was no significant difference as to ventilator days among the sedated vs no sedation group ($4.06 + 3.90$ vs $5.61 + 4.52$ days, $p = 0.217$), failure of extubation (16.7% vs 23.7%, $p = 0.732$), reintubation (33.3% vs 33.3%, $p = 0.764$), ICU length of stay ($6.28 + 3.847$ days vs $7.61 + 4.595$ days, $p = 0.293$), length of hospital stay ($19.7 + 12.56$ days vs $17.5 + 9.206$, $p = 0.463$) and mortality (6% vs 5%, $p = 1.000$). There is a trend towards higher self-extubation rate in the sedated group but it did not reach clinical significance (16.7% vs 5.3%, $p = 0.314$).

Conclusions: The use of early sedation in mechanically ventilated patients in this study did not show statistically significant difference when compared to no sedation group as to use of restraints, failure of extubation, self-extubation, reintubation, ICU and hospital length of stay and in-hospital mortality.

O-G-007

ACCURACY OF CAPILLARY VERSUS VENOUS BLOOD GLUCOSE ESTIMATION IN CRITICALLY ILL ADULT PATIENTS: AN OBSERVATIONAL STUDY

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Background: Strict glucose control to prevent both hyperglycaemia and hypoglycemia is believed to decrease morbidity and mortality in critically ill patients. Glucometers, though commonly used, have not been validated for the same purpose in intensive care units (ICU).

Objective: To determine the mean difference and correlation between capillary and central venous blood glucose estimation using glucometer in comparison to laboratory blood glucose value in critically ill adult patients.

Methods: This study included 53 patients aged >15 years admitted to ICU. Blood glucose estimation was done using glucometer (Accu-Chek Performa) from capillary and central venous access simultaneously, along with venous sampling for comparative laboratory analysis taken as gold standard. Data was analysed using SPSS version 16.

Results: Thirty two males (60.3%) and 21 females (39.7%) with a mean age 44.79 ± 17.01 were examined. Mean laboratory venous blood glucose (LVBG) and mean capillary glucometer value was 140.92 ± 52.59 mg/dl and 150.32 ± 59.89 mg/dl respectively (mean difference 9.4 mg/dl). Mean central venous glucometer reading was 140.58 ± 51.99 mg/dl (mean difference -0.34 mg/dl with respect to LVBG). The correlation coefficient for central venous measurement with laboratory value was higher (0.973) than that for capillary measurement (0.919). On comparing the influence of blood glucose measurement on insulin infusion protocol, 7 patients (13%) were found to be inappropriately titrated based on glucometer readings of which majority were from capillary blood ($n = 6$).

Conclusion: Central venous catheter samples were found to have the best correlation with laboratory glucose value. Though portable blood glucose measurement is a simpler way of measuring glycemic levels, a small but significant difference exists in the values of samples obtained from capillary or venous sources in critically ill patients. Hence, caution must be exercised in substitution of capillary glucometer reading for laboratory blood glucose results during insulin protocol titration, especially in haemodynamically unstable patients.

O-G-008

NUTRITIONAL STATUS OF CRITICALLY-ILL PATIENTS ADMITTED AT THE INTENSIVE CARE UNITS (ICUS) OF THE PHILIPPINE GENERAL HOSPITAL (PGH)

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Introduction: Critically ill patients admitted at the ICU present with a myriad of comorbidities, posing clinical difficulties in maintaining a normal nutritional status. The Subjective Global Assessment (SGA) is a tool that identifies malnutrition using instrument parameters such as weight history, diet history, primary diagnosis, stress level, and physical symptoms.

Method: A cross-sectional study of 93 adult critically-ill patients admitted at the ICUs of PGH was done using SGA to determine the prevalence and factors associated with malnutrition. Descriptive statistics, ANOVA, and logistic regression analysis were performed.

Results: The prevalence of malnutrition among critically-ill patients was 81.70%. Fifty-seven patients (61.3%) were assessed with SGA B, and nineteen (20.4%) with SGA C. Patients' mean age was 55.31 (SD + 16.43). Patients with severe malnutrition are significantly older than those who have normal nutritional status. The lowest recorded BMI is 16.07 kg/m² while the highest is 38.51 kg/m², with mean of 22.46 kg/m². Those who are severely malnourished have significantly lower mean weight and lower BMI. The prevalence of malnutrition for medical patients (80%) is not significantly different from the surgical patients (84%).

Conclusion: Majority (81.70%) of critically-ill patients admitted at the ICUs of PGH suffer from malnutrition, as classified by SGA. Significant predictors for malnutrition in this select group of patients are low BMI, low albumin level and severe disease. Identifying patients in whom nutritional therapy can alter outcome may help us assess the level of treatment required, to anticipate complications and to allocate scarce resources where it is most needed.

O-G-009

EFFICACY OF BI-LEVEL POSITIVE PRESSURE VENTILATION (BiPAP) OVER INVASIVE VENTILATION IN ACUTE EXACERBATION OF COPD WITH TYPE 2 RESPIRATORY FAILURE PATIENTS IN A CRITICAL CARE SETTING

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Objectives: To assess the efficacy Bi-level positive pressure ventilation (BiPAP) over mechanical ventilation for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) with type 2 respiratory failure patients in a critical care setting.

Methods: A prospective controlled trial was conducted in respiratory intensive care unit in National Institute of Diseases of Chest and Hospital (NIDCH) over 12 months. Total 217 AECOPD patients with $\text{pH} \leq 7.3$ and arterial partial pressure of carbon dioxide ($\text{PaCO}_2 \geq 60$ mm Hg) were recruited in this unit and treated with a standard medical treatment and BiPAP (group A, $n = 153$). Those who failed to respond to or unfit for non-invasive ventilation were treated with invasive mechanical ventilation along with standard medical treatment (group B, $n = 64$).

Results: The age (48 ± 12 vs 52 ± 19 yrs) and sex distribution in both groups were similar. Baseline pH was 7.31 ± 0.4 in group A and 7.29 ± 0.45 in group B which was insignificant statistically ($P = 0.023$). PCO_2 was 72 ± 9 mm of Hg in group A and 79 ± 13 mm of Hg in group B ($P = 0.017$). After 48 hours, the differences of pH , arterial partial pressure of oxygen (PaO_2) and partial pressure of carbon-dioxide (PCO_2) in group A (7.37 ± 0.05 , 92 ± 34 mm Hg, 52 ± 14 mm of Hg) were statistically insignificant ($P > 0.1$) compared with group B (7.39 ± 0.06 , 89 ± 22 mm Hg, 56 ± 16 mm of Hg). But nosocomial infections in both groups were significantly different (12 ± 8 vs 45 ± 16 ; $P < 0.001$). There were significant differences in mortality (28.8% vs 68% ; $P < 0.001$) and total hospital stay in both groups (8 ± 5 vs 17 ± 9 days; $P < 0.001$).

Conclusion: This study revealed that bi-level positive pressure ventilation (BiPAP) in our respiratory ICU was similarly effective in reduction of arterial gas alterations compared to invasive ventilation. But mortality rate and hospital stay was significantly low in BiPAP users.

ORAL PRESENTATION – ENVIRONMENTAL & OCCUPATIONAL HEALTH AND EPIDEMIOLOGY

O-H-001

ADVERSE RESPIRATORY HEALTH EFFECTS OF TEAR GAS

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Background: Tear gas is a term for the family of chemical compounds that can cause temporary disablement, most common agents is ortho-chlorobenzylidene malonitrile (CS). The most notorious effect as pulmonary edema has been well recognized. Respiratory system toxicity of CS included chronic cough and shortness of breath. During the 2013–2014 political turmoil in Bangkok, inadvertent use of tear gas was established.

Methods: A mobile station for interviewing and performing physical examination for the tear gas victims was set up as part of Medical Service Unit, near by the Democracy Monument, Rajdamnern Avenue, Bangkok. Spirometry and methacholine challenge testing were also performed in those without contraindications after informed consent.

Results: There were 37 victims; none had pre-existing respiratory disease, 4 had history of atopy, and 18 were active smokers. The mean exposure time was 7.7 hours. Two cases of chemical pneumonitis was demonstrated later by chest CT-scan. All of them had persistent cough, 34 had sputum production, 20 experienced shortness of breath, and 13 experienced wheezy. Nasopharyngeal inflammation could be observed in 29, and hand dermatitis in 1 victim. Abnormal spirometry was encountered in 8 patients, in whom 3 were smoker and 1 had history of atopy. Three victims had obstructive ventilatory defect, in which 1 also had airway hyperresponsiveness, and 5 had small airway obstruction.

Conclusion: Acute and late notorious respiratory health effects of tear gas were imminent. It is the responsibility of the medical community to collect objective evidence of tear gas toxicity among the victims, and handle to those in charge of public safety.

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O-H-002

EFFECT OF INCOMPLETE SMOKING CESSATION WITH VARENICLINE OR NICOTINE PATCH ON VASCULAR ENDOTHELIAL FUNCTION AS ASSESSED BY FLOW-MEDIATED VASODILATION

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Background: Although nicotine patch is effective in smoking cessation, it is contraindicated for patients with active ischemic heart diseases. Varenicline is a partial agonist of nicotinic acetylcholine receptors that is also effective in smoking cessation, but the risk of adverse cardiovascular events has been raised in some studies. However, the statistical significance of this risk is inconsistent across the studies. We have previously shown that vascular endothelial function, as assessed by flow-mediated vasodilation (FMD), improves after 3 months following complete smoking cessation using varenicline (BMJ Open, 2013). Here we report on the FMD data of nicotine-dependent outpatients with incomplete smoking cessation, despite the use of varenicline or nicotine patch.

Methods: Participants were evaluated by FMD prior to and between 2 to 4 months after the start of varenicline ($n = 6$) or nicotine patch ($n = 1$) therapy. Varenicline was titrated up to 1.0 mg twice daily for 12 weeks in total. Nicotine patch was tapered from 52.5 mg/day for 4 weeks to 35 mg/day for 2 weeks to 17.5 mg/day for 2 weeks, and then discontinued.

Results: FMD was significantly decreased from $5.4 \pm 3.1\%$ to $3.5 \pm 1.9\%$ ($p < 0.05$, $n = 7$) in participants who did not achieve complete smoking cessation (mean age, 57.4; M/F = 4/3). Although all of these participants did not achieve complete cessation, they did decrease their average number of cigarettes. The time-course of FMD after the initial approximate 3 months also showed a further decrease in most cases up until 1 year.

Conclusion: We observed a worsening of FMD data in participants who failed to achieve complete smoking cessation with varenicline or nicotine patch therapy. Smokers who wish to quit smoking with these therapies should achieve complete smoking cessation in order to improve vascular endothelial function.

O-H-003

NEWLY ESTABLISHED ELISA FOR N-ERC/MESOTHELIN IMPROVES DIAGNOSTIC ACCURACY IN PATIENTS WITH SUSPECTED PLEURAL MESOTHELIOMA

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Pleural mesothelioma is an aggressive tumour, commonly caused by exposure to asbestos. The prognosis of mesothelioma remains disappointing despite multimodal treatment. We previously reported that N-ERC/mesothelin could be a useful biomarker for the early diagnosis of pleural mesothelioma and developed an ELISA system for its detection. However, the reproducibility of our previous 7–16 ELISA system has been revealed to be unsatisfactory. To measure N-ERC/mesothelin more precisely, we developed a new 7–20 ELISA system. The subjects of this study were patients who were referred to our department with suspected pleural mesothelioma. The current study demonstrated that the newly established 7–20 ELISA system improved the sensitivity and specificity for diagnosing pleural mesothelioma compared with the previous system. Moreover, the 7–20 ELISA system showed better reproducibility and displayed the tendency of both higher sensitivity and higher specificity in plasma than in serum. Particularly for the epithelioid type, the area under the curve and the diagnostic accuracy of N-ERC/mesothelin were excellent; the area under the curve was 0.91, the sensitivity was 0.95, and the specificity was 0.76 in plasma. In conclusion, assessment of N-ERC/mesothelin with our newly established 7–20 ELISA system is clinically useful for the precise diagnosis of pleural mesothelioma.

O-H-004

WELDERS' SIDEROSIS: A RETROSPECTIVE COHORT STUDY ON WELDER'S PNEUMOCONIOSIS PATIENTS WITH SMALL ROUND OPACITIES ON CHEST RADIOGRAPH

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Objective: To study the radiographical changes and prognosis of welders' pneumoconiosis patients diagnosed within the last few years.

Methods: Occupational hygienics data (including years on welding work, welding materials exposed to and work environment), symptoms, lung function test results and follow-up data of 136 welders' pneumoconiosis patients were collected retrospectively. The follow-up lasted up till June 30, 2014, with follow-up interval being 1 year. Chest radiographs were read/reviewed together by 3 senior experts experienced in pneumoconiosis diagnosing and morphology/pattern, overall density, distributed lung areas of small opacities and pneumoconiosis stages were all logged.

Results: Of all 136 pneumoconiosis cases, five were of Stage II and 131 were Stage I, and they had been engaged in welding work for 9.2 ± 6.34 years. All patients were present with slight symptoms including coughing, chest distress and dyspnea, while their lung function remained normal. Small round opacities were found on chest radiographs of 88.9% of the 136 cases. Many years of follow-up on 131 cases of Stage I welder's pneumoconiosis showed that irregular small opacities remained fundamentally unchanged, while small round opacities tended to gradually lessen instead of clustering. Two years after primary diagnosing, the total affected lung zones of follow-up objects were noticed to start lessening, and reduced by 0.02 per patient among the 48 follow-up subjects. Of the 48 cases followed up up to six years after primary diagnosing, the affected lung zone number was reduced by 0.54 per patient while 4 cases (8%) went down to below Stage I. As of the 36 patients followed up 10 years after after primary diagnosis, the number of affected lung areas decreased by 1.14, and 22% (8 cases) appeared less than stage I on chest radiograph.

Conclusion: It seemed that the so-called Welders' pneumoconiosis featuring small round opacities tended to get alleviated/improved/lightened up over time, which suggested the possibility/diagnosis of siderosis.

O-H-005

INDOOR PM2.5 AND CO LEVELS WHILE BURNING MOSQUITO COILS AND ITS ASSOCIATED RESPIRATORY MORBIDITY

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Introduction: An estimated 29 billion mosquito coils (MCs) are used by 2 billion people worldwide every year. Laboratory-based studies have shown that MCs produce high levels of air pollutants including PM2.5 and CO. We aimed to (a) study the indoor levels of PM2.5 and CO inside a room while burning 3 brands of MCs with window-closed-door-closed (WCDC), window-open-door-closed (WODC), window-open-door-open(WODO), (b) study the prevalence of respiratory symptoms and allergic respiratory diseases in houses using MCs and liquid mosquito repellents (LMRs) in a rural community in India.

Methods: Each brand of MC was burnt 3 times, on 3 separate days in a room ($2.9 \times 5.8 \times 2.4$ m) [1 window (1.4×1.3 m) & 1 door (2.2×0.8 m)]. PM2.5 levels (mcg/m3) were measured online with Thermo PDR 1200 and CO (ppm) with Easylog USB sampler. 465 male & female subjects above the age of 18 years from 145 randomly selected homes were administered a questionnaire to capture demographic details and respiratory symptoms/illnesses.

Results: Mean PM2.5 and CO levels are shown in Table 1 with WCDC, WODC and WODO. 165 individuals used MC only, 214 used LMR only, 85 used MC + LMR. While burning MCs, 65% kept their WCDC. The prevalence rates (%) of diseases and symptoms between MCs and LMRs were: Asthma 3.6 vs 2.3, allergic rhinitis 9.7*vs 4.2, allergic conjunctivitis 9.0 vs 6.5, itchy nose 7.9 vs 5.1, itchy eyes 15.2 vs 13.1, runny nose 33.9 vs 28.9, blocked nose 17.7 vs 15.1, throat pain 15.1 vs 28.5* respectively.

Conclusion: Burning of MCs produced high indoor PM2.5 and CO levels which were markedly altered by keeping the window &/or door open. Use of MCs was associated with greater respiratory morbidity than LMRs.

	Mean PM2.5 ± SD (mcg/m3)			Mean CO ± SD (ppm)		
	WCDC	WODC	WODO	WCDC	WODC	WODO
Brand1 (n = 3)	1.031 ± 0.58	0.510 ± 0.511	0.084 ± 0.035	5.215 ± 3.20	1.214 ± 2.38	0.000 ± 0.00
Brand2 (n = 3)	0.848 ± 0.623	0.467 ± 0.514	0.061 ± 0.031	4.668 ± 2.94	1.478 ± 2.41	0.008 ± 0.09
Brand3 (n = 3)	0.355 ± 0.179	0.170 ± 0.142	0.062 ± 0.010	6.558 ± 3.775	1.968 ± 2.58	0.000 ± 0.00

O-I-002

ORAL PRESENTATION – INTERSTITIAL LUNG DISEASE

O-I-001

EFFICACY AND SAFETY OF NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS: RESULTS OF TWO 52-WEEK, PHASE III, RANDOMIZED, PLACEBO-CONTROLLED TRIALS (INPULSIS™)

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ON BEHALF OF THE INPULSIS™ TRIAL INVESTIGATORS

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Background: Nintedanib (formerly known as BIBF 1120) is an intracellular inhibitor that targets multiple tyrosine kinases. A phase 2 trial suggested that treatment with 150 mg of nintedanib twice daily reduced lung-function decline and acute exacerbations in patients with idiopathic pulmonary fibrosis.

Methods: We conducted two replicate 52-week, randomized, double-blind, phase 3 trials (INPULSIS-1 [NCT01335464] and INPULSIS-2 [NCT01335477]) to evaluate the efficacy and safety of 150 mg of nintedanib twice daily as compared with placebo in patients with idiopathic pulmonary fibrosis. The primary end point was the annual rate of decline in forced vital capacity (FVC). Key secondary end points were the time to the first acute exacerbation and the change from baseline in the total score on the St George's Respiratory Questionnaire, both assessed over a 52-week period.

Results: A total of 1066 patients were randomly assigned in a 3:2 ratio to receive nintedanib or placebo. The adjusted annual rate of change in FVC was –114.7 ml with nintedanib versus –239.9 ml with placebo (difference, 125.3 ml; 95% confidence interval [CI], 77.7 to 172.8; $P < 0.001$) in INPULSIS-1 and –113.6 ml with nintedanib versus –207.3 ml with placebo (difference, 93.7 ml; 95% CI, 44.8 to 142.7; $P < 0.001$) in INPULSIS-2. In INPULSIS-1, there was no significant difference between the nintedanib and placebo groups in the time to the first acute exacerbation (hazard ratio with nintedanib, 1.15; 95% CI, 0.54 to 2.42; $P = 0.67$); in INPULSIS-2, there was a significant benefit with nintedanib versus placebo (hazard ratio, 0.38; 95% CI, 0.19 to 0.77; $P = 0.005$). The most frequent adverse event in the nintedanib groups was diarrhoea, with rates of 61.5% and 18.6% in the nintedanib and placebo groups, respectively, in INPULSIS-1 and 63.2% and 18.3% in the two groups, respectively, in INPULSIS-2.

Conclusions: In patients with idiopathic pulmonary fibrosis, nintedanib reduced the decline in FVC, which is consistent with a slowing of disease progression; nintedanib was frequently associated with diarrhoea, which led to discontinuation of the study medication in less than 5% of patients. These data have been published (Richeldi et al. *N Engl J Med* May 2014;370[22]:2071–82).

CLINICAL CHARACTERISTICS OF SECONDARY PULMONARY ALVEOLAR PROTEINOSIS (SPAP): THE REASON FOR THE DIFFICULTY OF DIAGNOSIS AS SPAP (JSPS KAKENHI GRANT NUMBER 26305028)

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Background: We have studied the epidemiological research for secondary pulmonary alveolar proteinosis (sPAP) in Japan. As sPAP is a very rare lung disease compared with interstitial pneumonia, the review article of sPAP have few reports except for our reports (*Chest* 2009, *ERJ* 2011, *BMC pulmonary medicine* 2014) until now.

Purpose: The aim of this study is to define the clinical characteristics of sPAP because we have accumulated more clinical data of sPAP cases in Japan.

Methods: We researched the clinical data in sPAP cases diagnosed by the pathological findings and negative data of anti GM-CSF autoantibody. This is a retrospective cohort study approved by the Ethical Board of Kyorin University (H23-085-01). This work was supported by JSPS KAKENHI Grant Number 26305028.

Results: From 1999 to July 2014, we were able to accumulate the clinical data in 58 cases of sPAP in Japan. They had various underlying disorders (haematological disease: $n = 51$, autoimmune disease: $n = 5$, infectious disease: $n = 2$). The most common underlying disease was myelodysplastic syndrome ($n = 37$) and 5 cases (14%) of them complicated with Behcet's disease. Age at diagnosis of sPAP were wide range (24–77) and 48 cases (83%) had any symptoms. Also 20 cases had fever with respiratory symptoms. 2 years survival rate after diagnosis of sPAP were less than 50%.

Conclusion: sPAP is a very rare lung disease and it has poor prognosis. It is difficult to early diagnose as sPAP because they had various underlying and clinical symptoms. Therefore, we should to consider the complication of sPAP in patients with diffuse lung opacity, especially in hematological disorders.

O-I-003

LONG TERM FOLLOW-UP OF SERUM AUTOANTIBODY AGAINST GM-CSF LEVELS IN PATIENTS WITH AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Autoimmune pulmonary alveolar proteinosis (APAP) is a rare lung disease characterized by dysfunction of alveolar macrophages and neutrophils by neutralizing anti-granulocyte/macrophage colony-stimulating factor (GM-CSF) autoantibody. Measurement of the autoantibody in serum is considered to be useful for the diagnosis APAP. However, the level has been considered not to correlate with disease severity of APAP, which was determined by PaO₂ and symptoms (Inoue Y et al. *AJRCCM*, 2008), and long term changes of the serum levels have not well understood. To clarify the changes of the antibody and clinical courses, we measured the serum levels from patients with APAP who were followed more than 5 years in our hospital.

Subjects and Method: We enrolled 29 patients with APAP {11 female and 18 male, age 53 (25–78) years old}. We measured serum levels of autoantibody against GM-CSF by ELISA method at registration and 5 years later. We compared the data with the clinical data.

Results: The level of autoantibody against GM-CSF gradually and significantly decreased in 5 years ($p < 0.05$), although some patients increased. Some patients dramatically improved physiological and radiological findings in addition to serum GM-CSF level. However, %FVC, %DLco, or serum KL-6 did not significantly changed in total. 70% patients were treated with GM-CSF inhalation and/or whole lung lavage. All patients with autoantibody level more than 50 µg/mL had treatments.

Discussions and Conclusion: Serum levels of autoantibody, which did not cross-sectionally correlated with the disease severity as previously reported, gradually decreased year by year. To clarify the induction or maintenance of serum antibody levels, further studies will be required.

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O-I-005

A PRE-CLINICAL STUDY FOR DEVELOPMENT OF A NEW GM-CSF INHALATION DRUG AS A TREATMENT OF PULMONARY ALVEOLAR PROTEINOSIS

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Backgrounds: Studies in granulocyte/macrophage-colony stimulating factor (GM-CSF) knockout mice and series of patients with pulmonary alveolar proteinosis (PAP) showed that inhaled GM-CSF is promising as therapy for PAP. Our recent, multicenter study demonstrated that inhaled GM-CSF therapy of PAP is safe, efficacious, and provides a durable treatment effect in many patients. However, an investigator initiated clinical trial will be required for development of GM-CSF inhalation drug, because PAP is a very rare disease, discouraging pharmaceutical companies from conducting trials. The government authorities require a chronic toxicity study using animal models of inhalation as preclinical test data. Recombinant human GM-CSF (rhGM-CSF) demonstrates no physiological effect in mice or other rodents. We hypothesized that bioactivity of rhGM-CSF administered transtracheally can be detected in nonhuman primates, and planned an animal model of GM-CSF inhalation.

Methods: Nonhuman primates (*Macaca fascicularis*) were administered with 0.5 mg/body of rhGM-CSF derived from *E. coli*, yeast, CHO cells or saline for consecutive three days using a catheter sprayer (MicroSprayer, PennCentury), and evaluated by counts of blood cells, blood biochemistry, and analyses of bronchoalveolar lavage fluids (BALF) obtained through a slim bronchofiberscope (BF type XP60, Olympus).

Results: No abnormal symptom was observed in animals during the study. GM-CSF administered in trachea with microspray increased transiently (1) total cell counts in BALF; (2) white blood cells, especially neutrophils, monocytes, and eosinophils, in peripheral blood; and (3) serum C-reactive protein. Increased myeloid/erythroid ratio was observed in bone marrow of animals administered with GM-CSF. Surprisingly, GM-CSF was detected in serum by ELISA after trans tracheal administration of rhGM-CSF

Conclusions: This is the first report of detecting GM-CSF in serum after the trans tracheal administration of rhGM-CSF in an animal model of *Macaca fascicularis*. These results suggest that blood tests and analyses of BALF might be able to evaluate pharmacokinetics and bioactivities of administered rhGM-CSF by intratracheal spraying in primates.

O-I-006

TRANSBRONCHIAL LUNG BIOPSY FOR THE DIAGNOSIS OF LYMPHANGIOLEIOMYOMATOSIS

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Introduction: Lymphangioleiomyomatosis (LAM) is a rare cystic lung disease which occurs in fertile woman. LAM can be diagnosed by typical HRCT findings and clinical findings (angiomyolipoma, chylothorax, serum VEGF-D, and so on); however, pathological diagnosis is most important for definite diagnosis. In Japan, our previous study revealed 83% (surgical lung biopsy 65.3%, transbronchial lung biopsy (TBLB) 10.4%, autopsy 5.8%, and unknown 1.7%) of the LAM patients have been diagnosed based on the pathological findings (*Respirology* 2007; 12: 523).

Subject and Method: Until 2013, total 108 patients with LAM have been registered in National Hospital Organization Kinki-Chuo Chest Medical Center. TBLB was performed in 19 cases of them (17.6%) in our facility, and all of them were finally diagnosed as sporadic LAM. We analysed the sensitivity of diagnosis and safety of TBLB, comparing clinical status. The pathological specimens were examined by pathologists in our facility using haematoxylin and eosin stain, and immunohistochemical stain.

Results: All cases were women, median age was 43 (IQR 38.5–47.5), 14 non-smokers, 3 ex-smokers, and 2 smokers. The median percent-predicted FEV1, DLCO, and RV were 71.8 (IQR 62.8–98.3), 52.8 (IQR 40.25–68.35), and 170.2 (IQR 127.9–181.7), respectively. Median PaO2 on room air was 88.0 (IQR 78.45–93.95) Torr, and median Modified Medical Research Council dyspnea scale was 2 (IQR 0.5–2). All their HRCT scan images showed multiple thin regular wall cysts scattered throughout the lungs (100% positive), and 5 patients had histories of pneumothoraxes before TBLB. Median serum VEGF-D was 2068 (IQR 1489.5–2916.5) pg/ml and 17 of them were over 800 pg/ml (89.5% positive) (diagnostic, *Chest* 2010; 138: 674). Characteristic pathological findings of LAM, multifocal nodular proliferation of immature smooth muscle cells, so-called LAM cells were seen in 14 cases (73.7% positive) which was better sensitivity reported as 60% before (*Front Med* 2012; 6: 395). No remarkable complication including pneumothorax or bleeding was seen after TBLB.

Conclusion: We confirmed that TBLB is an effective and safe method to obtain enough specimens for pathological diagnosis of LAM.

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O-I-007

SUBGROUP ANALYSIS OF ASIAN PATIENTS IN THE INPULSIS™ TRIALS OF NINTEDANIB IN IDIOPATHIC PULMONARY FIBROSIS

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Background: The INPULSIS™ trials were two replicate, 52-week, randomized, double-blind, placebo-controlled, international Phase III trials that investigated the efficacy and safety of nintedanib 150 mg twice daily in patients with IPF. The primary endpoint was the annual rate of decline in forced vital capacity (FVC; mL/year). Key secondary endpoints were time to first acute exacerbation and change from baseline in St George's Respiratory Questionnaire (SGRQ) total score, both assessed over 52 weeks. This subgroup analysis of the INPULSIS™ results investigated the effect of nintedanib in patients from Asia.

Methods: A pre-specified subgroup analysis of Asian patients was undertaken for the primary and key secondary endpoints using pooled data from both trials. The frequency and severity of adverse events (AEs) in Asian patients were documented.

Results: Of the 1066 patients who participated in the INPULSIS™ trials, 322 were Asian (n = 194 in the nintedanib group and n = 128 in the placebo group). In the Asian subgroup, mean age was 66.0 years, 80.4% were male, and mean FVC % predicted was 81.2%. Baseline characteristics were comparable between the nintedanib and placebo groups. The adjusted annual rate of decline in FVC was -124.0 mL/year in the nintedanib group and -218.1 mL/year in the placebo group (a difference of 94.1 mL/year [95% CI: 33.7, 154.6]). The proportion of patients with ≥1 acute exacerbation was 4.6% in the nintedanib group and 7.0% in the placebo group (HR 0.66 [95% CI: 0.26, 1.68]). Mean change from baseline in SGRQ total score was 2.25 in the nintedanib group and 4.16 in the placebo group (a difference of -1.91 [95% CI: -5.19, 1.37]), with smaller increases indicating less deterioration in health-related quality of life. The most frequently reported AE in the nintedanib group was diarrhoea, reported in 56.2% of patients in the nintedanib group and 15.6% in the placebo group. Of patients who experienced diarrhoea, 4 (3.7%) patients receiving nintedanib and none of the patients receiving placebo prematurely discontinued treatment due to a diarrhoea event. The proportion of patients with serious AEs was similar in the nintedanib and placebo groups (33.5% versus 28.9%, respectively).

Conclusion: Results from a pre-specified subgroup analysis of Asian patients with IPF participating in the INPULSIS™ trials were in line with results from the overall patient population, demonstrating a consistent effect of nintedanib on slowing disease progression and a manageable side-effect profile.

O-I-008

CYTOKINE PROFILE OF LUNG TISSUES AND SERUM IN PATIENTS WITH INTERSTITIAL LUNG DISEASES

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Pulmonary fibrosis (PF), especially IPF (Idiopathic pulmonary fibrosis), is progressive disease, and yet there is no effective treatment. Modulation of cytokine expression represents a potentially useful approach for the treatment of PF/IPF. To identify potential targets for such intervention, Real-time RT-PCR was used to compare the expression of messenger ribonucleic acids (mRNAs) coding for 21 cytokines in lung tissue obtained from patients with PF and control subjects. Some cytokines were also studied at the protein level in serum with luminex workstation. RNAs coding for all of the cytokines evaluated were detected in most lung samples. Indeed, when the amounts of cytokine mRNA were compared, mRNAs coding for TGF-β1, TGF-β3, IL-13Rα1, IL-13Rα2, IL-4Rα, MCP-4, MDC and CCL18 were significantly more abundant in lung biopsies from patients with PF compared with those of controls (P < 0.05–0.01). Furthermore, expression of TGF-β1, TGF-β2, TGF-β3, IL-4Rα, IL-13Rα1, IL-13Rα2, TGFα, EMMPRIN, MMP2, TARC, MCP-4, MDC, CCL24, MMP12, CCL18 mRNAs were shown more than 1.5 fold higher in lungs from IPF subjects than those in the control tissues, however, statistical analysis indicated only expression of TGF-β1 mRNA displayed significant difference between IPF and the control group (P < 0.05). When compared with the controls, serum from pulmonary fibrosis patients contained significantly higher levels of MCP-1, TGFβ1 (P < 0.05 or <0.01). Conversely, no significant differences were found in the expression of Eotaxin, IL-13, IL-4, TGFα, MMP2, MMP9, MMP12, TGFβ2 and TGFβ3 between the two groups. There were higher expressions of IL-4, IL-13, TGFβ1, TGFβ3 and MCP-1 in the serum from the 3 IPF patients than these in the controls. And the levels of IL-4, TGFβ1 and MCP-1 showed statistical difference between the two groups (P < 0.05 or 0.01). These results suggest the signal transduction pathway of IL-4/IL-13 is potential therapeutic target and cytokines, TGF-β1, TGF-β3, MCP-4, MDC, CCL18 and MCP-1, may be implicated in the pathogenesis and progression of PF/IPF, therefore, may also be attractive targets in therapeutic intervention.

O-I-009

PREDICTIVE FACTORS FOR THE EFFECT OF PIRFENIDONE IN IDIOPATHIC PULMONARY FIBROSIS

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Backgrounds: Pirfenidone (PFD) is one of anti-fibrotic drugs used for the treatment of idiopathic pulmonary fibrosis: IPF. PFD has been approved in some Asian and European countries recently, but usage experience in practical clinics is still limited. The purpose of this study was to clarify the difference of the baseline parameters in each PFD response group and the clinical and diagnostic change between pre- and post-PFD therapy.

Methods: We retrospectively analysed general information and clinical characteristics of twenty IPF cases, treated with PFD from April 2009 to March 2014 in one university hospital in Japan. Deterioration of respiratory status was defined as 10% or greater decline in percentage predicted value of FVC (%FVC) after 6-month treatment. We categorized three PFD treatment response groups as following: worse group (WG); <= -10%, inhibition group (IG); -10%–0%, better group (BG); 0%. We used Sumikawa score (AJRCCM 177 433, 2008) to evaluate the CT findings.

Results: PFD improved %FVC in seven patients (BG: 35%) and stabilized %FVC in eight patients (IG: 40%) of total 20 cases. Autoimmune antibodies were more detected in IG and BG. WG had more ground-glass attenuation: GGA (p < 0.01), more airspace consolidation (p = 0.045), more reticular opacity (p = 0.05) and less fibrosis score (p = 0.03) than IG and BG in CT findings. After 6-month PFD administration, KL-6 and LDH were reduced in each group (p = 0.03 and 0.05). PFD therapy improved GGA (p = 0.001) and consolidation (p = 0.02) in BG. In contrast, WG had more airspace consolidation and honeycombing after PFD therapy.

Conclusions: Among baseline CT parameters, GGA, airspace consolidation, reticular opacity and fibrosis score were different in the groups categorized by PFD response. The laboratory and diagnostic change were detected after PFD therapy.

O-I-010

EXPERIMENTAL STUDY OF HYPERSENSITIVITY PNEUMONITIS IN GUINEA PIG INDUCED BY INHALATION OF HAIR DYE INGREDIENTS

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Background: Hypersensitivity pneumonitis (HP) is a pulmonary disease with symptoms of dyspnea and cough resulting from the inhalation of an antigen to which the subject has been previously sensitized. Case has reported that some HP patients were due to hair dye, which is lack of relevant experimental basis. In this study we explored if inhalation of hair dye ingredients can induced HP in guinea pigs.

Methods: 45 Hartley guinea pigs weighed (300 ± 50) g were randomly divided into 9 group according to duration and solvents of inhalation. The experimental groups were group A (1/2), group B (1/2), group C (1/2) and group D (1/2), respectively inhaling colouring agent, colour-developing agent, emulsion and mixture agent. Group 1 and group 2 stood for intermittent inhalation group and long-term inhalation group. Group E was the normal control group. Each group tested pulmonary function at 4 time points. Bronchoalveolar lavage fluid (BALF) was obtained from the left lung of guinea pigs, and the right lung was made into histological specimen after 3 weeks. The concentrations of IFN- γ , IL-4 and IL-12 in isolated BALF were measured by enzyme-linked immunosorbent assay.

Results: Guinea pigs in group A1 and D1 had hair loss and weight loss. Compared with group E, the percentage of lymphocytes in BALF of group D1 was significantly increase. In terms of histopathology, the lung tissue in group A1 was filled with inflammatory cells in the alveoli, alveolar structure slightly disordered, in group D1 was significant thickening of the alveolar septa, infiltrated with inflammatory cells and fibrosis in some area, group A2 had alveolar structural disorder, group D2 had alveolar septa slightly thickened. Also the concentration of IFN- γ in group D1, the concentration of IL-4 and ratio of IL-4/IL-12 in group D2 was higher than group E.

Conclusions: The effect of coloring agent and emulsion on alveolar injury was not obvious. The mixture agent, containing coloring agent and color-developing agent, can induce HP in guinea pig with typical pathology.

O-I-011

CASE ANALYSIS OF INTERSTITIAL LUNG DISEASES INDUCED BY BREAST CANCER CHEMOTHERAPY

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Backgrounds: The incidence of and number of deaths due to breast cancer are rising in Japan, commonly affecting women of childbearing and working age. Drug-induced interstitial lung disease due to chemotherapeutic agents against breast cancer is becoming less of a rare encounter for pulmonary physicians; however, little is known about its frequency, clinical characteristics, and treatment outcomes.

Methods: We reviewed our medical records from August 2003 to June 2014 and identified all breast cancer patients who developed interstitial lung disease after exposure to breast cancer chemotherapy and met the diagnostic criteria for drug-induced lung disease set by the Japanese Respiratory Society.

Results: Twenty-four patients were identified. All were women, with mean age of 56 years (range: 37 to 78). Fourteen (58%) were never smokers. The mean time duration from exposure to onset of disease was 62 days (range 20 to 110) and typical symptoms included fever, non-productive cough, and shortness of breath. The mean lactate dehydrogenase and Krebs von den Lungen-6 levels at the time of diagnosis were 310 U/L (range: 201 to 502, reference values: 118 to 223) and 633 U/mL (range: 222 to 2226, reference values: 0 to 500), respectively. The most common drugs responsible were docetaxel ($n = 11$), paclitaxel ($n = 5$), and cyclophosphamide/epirubicin/5-fluorouracil (CEF) ($n = 4$). Eleven out of the 16 cases caused by the taxane agents had radiological patterns that resemble hypersensitivity pneumonitis. Eleven cases (46%) improved by discontinuation of the responsible drug(s) alone without administration of corticosteroids. One patient, induced by vinorelbine, died despite initiation of corticosteroid pulse therapy.

Discussion and Conclusion: Preliminary analysis based on our medical case records indicated that the incidence of drug-induced interstitial lung disease among breast cancer patients undergoing chemotherapy was 0.8%. Studies looking into larger number of cases are warranted for further clarification of above findings, perhaps leading to early detection of lung toxicity and less disruption to breast cancer management.

O-I-012

FLUOROFENIDONE ATTENUATES BLM-INDUCED PULMONARY INFLAMMATION AND FIBROSIS IN MICE VIA INHIBITING THE ACITIVATION OF NALP3 INFLAMMASOME AND IL-1B/IL-1R1/MYD88 SIGNALLING PATHWAY

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IL-1 β plays an important role in the pathogenesis of idiopathic pulmonary fibrosis. The production of IL-1 β was dependent upon the signal via caspase-1-containing multiprotein complexes called inflammasomes and IL-1R1/MyD88 signalling. We previously showed that fluorofenidone (FD) can attenuate BLM-induced lung inflammation and fibrosis. In this study, we explore mainly the anti-inflammatory and anti-fibrotic effect of FD and whether FD exerts these effects through suppressing activation of NALP3 inflammasome and the IL-1 β /IL-1R1/MyD88 signalling pathway *in vivo*. Male C57BL/6J mice were intratracheally injected with BLM or saline. FD, YVAD-fmk, or Anakinet was administered throughout the course of the experiment. Mice were killed on day 1 and day 14. Lung tissue sections were stained with H&E and Masson's trichrome. The expressions of IL-1 β , IL-6, MCP-1 and MPO were measured by ELISA and/or RT-PCR. The expressions of α -smooth muscle actin (α -SMA), fibronectin, collagen I, caspase-1, IL-1R1 and MyD88 were measured by Western blot and/or RT-PCR. FD significantly attenuated BLM-induced lung inflammation and fibrosis. FD also markedly reduced the protein and/or mRNA expressions of IL-1 β , IL-6, MCP-1, MPO, α -SMA, fibronectin and collagen I, caspase-1, IL-1R1 and MyD88 in mice lung tissues. These studies demonstrate that FD, a potential anti-fibrotic agent, attenuated BLM-induced pulmonary inflammation and fibrosis in mice via inhibiting the activation of NALP3 inflammasome and IL-1 β /IL-1R1/MyD88 signalling pathway.

O-I-013

PREPARATION OF LUNG-TARGETING, EMODIN-LOADED PLGA MICROSPHERES AND THEIR PROPERTIESCHEN X^{1,2}, YANG Z¹, SUN R⁴, MO Z¹, JIN G¹, WEI F³, HU J¹, GUAN W¹, ZHONG N¹

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Emodin (1, 3, 8-trihydroxy-6-methylantraquinone) has been identified to have the potential to improve lung fibrosis and lung cancer. To avoid liver and kidney toxicities and the fast metabolism of emodin, emodin-loaded poly(lactic-co-glycolic) acid microspheres (ED-PLGA-MS) were prepared and their characteristics were studied. ED-PLGA-MS were prepared by the organic phase dispersion-solvent diffusion method. By applying an orthogonal design, our results indicated that the optimal formulation was 12 mg/ml PLGA, 0.5% gelatin, and an organic phase : glycerol ratio of 1:20. Using optimal experimental conditions, the drug loading and encapsulation efficiencies were 19.0% (± 1.78) and 62.2% (± 2.63), respectively. The average particle size was $9.68 \pm 0.65 \mu\text{m}$. *In vitro* studies indicated that the ED-PLGA-MS demonstrated a well-sustained release efficacy. The microspheres delivered emodin primarily to the lungs of mice upon intravenous injection. It was also detected by microscopy that there was partial lung inflammation in lung tissues and no pathological changes were found in other tissues of the ED-PLGA-MS-treated animals. These results suggested that ED-PLGA-MS are of potential value in treating lung diseases in animals.

O-I-014

O-I-016

IMPROVEMENT OF AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS AFTER INFECTIOUS EPISODES

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Introduction: Pulmonary alveolar proteinosis (PAP) is a rare disease of unknown aetiology, characterized by accumulation of periodic acid-Schiff stain positive intraalveolar proteinaceous material. More than 90% cases of PAP are autoimmune PAP (APAP) with anti-granulocyte/macrophage colony-stimulating factor (GM-CSF) autoantibody in the serum. The experience of spontaneous resolution occurs in about 30% of APAP (Inoue Y, et al. AJRCCM 2008).

Subjects and Methods: From 2000 to 2013, 98 cases of APAP were diagnosed in our institute. Diagnosis of APAP was performed using radiological findings, pathological findings of transbronchial lung biopsy specimens, and existence of positive anti-GM-CSF autoantibody. Two in 98 cases (2%) showed improvement after infectious episodes.

Results: CASE 1 – A 40-year-old female with cough and dyspnea was diagnosed with APAP in 2002. She suffered from a viral infection, herpes encephalitis, in 2013 and was treated with an antiviral drug. Her symptoms and radiological findings resolved after the recovery from the encephalitis. Serum level of KL-6, a serum marker for APAP, dramatically decreased from 9837 U/mL to 4819 U/mL according with the symptom, and Disease severity score (Inoue Y, et al. Respirology 2006) (grade 3 to 2). CASE 2 – A 53-year-old male current smoker with dyspnea and cough was diagnosed with APAP in 2005. He was admitted due to high body temperature in November 2009. Infiltrative shadows on chest X-ray and HRCT worsened. His APAP was considered to get worse complicated with pneumonia. After the treatment with antibiotics (Ciproxan 200 mg twice per day), the radiological findings and symptoms improved, and serum level of KL-6 decreased from 3980 U/mL to 3180 U/mL. In February 2012, he experienced the similar improvement of APAP after infectious episode.

Discussion and Conclusion: We suppose that spontaneous remission of APAP might be triggered by some factors such as GM-CSF induction after viral or bacterial infection.

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IMPACT OF PULSE I.V. CYCLOPHOSPHAMIDE ON SCLERODERMA RELATED INTERSTITIAL LUNG DISEASE: AN INDIAN EXPERIENCE

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Introduction: Systemic sclerosis (SSc) is a rare connective tissue disorder of unknown aetiology with characteristic involvement of lungs, skin, heart, kidneys and the gastrointestinal tract, but pulmonary involvement contributes maximally to its mortality and morbidity.

Aim of the Study: Cyclophosphamide (CYC) is a well accepted therapy for systemic sclerosis associated interstitial lung disease (SSc-ILD), but the ideal dosage and length of treatment continues to remain elusive. Again, similar studies in the Asian scenario are scarce, if at all present. Our objective was to evaluate the effect of a six-month pulse intravenous CYC therapy on SSc-ILD.

Materials and Methodology: In a single-centre, prospective, observational study, nine patients (eight females, one male) with SSc-ILD were given pulse intravenous cyclophosphamide at monthly interval (600 mg/m² body surface area) for six cycles with oral prednisolone (0.75 mg/kg daily) over a six month period. Over the next six months, azathioprine (2–3 mg/kg) was administered along with same dose of prednisolone. Primary end points were forced vital capacity and high resolution CT scan of thorax score. Secondary end-points were quality of life, as measured by health assessment questionnaire-disability index (HAQ-DI) and six-minute walk test.

Results and Discussion: One year follow ups have been completed in nine patients. Statistical analysis of FVC showed significant improvement ($p = 0.003$), with statistical significance between 6 months and baseline, and also between 12 months and baseline. Six-minute walk distance also improved significantly ($p = 0.0028$). There was no significant improvement in HRCT scan scoring and HAQ-DI score. However on HRCT scan of thorax, there was regression of ground glass opacities but fibrosis remained unchanged.

Conclusion: Pulse IV CYC for six months with low dose corticosteroids produces significant improvement in FVC and six-minute walk distance which is sustained at 12 month follow-up.

O-I-015

SARCOIDOSIS – INDIAN PERSPECTIVE

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Sarcoidosis once thought to be rare in our country has become quiet common and is often misdiagnosed and mistreated as tuberculosis. All age group affection is seen with predominance in young population and shown to have equal sex distribution. The role of negative Montoux test along with typical findings on HRCT and characteristics of the mediastinal nodes gives diagnosis in almost 40%. Transbronchial needle aspiration along with transbronchial biopsies gives the diagnosis in remaining 60%. The role for ACE levels is virtually non-diagnostic and may be used for prognostic significance. If suspicion of sarcoidosis is kept in mind, the diagnostic rate improves and patients can be saved from tuberculosis treatment. Analysis of 50 proven cases of sarcoidosis seen over a period of 1 year is done along with epidemiological, radiological and bronchoscopic findings. The data is compared with the available global data to know exactly the difference between Indian Sarcoid to the western world.

ORAL PRESENTATION – LUNG CANCER

O-J-001

INTEGRATIVE ANALYSIS OF DNA COPY NUMBER IN METASTATIC NSCLC IDENTIFIES DRUG SENSITIVITY TO AFATINIB

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Background: Afatinib (BIBW-2992) has been approved for patients with untreated metastatic non-small cell lung cancer (NSCLC) harbouring EGFR exon 19 deletions or exon 21 L858R substitution mutations. Pharmacogenomic studies have found that genome-wide assays is the unbiased discovery of genomic alterations which is associated with drug response to targeted therapy. The aim of our study is to identify the correlation between DNA copy number profiles and treatment response to afatinib.

Methods: Integrative analysis of DNA copy number alterations (CNA) from 32 metastatic NSCLC patients were performed to identify recurrent regions of genomic change associated with primary response to afatinib using Affymetrix Mapping 250 K Nsp SNP array. Copy number-associated transcriptome profiling was identified using Affymetrix Human genome U133 Plus 2.0 array. Comparison of candidate genes correlated with copy number variation and clinical outcome of afatinib treatment was conducted by quantitative-PCR (qPCR).

Results: Predictive model scores generated from cross-validation was correlated with sensitivity to afatinib. Eight distinct genomic regions were identified in predictive model for afatinib sensitivity. Regions contained chromosomal gain of EGFR (7p11.2) as well as chromosomal loss of HSD3B2 (1p12) and MTAP (9p21.3). The extreme concordance between DNA copy number and transcript abundance was highly significant for the genes mapping to 7p11.2 in afatinib-sensitive group. Specially, amplification of CCT6A was related to the intrinsic resistance to afatinib.

Conclusions: These data show that integrative analysis of DNA copy number analysis can be used to identify genetic alterations which can be used to discover clinically relevant predictors of drug sensitivity to afatinib.

O-J-002

miR-15a INDUCES CELL APOPTOSIS AND INHIBITS METASTASIS BY TARGETING BCL2L2 IN NON SMALL CELL LUNG CANCER

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Objective: Increasing evidence has demonstrated that microRNAs (miRNAs) play a critical role in cancer development and progression. Aberrant expression of miR-15a has recently been reported in several cancers, but its role in non small cell lung cancer (NSCLC) still remains obscure. We investigated the effects of miR-15a on proliferation, apoptosis and metastasis in A549 cells.

Material and Methods: 18 paired NSCLC and adjacent non-tumour lung tissues were surgically removed and immediately snap frozen until total RNA was extracted and confirmed by two independent pathologists. The targets of miR-15a were predicted by bioinformatics tools. RNA isolation and quantitative real-time PCR (qRT-PCR), Western blot analysis, cell proliferation assay, cell cycle analysis, cell apoptosis assay, migration and invasion assay were done. The WT or MT 3'-UTR vectors were co-transfected with miR-15a or negative control into A549 cells, and after 24 hours of transfection luciferase activity was measured using the Dual-Glo luciferase assays kit. Statistical analysis was performed using SPSS13.0 software (SPSS, Chicago, IL, USA). P values of less than 0.05 were considered statistically significant.

Results: miR-15a was significantly downregulated in NSCLC than in adjacent non-cancerous tissues. miR-15a overexpression remarkably inhibited cell viability, invasion, migration and promoted the apoptosis of NSCLC cells. Additionally, inhibition of miR-15a expression had the opposite effects on tumour progression, while cell cycle remained unaltered. Furthermore, we identified that BCL2L2 was a target of miR-15a and negatively regulated by miR-15a at the translational level.

Conclusion: miR-15a act as a tumour suppressor in NSCLC by directly targeting BCL2L2 and may serve as a potential diagnostic biomarker and therapeutic target for NSCLC.

O-J-003

SIMPLE SHIPPING PROCEDURE USING FILTER PAPER FOR DETECTION OF EGFR AND KRAS MUTATION IN MALIGNANT PLEURAL FLUID FROM REMOTE AREA IN INDONESIA: PRELIMINARY STUDY

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Background: Indonesia has more than 6000 inhabitant islands stretching across 2 millions square miles. With new cases of lung cancer is increasing, many suspected lung cancer patients with pleural effusion in remote area are needed to be diagnosed properly that could only be done in referral laboratory, therefore simple and accurate shipping procedure are needed.

Objective: To evaluate the possibilities of using filter paper as transport medium in remote area for lung cancer pleural fluid cytogenetic analysis.

Methods: Whatman filter paper was simply bathed in pleural fluid from 29 lung cancer patients, then dried in room air, and send to our laboratory. DNA were isolated and EGFR and KRAS mutation were analysed using HRM-PCR and Restriction Fragment Length Polymorphism (RFLP).

Result: Good quality DNA could be isolated from dried filter paper (100%). KRAS mutation could be detected in 6.9% (2/29) samples. EGFR mutation could be detected in 17.2% (5/29) samples. KRAS mutation was found as mutation codons 12, the type of EGFR mutation were L858R point mutation (2 samples) and deletion of exon 19 (3 samples)

Conclusion: Filter paper could be used as simple transport medium for cytogenetic analysis in lung cancer pleural effusion.

O-J-004

O-J-006

SIMPLE LATEX BALLOON RESERVOIR SYSTEM FOR EXHALED BREATH CONDENSATE AS NONINVASIVE MOLECULAR DIAGNOSTIC METHODS IN LUNG CANCER: PRELIMINARY STUDY

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Background: Trained dogs could differentiate lung cancer and normal subject through sniffing. DNA component in exhaled breath condensate (EBC) is thought to be different between lung cancer and normal subjects. Methylation of APC were found in bronchial samples in lung cancer. To prove that simple latex balloon reservoir system for EBC is a noninvasive method to detect lung cancer, we evaluate DNA content and APC methylation status from EBC collected using latex balloon reservoir system.

Methods: Histologically confirmed lung cancer patients were asked to blow latex balloons for certain volume. DNA and APC methylation status APC were evaluated from EBC inside latex balloon.

Result: Fifteen lung cancer cases, 14 males and 2 females (23 to 65 year old) were enrolled in the preliminary study. 14 cases were lung adenocarcinoma and 2 cases with lung squamous cell carcinoma. APC methylation could be detected from serum and sputum of subjects. DNA and APC methylation was detected from EBC inside latex balloon reservoir system.

Conclusions: Latex balloon reservoir system is a simple, noninvasive, and promising procedure for early detection procedure in lung cancer. However, this system needs further adjustment to enhance DNA recovery.

TRANSLATIONAL EVIDENCE OF ZINC-FINGER E-BOX BINDING HOMEBOX 1 INVOLVEMENT IN ACQUIRED RESISTANCE TO GEFITINIB IN NON-SMALL CELL LUNG CANCER

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Rationale: Acquired resistance to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) limits the progression-free survival of non-small cell lung cancer (NSCLC) harbouring activating EGFR mutation. Several molecular mechanisms of acquired resistance have been identified, such as epithelial-mesenchymal transition (EMT) and involvement of cancer stem cells (CSCs). However, master regulator responsible for these two mechanisms remains unknown.

Purpose of Study: Using in vitro, in vivo model, and clinical specimens, here we investigate the role of Zinc-finger E-box binding homeobox 1 (ZEB1) in the acquired resistance to gefitinib.

Methods: NSCLC cell line harbouring exon 19 deletional mutation, PC9, was used in this study. We exogenously overexpressed ZEB1 gene by lentivirus-mediated transduction and injected the ZEB1-overexpressed PC9 cells into NOG mice and treated them with gefitinib. ZEB1 and CSCs-related factors, such as polycomb ring finger oncogene BMI1, and aldehyde dehydrogenase 1A1 (ALDH1A1), were analysed in lung cancer specimen of patients with acquired resistance to EGFR-TKI.

Results: ZEB1 overexpression induced gefitinib resistance in vitro. ZEB1-overexpressing PC9 (PC9-ZEB1) tumour grew faster as compared to PC9-mock tumour in mice. Moreover, extent of the tumour inhibition by gefitinib was significantly lesser in PC9-ZEB1 tumours as compared to that in PC9-mock tumours in vivo. ZEB1, BMI1, and ALDH1A1 were highly expressed in lung cancer specimens of patients with acquired resistance.

Conclusions: Our in vitro, in vivo, and clinical data strongly suggest that ZEB1 is involved in the acquired resistance of NSCLC to EGFR-TKI. Therefore, ZEB1 should be considered as potential target to prevent acquired resistance to gefitinib in NSCLC.

O-J-005

O-J-007

EPIGENETIC ALTERATIONS OF IGF1 REGULATE TAZ EXPRESSION IN LUNG CANCER

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The insulin-like growth factor (IGF) system has been implicated in the oncogenesis of epithelial malignancies. Epigenetic alterations have emerged as common hallmarks of many cancer types, including lung cancer. However, the epigenetic alterations of IGF1 in lung cancer is not yet known. Herein, we studied the role of IGF1 pathway during lung cancer progression, emphasizing its epigenetic regulation and the interaction between IGF1 and its downstream signalling in lung cancer. The results reveal DNA methylation in promoter site 1 (P1) of IGF1 gene in lung cancer cells. 5-Aza-2'-deoxycytidine treatment on lung cancer cell line HTB-57 repressed both IGF1 and TAZ protein expression levels, indicating that IGF1 expression was at least partially upregulated by promoter hypermethylation. Enhanced IGF1 expression in NCI-H3255 cells promoted phosphorylation of Akt, promoted cell proliferation and inhibited anoikis. Silencing IGF1 with shRNA transfection attenuated Akt activity and promoted anoikis in NCI-H1975 cells. Using methylation specific-polymerase chain reaction (MS-PCR), we found that 58.8% of patients with lung adenocarcinoma displayed hypermethylation at IGF1. IGF1 was epigenetically upregulated by hypermethylation in human lung cancer tissues, which was relevant to the function of IGF1 to upregulate TAZ expression via PI3K/Akt pathway.

CONSTRUCTION OF EXPRESSION VECTOR, ESTABLISHMENT OF STABLY TRANSFECTED A549 CELL LINE AND PRELIMINARY RESEARCH ON THE FUNCTION OF RBM5 GENE

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Background and Aim of Study: RBM5 (RNA-binding motif protein 5, also named H37/LUCA-15) gene from chromosome 3p21.3 is a known putative tumour suppressor gene. In this study, through the construction of an expression vector and establishment of a stable transfected RBM5 A549 cell line, we researched the influence to cell proliferation and expression of DHX15 (DEAH-box polypeptide 15, a splicing-related factor) in A549 which overexpressed RBM5 gene.

Methods: A two-step PCR technique was applied to clone the full-length RBM5 coding region to construct the eukaryotic expression vector pcDNA3.1 (+)/RBM5. Then, the sequenced recombinant plasmid pcDNA3.1 (+)/RBM5 transfected in lung adenocarcinoma cell A549. After screened by G418, the positive cells were identified by Western Blotting. Flow cytometry was used to analyse the cell cycles of the pcDNA3.1 (+)/RBM5 and pcDNA3.1 (+) transfection groups. At last, using RT-PCR technology to detect the expression of DHX15 in the A549 cell line which overexpressed RBM5.

Results: It has constructed pcDNA3.1 (+)/RBM5 eukaryotic expression vector, screened out the A549 cells that stably transfected with RBM5 gene. Compared with blank plasmid pcDNA3.1 (+) transfected cells, the recombinant plasmid pcDNA3.1 (+)/RBM5 transfected cells in G1 phase cells is increased, the proportion of cells in S phase is decreased ($P < 0.01$). A549 cell line that was overexpressed RBM5 upregulated the expression of DHX15 ($P < 0.01$).

Conclusion: We have successfully recombinated plasmid pcDNA3.1 (+)/RBM5 and established a RBM5 stably transfected A549 cell line, and preliminary confirmed RBM5 overexpression inhibits the cell cycle of lung adenocarcinoma A549 cell line and makes DHX15 upregulated.

O-J-008

CISPLATIN-INDUCED DOWNREGULATION OF RBM5 INCREASES DRUG RESISTANCE BY ACTIVATING AUTOPHAGY IN NON-SMALL CELL LUNG CANCER CELLS

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Background: RNA binding motif 5 (RBM5) is a tumour suppressor gene which is involved in the cell proliferation, apoptosis and cell cycle. Recent study shows that RBM5 is also involved in cisplatin resistance in non-small cell lung cancer (NSCLC). However, the underlying mechanism is not fully understood especially the involvement of autophagy. The aim of this study is thus to investigate whether cisplatin resistance is associated with alteration of RBM5 expression and its relationship with alteration of autophagy in NSCLC.

Methods: The cisplatin resistant clone (A549/cis) of A549 cells was established by exposing the cells with gradually increasing concentrations of cisplatin until chemoresistance acquisition was elucidated by MTT and A549/cis cells could stable grow and be passaged. Degree of autophagosome formation was evaluated by acridine orange (AO) and monodansylcadaverine (MDC) staining in A549/cis cells and parental cells. The level of LC3 and RBM5 was examined by western blot analysis.

Results: A549/cis cells exhibited irregular shape with ~8-fold resistant to cisplatin-induced apoptosis compared with A549 cells. Proteins analysis for LC3 and RBM5 indicated that the LC3 expression was significantly higher in A549/cis cells than that in A549 cells, while RBM5 expression was much lower in resistant cells than that in parental cells, respectively. Moreover, autophagosome formation detected by AO and MDC staining was dramatically increased in the resistant cells, suggesting the important role of autophagy in attenuating of cisplatin-induced cell death.

Conclusions: This study shows that inactivation of RBM5 induced by long-term cisplatin exposure activated autophagy, which, at least in part, was responsible for cisplatin resistance in human NSCLC.

O-J-009

A SPECIFIC SERUM CHEMOKINE NETWORK CORRELATES WITH TUMOURIGENESIS IN AND PROGNOSIS OF PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Rationale: Inflammation plays an important role in the microenvironment of lung cancer.

Objectives: The present study aimed to evaluate the association of inflammatory biomarker networks with chemotherapies for patients with non-small cell lung cancer (NSCLC).

Methods: Sera of healthy non-smokers (n = 14) and patients with NSCLC (n = 50), 36 with adenocarcinoma and 14 with squamous cell carcinoma, were collected on 1, 2 and 3 admissions following chemotherapeutic treatment (0, 21 and 42 days post-diagnosis).

Measurements: Cytokine concentrations were measured using multiplexed cytokine immunoassays. Clinical informatics was scored by a Digital Evaluation Score System (DESS) to assess the severity of the patients. All of the patients completed follow-up for up to 2 years.

Main Results: Among the 40 mediators measured, 13 showed significant differences between patients with lung cancer and healthy controls, 9 between untreated patients and patients with adenocarcinoma at stage IV who had undergone the first chemotherapy course and 13 between untreated patients and patients who had undergone the second chemotherapy course. The protein network of cytokines in NSCLC was similar to that of normal persons after multiple courses of chemotherapy. The DESS values for adenocarcinoma differed from those for squamous carcinoma. The survival analysis of these NSCLC patients suggested that MIP-3 α is the most crucial biomarker for predicting survival rates. Network analysis of the serum chemokines suggested that the connection between these proteins gradually decreased as the disease progressed.

Conclusions: Our data identify an NSCLC-specific profile of inflammatory mediators that may be useful for cancer sub-classification and the evaluations of therapeutic effects and overall survival.

O-J-010

KRUPPEL-LIKE FACTOR 2 IMPROVES POSTOPERATIVE PROGNOSIS OF LUNG ADENOCARCINOMA PATIENTS

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Background: Lung Krueppel-like factor (LKLF, KLF2) is a member of the family of the Krueppel-like factors (KLFs). KLF2 was initially described as a lung-specific transcription factor. KLF2 is reported to regulate some malignant cells. We examined and evaluated the effect of KLF2 on lung adenocarcinoma and the relationship of their mRNA expression with CC-chemokine receptor 7 (CCR7) and TP53 gene mutations in lung adenocarcinoma.

Methods: A total of 120 patients of stage I to IV with lung adenocarcinoma were included in this retrospective analysis. The mRNA expression of KLF2, CCR7, CCR7 ligands (CCL19 and CCL21) in surgically resected lung adenocarcinoma specimens were examined and evaluated the relation to genetic mutations.

Results: High mRNA expression of KLF2 in lung cancer patients indicated significantly good prognosis than the groups of low expressions (p = 0.007, HR = 2.00, 95% CI of ratio 1.22 to 3.32). The expression of KLF2 mRNA had relationships with CCR7, CCL21 and CCL19 mRNA expression in lung adenocarcinoma. Moreover the mRNA expression of KLF2 in lung adenocarcinoma specimens was influenced by the TP53 mutation in lung cancer specimens. The expression of KLF2 was confirmed with immunohistochemical analysis and mRNA expression extracted from tissue sections of lung adenocarcinoma specimens by laser capture microdissection.

Conclusion: We propose KLF2 as clinical good prognostic factors and that KLF2 has strong relation with CCR7 and the ligands mRNA expression in lung adenocarcinoma. And the mRNA expression of KLF2 was regulated with TP53 mutations.

O-J-011

IMPROVING THE QUALITY OF LIFE FOR AMBULATORY PATIENTS WITH ADVANCE LUNG CANCER THROUGH PHONE TRIAGING

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Introduction: PROBLEM – Palliative care strives to improve the quality of life for patients and their families by impeccable assessment and management using an interdisciplinary approach. However, patients with lung cancer-related pain and other symptoms tend to be undertreated because of limited follow-up visits due to late referrals and logistics. Thus, Patients have to deal with the complex and time consuming logistics of ambulatory cancer care. At the same time, members of staff often waste considerable time and energy in organizational aspects of care that could be better used in direct interaction with patients.

Methods: DESIGN – Quality improvement study using the Edmonton Symptom Assessment Scale (ESAS) is a formalized symptom assessment tool used to capture patients' subjective measurement of symptoms and focus group meetings with patients and families regarding how to complete the ESAS and rate their symptoms by using the numerical 0 to 10 rating scale. SETTING – Outpatient palliative care clinic at Supportive Care Center, Vancouver General Hospital, Vancouver, where lung cancer patients receive chemotherapy and complementary palliative care. METHODS – At each clinic visit, a nurse trained in palliative care explains the ESAS to the patient and caregivers to ensure the scale is understood and properly filled out. Symptoms included on the ESAS are pain, fatigue, depression, nausea, anxiety, drowsiness, best appetite (with a score of zero signifying no subjective report of appetite issues), best feeling of well-being, no shortness of breath (SOB), and best sleep. While the ESAS is systematically used with each phone call, the numerical 0 to 10 rating scale is also used to assess current patient distress. The phone triage nurse has access to previous ESAS scores through the patient's medical record to determine the patient's goals for pain control, recent symptom scores, and recent changes in medication regimen. ESAS scores are included in this study for the 42 lung cancer patients (with mean age 54.6, the male/female ratio 3/1) to illustrate the effects of continued patient contact between as well as after clinic visits in abetting an overall decrease in symptom distress.

Results: The first ESAS consultation revealed a high symptom burden. Initial management of symptoms focused on pain, nausea, appetite, anxiety, and sleep. Time from the first consultation to the final clinic visit was 2 months, at which time symptom burden had decreased overall. Phone conversations between the palliative care nurses and the patients took place between visits and continued after their final visit and until their ultimate decision to transition to hospice care. Because the patient's subjective feeling of SOB increased with disease progression, home oxygen, and short-acting opioid therapy were introduced to lessen their distress; subsequent follow-up phone calls with palliative care nurses noted a decrease in symptom burden and an increased sense of comfort and control with self-managing care at home.

Conclusion: The information from the cases included in this study, as well as our experience with other palliative patients regarding the importance and effectiveness of an outpatient palliative care phone triaging staffed by designated nurses, is limited. Nevertheless, the results suggest that patients, as well as their family members and at-home caregivers, benefit from having this resource available to discuss questions and concerns regarding symptom management and emotional support throughout their cancer journey. Further studies of the effectiveness of such a programme are warranted.

O-J-012

DIFFERENTIALLY EXPRESSED GLYCOSYLATED PATTERNS OF ALPHA-1-ANTITRYPSIN AS SERUM BIOMARKERS FOR THE DIAGNOSIS OF LUNG CANCER

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Objective: Lung cancer is the most common malignant tumour worldwide. Diagnostic biomarkers with adequate sensitivity and specificity for lung cancer detection are desperately looked-for. Glycans in glycoprotein are significantly altered in cancer, and may serve as a tool to identify potential diagnostic biomarkers. Recent studies have reported changes in alpha-1-antitrypsin (A1AT) glycosylation in serum, tissue and cell lines of lung cancer.

Materials and Methods: Herein, a lectin-microarray was used to detect glycosylation changes of serum A1AT from patients with lung adenocarcinoma (ADC), squamous cell lung cancer (SCLC), small-cell lung cancer (SCLC) and those with benign pulmonary diseases. The differentially expressed glycosylated pattern of A1AT identified by lectin-arrays was further confirmed by lectin-based ELISA assays.

Result: We found that galactosylated A1AT could distinguish NSCLC from benign diseases (AUC = 0.834), fucosylated A1AT showed exceptional capability in distinguishing ADC from benign diseases (AUC = 0.919) or other lung cancer subtypes (AUC = 0.844) and A1AT containing poly-LacNAc could detect SCLC from benign diseases (AUC = 0.905) or NSCLC (AUC = 0.707).

Conclusion: The present study indicates that glycosylated patterns of A1AT may serve as potential biomarkers for detection of lung cancer. Further studies in larger sample sizes are necessary to validate the clinical utility of these markers.

O-J-013

EPIDERMAL GROWTH FACTOR RECEPTOR MUTATIONS IN LUNG SQUAMOUS CELL CARCINOMA IN SMOKERS AND NEVER SMOKERS

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Objective: To determine the frequency of epidermal growth factor receptor (EGFR) mutation in squamous cell carcinoma (SCC) of the lung in smokers and never smokers.

Methods: The clinical and CT scan features of consecutive patients diagnosed with lung SCC at the University of Malaya Medical Centre, Kuala Lumpur from 2009 to 2013 were studied. Somatic EGFR mutations in lung SCC biopsy specimens were detected by allele-specific real-time polymerase chain reaction.

Results: EGFR mutations were detected in the tumours of 12 (12.4%) out of a total of 97 patients. These consisted of deletion mutation in exon 19 in seven patients, substitution (L858R) mutation in exon 21 in four patients and insertion mutation in exon 20 in one patient. EGFR mutations were more frequently detected in the tumours of female [6 of 24 (25.0%)] than male patients [6 of 73 (8.2%)] (OR, 3.04; 95% CI, 1.08–8.55; p = 0.04), never smokers [7 of 27 (25.9%)] than ever smokers [5 of 70 (7.1%)] (OR, 3.63; 95% CI, 1.26–10.26; p = 0.03) and peripheral SCCs [7 of 34 (20.6%)] than central SCCs [5 of 63 (7.9%)] (OR, 1.83; 95% CI, 1.04–3.25; p = 0.11). Multivariate analysis with gender and smoking history (never versus ever smoker) as covariates showed that only a never smoking status was an independent predictor of EGFR mutation positivity (adjusted OR, 4.55; 95% CI, 1.30–15.92; p = 0.018).

Conclusions: The frequency of EGFR mutation in SCC of our patients is 12.4% which is higher than that reported in the West. EGFR mutation-positive SCC are 3.6 times more common in never smokers compared to ever smokers and 3.0 times more common in females compared to males. A never smoking status is an independent predictor of EGFR mutation positivity in SCC.

O-J-014

STUDY OF MECHANISM OF REVERSE OF COX-2 INHIBITOR CELECOXIB ON ACQUIRED RESISTANCE TO GEFITINIB IN NON-SMALL CELL LUNG CANCER

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Background and Objective: Overexpression of cyclooxygenase-2(COX-2) and epidermal growth factor receptor (EGFR) has been detected in non-small cell lung cancer (NSCLC). The interaction of COX-2 and EGFR play an important role in tumour development and progression. Previous studies had shown that combined use of COX-2 inhibitor celecoxib and EGFR tyrosine kinase inhibitors (TKIs) may have synergistic inhibitory effect on the proliferation of EGFR mutation cell lines. In this study, we explored the role of celecoxib and relevant signalling pathway in acquired gefitinib resistance in NSCLC.

Methods: Gefitinib-resistant PC9/G cell lines was induced by exposure of PC9 cell lines to MNNG and gefitinib and maintained in the media containing 0.05 umol/L of gefitinib. The inhibitory effects of gefitinib and/or celecoxib on cellular proliferation were tested by MTT assay. Cell cycle and apoptosis were analysed by flow cytometry. Western Blot was used to detect expression of COX-2, EGFR, phospho-EGFR, Akt and phospho-Akt, Erk, phospho-Erk.

Results: Resistant index of PC9/G cells to gefitinib was about 147- to 198-fold higher than PC9 cells, and it was accompanied by significant increase of COX-2 expression in PC9/G cells. Inhibition of COX-2 with celecoxib in PC9/G resulted in dramatic inhibition of proliferation and promotion of apoptosis in response to gefitinib. PC9/G cells' sensitivity to gefitinib is restored. The combination of celecoxib and gefitinib significantly induced G0/G1 arrest. Furthermore, the combination as compared with effect of single agents showed strong reductions of p-AKT, p-ERK of PC9/G cell line.

Conclusions: These findings suggest that COX-2 signalling by PI3K/Akt and ERK pathway may be an important mechanism of acquired gefitinib resistance and may serve as an alternative therapeutic target for NSCLC unresponsive to EGFR TKIs.

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O-J-015

DIAGNOSTIC TIME FOR LUNG CANCER PATIENTS AND THE ROLE OF A SERUM BASED BIOMARKER PANEL IN THE EARLY DIAGNOSIS FOR A COHORT OF HIGH-RISK PATIENTS

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Background and Objective: In this study, we applied a combined cancer biomarker panel to help clinically identify small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) in a high-risk population.

Methods: Serum levels of four biomarkers (ProGRP, CEA, SCC and CYFRA21-1) were determined in 153 patients with a high-risk of lung cancer (12 with a new diagnosis of SCLC, 52 with NSCLC and 89 without lung cancer). The diagnosis delay information was collected by interviewing all the participants.

Results: We found significantly higher serum levels of ProGRP ($p < 0.0001$) among SCLC patients vs. the rest of population. By receiver operating characteristic curve analysis, we established the cut off values of ProGRP, CEA, SCC and CYFRA21-1 at 300 pg/mL, 7.3 ng/mL, 3 ng/mL and 6.5 ng/mL, respectively. Sensitivity and specificity of ProGRP in diagnosing SCLC was 75% and 100%, respectively. Among the 14 lung cancer patients with a false negative CT result, the diagnostic panel detected eight additional cancers.

Conclusions: This panel increased the diagnostic specificity among high-risk subjects (excluding those with renal failure) and increased sensitivity in patients with lung cancer auxiliary to CT scan. These results might be applied to shorten the diagnosis delay in healthcare institutions in China.

O-J-016

PALLADIUM (II)-SACCHARINATE COMPLEX OF TERPYRIDINE SEEMS TO BE A PROMISING NOVEL COMPOUND FOR THE TREATMENT OF LUNG CANCER IN VITRO

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Successful management of lung cancer is still poor. Thereby, novel compounds/approaches are required. In this study, we investigated the cytotoxic/apoptotic effect of our patented novel palladium (Pd)-based compound ([PdCl(terpy)](sac)•2H₂O) against lung cancer cell lines (A549 and PC3). The MTT and ATP assays were performed as cytotoxicity assays. Caspase-cleaved cytokeratin 18 (M30) levels were measured to measure apoptosis. To elucidate the mechanism of apoptosis, p53, Bik, Bax and FasL genes were silenced by transfection method. To determine whether the Pd(II) complex causes DNA damage or not, γ H2AX (phosphorylated H2AX) assay was performed. Based on MTT and ATP assays, Pd(II) compound showed cytotoxic activity in a dose dependent manner in both cell lines. Transfection results showed that A549 and PC3 cells viability was not changed after the transfection. Caspase 3/7 activity was found to play a role in apoptosis. γ H2AX assay results indicated that Pd(II) compound cause to DNA damage both cell lines in a dose dependent manner. In conclusion, this Pd(II) compound deserves further attention to be evaluated in vivo in terms of its possible anticancer activity against lung cancer.

O-J-017

LUNG CANCER AND COMPLEMENTARY-ALTERNATIVE TREATMENT USE AND REASONS

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In cancer patients, high symptom load and poor prognosis, causes more complementary-alternative treatment (CAT) use. Although very few of CAT methods tested and most not proved, these methods remains to be popular. This study was done to find out, CAT application frequency, its causes, methods and life quality and depression-anxiety level possible effect on CAT usage, to compare CAT users and nonusers sociodemographic, medical, psychosocial variables in lung cancer patients.

Material and Methods: Research was done in Akdeniz University Medical Faculty, Internal Medicine Medical Oncology and Chest Medicine Clinics, between the dates June 2012 and October 2012, with patients, diagnosed as lung cancer at least 3 months ago, in the form face to face questionnaire. In data collection, CAT inquiry form, Hospital Anxiety-Depression Scale (HAD) and life quality questionnaire (EORTC QLQ-LC13) were used, while in data descriptive statistics, mean, standart deviation, frequency and ratio values were used. Variant distribution was controlled with Kolmogorov-Smirnov test. In qualitative data analysis independent samples t-test and Mann-Whitney u-test, in quantitative data analysis, ki-square test, in conditions not provides, fisher test and for the analysis SPSS 20.0 programme was used.

Findings: 161 patients (10 women, 151 men) was included in the study, 61 (%36.96) were CAT user. Most used CAT method was plants, most used plant was stinging nettle and its seeds. There were no significant difference between CAT users and nonusers in respect to sociodemographic, socioeconomic features such as medical conditions, age, sex, marital-education-economic status and EORTC QLQ-LC13 life quality scale average total score, HAD average total anxiety score and mean depression score. In CAT users, anxiety incidence was significantly lower than in CAT nonusers. CAT users were found to be more consulting to psychiatrist and were using more antidepressant drugs.

Results: It was found out in our study that lung cancer patients perceive their disease independently from their sociodemographic, socioeconomic and medical status, they tend to CAT as complementary to their conventional treatment. Despite there is no significant difference between CAT users and nonusers depression and anxiety score mean, anxiety was seen much more less in CAT users. Reason for this, might be CAT users were going to psychiatrist and were using antidepressants more frequently than CAT nonusers. Our study shows that, we should give much more information about CAT to our patients regardless their sociodemographic, socioeconomic and medical status, we should ask CAT usage status to all patients, especially patients who are taking psychological support and treatment as they tend to be seen more prone to CAT usage.

O-J-018

O-J-020

HIGH-DOSE CISPLATIN EXPOSURE INCREASED AUTOPHAGY AND CAUSED CISPLATIN RESISTANCE IN HUMAN LUNG CANCER A549 CELLS

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Background: Cisplatin is a well-known apoptotic inducer and one of the most active antitumour agents used in human chemotherapy of non-small cell lung cancer (NSCLC). However, cisplatin-based chemotherapy always results in acquired resistance. The underlying mechanism of such resistance is not fully understood, especially the involvement of autophagy. The objective of this study is thus to investigate whether an alteration in autophagy could be induced by cisplatin and the relationship between autophagy and drug resistance.

Methods: Human lung adenocarcinoma cell line A549 cells were tested *in vitro* to evaluate the effect of cisplatin using different doses. Cell growth inhibition was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-dephenyl tetrazolium bromide (MTT) assay after treatment with cisplatin for 24 h. Degree of autophagosome formation were evaluated by acridine orange (AO) and monodansylcadaverine (MDC) staining.

Results: Proliferation of A549 cells was inhibited after cisplatin treatment in a dose-dependent manner at a concentrations ranging from 2.5 to 30 µg/ml as determined by MTT assay. Nevertheless, as cisplatin dose increasing from 60–180 µg/ml, viability of A549 cells was significantly increased resulting in a high dose drug-resistance of cisplatin. Meanwhile, autophagosome formation detected by AO and MDC staining was observed slightly increased at concentrations ranging from 2.5 to 30 µg/ml, but increased greatly at concentrations ranging from 60 to 180 µg/ml.

Conclusions: High-dose cisplatin treatment induced autophagy in a dose-dependent manner and caused cisplatin resistance in human lung cancer A549 cells.

ONCOLOGICAL EMERGENCIES ARISING AT DIAGNOSIS OF LUNG CANCER IN OUR HOSPITAL

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Background: Oncological emergencies in lung cancer, often encountered during the course of the disease, are associated with high morbidity and mortality rates, and early diagnosis and treatment of these conditions can significantly affect clinical outcomes.

Purpose: This study retrospectively investigated oncological emergencies encountered when diagnosing lung cancer.

Methods: Among 596 newly diagnosed lung cancer patients treated at our hospital between April 2005 and December 2010, 60 (48 men, 12 women; mean age, 66.8 years) showed complications with oncological emergencies at diagnosis. We investigated the background, frequency, and treatment of oncological emergencies in these patients.

Results: Histological diagnosis was adenocarcinoma in 41 cases, squamous cell carcinoma in 7, large-cell carcinoma in 3, pleomorphic carcinoma in 1, and small cell carcinoma in 8. The most common oncological emergencies were superior vena cava syndrome in 11 cases, unilateral massive pleural effusion in 11, spinal cord compression in 10, cardiac tamponade in 9, and tracheobronchial stenosis in 9. Hypercalcaemia and disseminated intravascular coagulation were also recognized in a few cases. The approach to definitive therapy was commonly multi-disciplinary, involving medical oncologists, surgeons, radiation oncologists, and other medical specialists. After intervention for each oncological emergency, systemic chemotherapy or molecular-targeted therapy was added on a case-by-case basis.

Conclusion: Oncological emergencies in lung cancer patients are not rare, even at onset, and most are related to structural dysfunction. A multi-disciplinary approach and swiftness in establishing appropriate therapeutic measures are crucial to optimize the functional and vital prognoses of these patients.

O-J-019

O-J-021

GENETIC ANALYSIS OF HYPOXIA INDUCIBLE FACTOR-2 ALPHA IN LUNG CANCER

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Introduction: Hypoxia-inducible factor-2α (HIF-2α), a member of the hypoxia-inducible transcription factor (HIF) family, is known to promote cancer cell malignancy. To date, several reports showed possible roles of HIF2A SNPs in physiologic adaptation in high altitude and susceptibility to complex diseases including cancers. In this study, to determine whether any of HIF2A SNPs associate with progression of lung cancers, we investigated associations of eight SNP loci of HIF2A gene (rs4953354, rs13419896, rs17039192, rs1867785, rs1868085, rs4953347, rs11894252, rs7579899).

Material and Methods: We prepared genomic DNA from 83 lung cancer patients (42 adenocarcinoma, 30 squamous cell, 4 adenosquamous cell, and 7 small cell carcinomas) then PCR and direct sequencing analyses were utilized to genotyping of HIF2A.

Results: Direct-sequencing analyses revealed that frequencies of minor allele of two loci (rs13419896 or rs7579899) were significantly higher in female (P = 0.037 or 0.035), and those of 4 loci (rs13419896, rs1867785, rs11894252, or rs7579899) were significantly higher in patients with well-differentiated cancers (P = 0.045, 0.048, 0.023 or 0.041). Notably, one locus (rs13419896) as well as clinical staging status significantly associated with overall survival of lung cancer patient: Patients who had a minor allele or an advanced cancer showed significantly poorer survival (P = 0.012 or 0.0074, log-rank test). Multivariate analyses revealed the minor allele of the HIF2A locus (rs13419896) was an independent prognostic factor of lung cancer as well as advanced clinical stage (RR = 2.22; 95%CI = 1.23–4.12; P = 0.0079 and RR = 2.41; 95%CI = 1.35–4.45; P = 0.003).

Conclusion: Genetic polymorphism of the HIF2A might be a useful prognostic marker in lung cancer patients.

AFATINIB IN MANAGEMENT OF NON-SMALL CELL LUNG CANCER (NSCLC): WHAT IS EVIDENCE SO FAR?

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Afatinib is an oral, irreversible ErbB family blocker of epidermal growth factor receptor (EGFR), HER2 and ErbB4 signalling and ErbB3 transphosphorylation. Preclinical studies indicate that afatinib inhibits the kinase activity of both wild-type and mutant forms of EGFR and HER2 and of wild-type ErbB4. It also shrinks tumours resistant to first-generation EGFR TKIs (i.e., gefitinib or erlotinib) including EGFR L858R/T970M double-mutant tumours in animal models. Clinical efficacy of afatinib has been extensively evaluated in a series of LUX-Lung trial programme. LUX-Lung 1, 4 and 5 studied efficacy of afatinib in NSCLC patients pretreated with chemotherapy and gefitinib/erlotinib, while the efficacy in first line or second line (EGFR-TKI-naïve) setting in EGFR mutation positive NSCLC was tested in LUX-Lung 2, 3, 6 and 7. LUX-Lung 8 evaluates the clinical relevant advantage of afatinib over erlotinib in second line squamous subtype of NSCLC, whereas the advantage over gefitinib is assessed in first line EGFR common mutation positive NSCLC in LUX-Lung 7. While LUX-Lung 7 and 8 are ongoing, LUX-Lung 3 has demonstrated a superior progression-free survival (PFS) of afatinib compared with cisplatin/pemetrexed chemotherapy in overall study population (median 11.1 vs 6.9 months, HR = 0.58, p = 0.0004) and in those with EGFR common (Del19/L858R) mutations (median 13.6 vs 6.9 months, HR = 0.47, p = 0.001) of first line NSCLC. The PFS improvement is associated with significant improvement in patient-reported outcomes and the quality of life. These results have been further confirmed by LUX-Lung 6 of afatinib versus cisplatin/gemcitabine chemotherapy. The recent combined analysis on the mature overall survival (OS) data of LUX-Lung 3 and 6 indicated that OS was significantly improved with afatinib versus chemotherapy (median 27.3 vs 24.3 months, HR = 0.81, p = 0.037) in 1st line NSCLC harbouring EGFR common (Del19/L858R) mutations. In both trials, when analysed individually, 1st line NSCLC patients with EGFR Del19 mutation receiving afatinib had more than one year additional survival compared to chemotherapy (LUX-Lung 3: median OS 33.3 vs 21.1 months, HR = 0.54, p = 0.0015; and LUX-Lung 6: median OS 31.4 vs 18.4 months, HR = 0.64, p = 0.0229). Diarrhoea and rash are the most frequent adverse events of afatinib; they are manageable with low treatment discontinuation rate.

O-J-022

FREQUENCY OF EPIDERMAL GROWTH FACTOR RECEPTOR MUTATIONS IN SQUAMOUS CELL CARCINOMA OF THE LUNG IN SMOKERS AND NEVER SMOKERS

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Objective: To determine the frequency of epidermal growth factor receptor (EGFR) mutation in squamous cell carcinoma (SCC) of the lung in smokers and never smokers.

Methods: The clinical and CT scan features of consecutive patients diagnosed with lung SCC at the University of Malaya Medical Centre, Kuala Lumpur, from 2009 to 2013 were studied. Somatic EGFR mutations in lung SCC biopsy specimens were detected by allele-specific real-time polymerase chain reaction.

Results: EGFR mutations were detected in the tumours of 12 (12.4%) out of a total of 97 patients. These consisted of deletion mutation in exon 19 in seven patients, substitution (L858R) mutation in exon 21 in four patients and insertion mutation in exon 20 in one patient. EGFR mutations were significantly more frequently detected in the tumours of female [6 of 24 (25.0%)] than male patients [6 of 73 (8.2%)] (OR, 3.04; 95% CI, 1.08–8.55; $p = 0.04$) and never smokers [7 of 27 (25.9%)] than ever smokers [5 of 70 (7.1%)] (OR, 3.63; 95% CI, 1.26–10.26; $p = 0.03$). Although a higher proportion of peripheral SCCs harboured EGFR mutations [7 of 34 (20.6%)] compared to central SCCs [5 of 63 (7.9%)], the difference was not statistically significant ($p = 0.11$). Multivariate analysis with gender and smoking history (never versus ever smoker) as covariates showed that a never smoking status was an independent predictor of EGFR mutation positivity (adjusted OR, 4.55; 95% CI, 1.30–15.92; $p = 0.018$).

Conclusions: The frequency of EGFR mutation in SCC of our patients was 12.4% which is higher than that reported in the West. EGFR mutations should be tested in the SCC of Asian patients, particularly in never smokers, 25.9% of whom have EGFR mutation-positive tumours, to identify those who may benefit from treatment with EGFR-tyrosine kinase inhibitors.

ORAL PRESENTATION – OTHERS

O-K-001

ASSOCIATIONS OF SRAGE AND S100A12 ON POSTOPERATIVE RESPIRATORY COMPLICATIONS ACCORDING TO DIFFERENT TWO VENTILATION MODES AFTER LAPAROSCOPIC-ASSISTED COLORECTAL SURGERY

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Introduction: The aim of this prospective randomized trial was to evaluate the impact of ventilator mode on the development of respiratory complications in colorectal surgery and to investigate whether plasma soluble receptor for advanced glycation end products (sRAGE) and S100A12 levels are associated with the occurrence of respiratory complications after colorectal surgery.

Methods: Forty-six patients undergoing laparoscopic colorectal surgery were randomly allocated to receive mechanical ventilation using either volume controlled ventilation (VCV) ($n = 23$) or pressure controlled ventilation (PCV) ($n = 23$) mode. In the VCV group, ventilation mode was VC mode (tidal volume (TV) of 8 mL/kg of ideal body weight (IBW)) during the operation. In the PCV group, initial ventilation mode were VC mode (TV of 8 mL/kg of IBW) and after pneumoperitoneum ventilator mode were changed to PC mode (inspiratory pressure to provide TV of 8 mL/kg of IBW) and then ventilator mode were changed to VC mode after decompression of CO₂ gas. Respiratory parameters were measured and plasma sRAGE and S100A12 were collected at 5 minutes after induction (T1), 40 minutes after pneumoperitoneum (T2), the end of operation (T3) and 24 hours after operation (T4).

Results: Peak airway pressure was significantly higher in the VCV group compared with that in the PCV group (T2). Plasma sRAGE and S100A12 levels were also significantly higher in the VCV group compared with that in the PCV group (T2, T3) and sRAGE and S100A12 levels at T2 and T3 were positively correlated with a peak airway pressure (sRAGE: $r = 0.210$; $P = 0.013$; S100A12: $r = 0.238$; $P = 0.005$). In the receiver-operator characteristic (ROC) analysis, the areas under the curve (AUC) of sRAGE and S100A12 at T2 and T3 for respiratory complications were 0.708 (95% CI, 0.599 to 0.817) and 0.670 (95% CI, 0.559 to 0.781), respectively. However, incidences of respiratory complications were not statistically different between groups.

Conclusion: PCV during pneumoperitoneum in patients undergoing laparoscopic colorectal surgery showed lower peak airway pressure and less increase of sRAGE and S100A12 but did not decreased incidence of respiratory complications compared with VCV. The plasma levels of sRAGE and S100A12 were positively correlated with peak airway pressure and could be helpful for early detection of postoperative respiratory complications following laparoscopic-assisted colorectal surgery.

O-K-002

THE ASSOCIATION OF OXYGEN DESATURATION INDEX AND LIPOPROTEIN PHOSPHOLIPASE A2 TOWARDS CORONARY ARTERY DISEASE IN OBSTRUCTIVE SLEEP APNOEA MALE SUBJECTS

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Background: The mechanisms of coronary artery disease in obstructive sleep apnoea (OSA) are not well understood. The inflammatory cells produce lipoprotein phospholipase A2 (Lp-PLA2) and it may promote oxidation of low density lipoprotein and hydrolysing phospholipid to become lysophosphatidylcholine and oxidized fatty acid which have proatherogenic effect.

Objective: The aim of the study is to determine the association of oxygen desaturation index (ODI) with Lp-PLA2 towards CAD in OSA male patients.

Material and Method: This was a cross sectional design study with 74 samples, age 45–75 years old, with positive Berlin questionnaire, visiting Siloam Lippo Village Hospital for medical check up. Lp-PLA2 levels were measured in serum using PLAC test. Sleep test was performed according to their best time.

Results: Bivariate analysis showed that ODI with cut off point of 11.09 became a significant risk factor for CAD ($p = 0.02$, odds ratio (OR) 3.02). Lp-PLA2 had a protective effect on CAD ($p = 0.02$, OR = 0.32, 95% Confidence Interval (CI) 0.10–0.95) but had no significant results with the association to ODI or AHI. Plasma oxLDL levels were not significantly associated with either CAD or ODI. In multivariate analysis only ODI, BMI, Lp-PLA2 hs-CRP showed significant results.

Conclusion: ODI, Lp-PLA2 and another risk factors such as BMI and hs-CRP should be taken into account when considering risk factors for coronary artery disease in OSA male patients.

O-K-003

THE CORRELATION ANALYSIS BETWEEN SMOKING AND THE DISTAL LOWER LIMB ARTERIAL ABNORMALITY AS DETECTED BY IRTI AND CPUS IN A DOUBLE BLIND CONTROLLED CLINICAL STUDY

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Background: Infrared thermal imaging (IRTI) is a novel technique for non-invasive imaging detection of vessel function. Our previous research showed that IRTI could be used in diagnosing lower limb deep venous thrombosis (DVT). Other studies also reported that IRTI mainly detects disorders of peripheral arteries. In light of compression ultrasonography (CPUS) as currently the first-line noninvasive modality to detect DVT, we used IRTI and CPUS in detecting lower limb vessels of 124 healthy adults to analyse whether the distal lower limb arterial abnormality was associated with smoking and to evaluate the consistence between IRTI and CPUS detecting vascular abnormal.

Method: 124 healthy adults were included in the CPUS and IRTI double blind controlled clinical study. Meanwhile, the smoking status of these subjects was obtained. Abnormal CPUS or IRTI findings in a subject was defined as positive (+) and normal as negative (–) respectively. The correlation analysis between smoking and lower limb vascular abnormality was carried out by Pearson chi-square test, and the value of IRTI and CPUS detect on vascular abnormal was evaluated by McNemar chi-square test.

Results: Among the 124 subjects, there were 67 males and 57 females, including 31 smokers and 93 non-smokers, with a mean age of 42 ± 12 years old. Among 31 smokers, 29 were male and 2 female (mean duration of smoking: 19.33 ± 10.64 years). The number of both IRTI and CPUS negative subjects were 43, and both positive 47, CPUS negative but IRTI positive 34. Among the CPUS positive subjects, 18 were smokers and 29 nonsmokers; among the CPUS negative subjects, 13 were smokers and 64 nonsmokers. These figures were 28 and 53 among IRTI positive subjects, 3 and 40 among IRTI negative subjects, respectively. Smoking was related closely to the distal lower limb arterial abnormality (IRTI: $X^2 = 11.404$, $P = 0.001$; CPUS: $X^2 = 7.138$, $P = 0.008$). IRTI and CPUS detection of low limb arterial abnormality did not completely coincide with each other ($P = 0.000$).

Conclusion: Smoking is related to the distal lower limb arterial abnormal, and IRTI can discover the vascular dysfunction earlier than CPUS. IRTI and CPUS could be complementary.

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O-K-004

LONG-TERM RESULTS OF SMOKING CESSATION AND FACTORS INFLUENCING THE SUCCESS OF SMOKING CESSATION

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Objective: In view of the high prevalence of smoking, both public campaigns against smoking and smoking cessation programmes are of great importance for the protection of public health. In this study, the long-term success of patients, who had applied to a smoking cessation centre, in quitting smoking was investigated. The impact of the availability of cost-free treatment and the specialization of the treating doctor on the success of cessation was also investigated.

Method: This is a retrospective cohort study. Patients treated at a smoking cessation centre by pulmonologists and psychiatrists, from 01.06.2011 to 01.06.2012, constituted the study population. Data was obtained from the patient files, while the success of the patients in quitting smoking was determined by telephone interviews with the patients. Logistic regression analysis was performed to assess the success of smoking cessation.

Results: Data pertaining to 980 patients, 70.4% of which were male, was analysed. The mean age of the patients, who had consulted for smoking, was 41.3 years, and the mean age at smoking initiation was 16.4 years. The Fagerström Nicotine Dependence score was 6.2 and the total cigarette consumption per smoker was 26.6 packages/year. Only 3.6% of the patients had been referred to the centre by their doctor. The percentage of the patients, who visited the centre for post-treatment control, was 18.5%. While 50.8% of the patients were treated with bupropion, 30.6% were treated with varenicline, 9.8% received behaviour therapy alone, and 8.8% received nicotine replacement therapy. Of the 980 people, who had applied to the centre, only 660 (67.3%) were able to be reached. Of these people, who were interviewed on telephone, 53% declared to have never quit smoking and 25.5% to have restarted smoking, and the rate of long-term smoking cessation (on average for 20 months) was determined as 21.5%. Two main factors were influential on the success of smoking cessation: the age and the level of nicotine dependence of the smoker. Cessation success is 1.6 times higher in smokers aged 50 and above, compared to young smokers. The success of smokers with low nicotine dependence is approximately 2.3 times higher ($p < 0.01$).

The availability of cost-free treatment, the specialization of the treating doctor, and the treatment method applied were not effective on the success of cessation ($p > 0.05$).

Discussion: One out of five smokers succeeded in quitting smoking in the long-term. One-fourth of the smokers, who attempt to quit smoking, restart smoking. Unsurprisingly, the success of smokers with low nicotine dependence in quitting smoking is approximately two-fold higher.

It was noteworthy that only 18.5% of the patients, who had applied to the smoking cessation centre, attended post-treatment controls.

Conclusion: Irrespective of the treatment method applied, the specialization of the treating doctor and the cost of the treatment, the success rates achieved for smoking cessation are similar.

O-K-005

SYRINGO-PLEURAL SHUNT AFTER FIFTEEN YEARS – A RARE CAUSE OF RECURRENT PLEURAL EFFUSION

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This is a case report of one of the rarest cause of recurrent pleural effusion because of syringe-pleural shunt which after fifteen years has led to the said complication. The patient reported is case of post spinal tuberculosis who developed syringomyelia which itself is a rare sequelae of tuberculosis, has undergone syringopleural (SP) shunting. After fifteen years of normal working of shunt, the patient developed recurrent pleural effusion. Thoracentesis both diagnostic and therapeutic has been done. The fluid repeatedly examined was transudative and every effort to find out the cause was non-yielding. Computed tomography (CT) done focusing the shunt showed that it was in exact place. Pleural fluid was positive for beta-2 transferrin. Video-assisted thoracoscopic (VATS) exploration done and it was found that distal tip of shunt was adhered with the lung parenchyma. The pleural biopsy was negative for any malignancy or tuberculosis. The effusion did not progress further after the dislodgement of distal tip from lung parenchyma.

O-K-007

ASSESSMENT OF KNOWLEDGE, ACCESSIBILITY AND UTILIZATION OF PALLIATIVE CARE SERVICES AMONG ADULT CANCER PATIENTS AT TIKUR ANBESA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2014

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Background: Cancer has been the leading cause of death worldwide for more than two decades. More than 150,000 cancer cases were estimated to exist in Ethiopia each year. The goal of Palliative Care (PC) is to prevent and relieve suffering and to support the best possible Quality of Life (QOL) for patients and their families, regardless of the stage of the disease or the need for other therapies. This study attempted to assess the knowledge, accessibility and Utilization of PC Services for adult cancer patients by their perspective at Tikur Anbesa Specialized Hospital (TASH), Addis Ababa, Ethiopia.

Method: A cross-sectional Institution based study was conducted among respondents who had Cancer at TASH. TASH was the only referral centre of PC and cancer treatment in Ethiopia. So it was selected purposively. Data was collected by interviewing the client's using a pretested Amharic version questionnaire. During the survey, 384 respondents with cancer were interviewed. Data entry was done using Epi Info version 3.5.2 and exported to SPSS version 21 for analysis. Logistic regression model was applied to control confounders.

Result: Of the total clients interviewed, more than 62.2% respondents who had treatment in TASH were knowledgeable about PC for cancer. About 86% of client's were in the age 35 years and older. About Nine out of ten (89.8%) respondents reported problems on accessibility of Palliative Care (PC) services for cancer in TASH. Respondents knowledge of PC services (AOR = 26.9, 95% CI; 12.3, 59), presence of little physical wellbeing to the respondents (AOR = 3.1, 95% CI; 1.96, 4.9), full social wellbeing of the respondents (AOR = 1.7, 95% CI; 1.01, 2.8); monthly income \$US 25–50 of the respondents (AOR = 0.25, 95% CI; 0.09, 0.7) and single marital status of the respondents (AOR = 55.4, 95% CI; 1.2, 2660.4) were statistically significantly associated with respondents utilization of PC services for cancer at TASH.

Conclusion: High number of respondents reported problems on accessibility of PC services for cancer in TASH and more than just an average of respondents reported as they had knowledge. Respondent's knowledge on PC, physical wellbeing, social wellbeing, income and marital status were a concern for utilization of PC services for cancer at TASH. Health care providers at TASH are recommended to have a sustained health education session focusing on PC services to the clients with cancer. Facilitations required for the clients have to be made easily accessible based on the standards mentioned in this study in this Hospital. Community Mobilization through the media, posters and face to face on Community Health Day (CHD) focusing on PC services to cancer must be addressed by Addis Ababa Town administrations and policy makers. The Federal Democratic Republic of Ethiopia, Ministry of Health must plan to build more additional centre in Addis or elsewhere in the country for more awareness creation to the clients and achievement of PC services by the majority.

ORAL PRESENTATION – PAEDIATRICS

O-L-002

O-L-001

LUNG FUNCTION AMONG EARLY ADOLESCENTS DELIVERED TERM WITH LOW BIRTH WEIGHT

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Background: Conflicting results on the effect of low birth weight (LBW) on lung function among adults delivered with LBW had been reported in literature. Several studies have documented alterations in lung function; however some studies showed no correlation between LBW and abnormal lung function.

Objectives: The objective of the study is to determine the correlation of LBW with the present lung function of early adolescents who were delivered term, healthy and with LBW. Furthermore, the authors would like to determine the differences in the mean forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) among subjects with a) maternal history of active smoking during pregnancy, b) passive smoking, c) asthma, and d) pneumonia.

Methodology: In this cross-sectional study, 41 subjects in early adolescence (10–13 years old) delivered term healthy with LBW (<2.5 kg) underwent pulmonary function test to determine FEV1 and FVC. Other recorded information included birth weight, present weight and height, body mass index (BMI), smoking, and childhood illnesses.

Results: There is a weak correlation between LBW and abnormal lung function studies among early adolescence (Spearman's correlation coefficient range 0.002–0.160 or less than +1, $p = 0.17–0.495$). No statistically significant difference in mean FEV1 and FVC values were noted among those with history of maternal smoking, passive smoking and asthma. Only those with history of pneumonia at less than 2 years old had statistically significant mean predicted FVC values ($p = 0.042$).

Conclusion: We therefore conclude that LBW has a weak correlation with FEV1 and FVC among early adolescents.

Recommendations: The authors recommend that parental education and physician initiated efforts in promoting wellness aimed at preserving normal lung growth pre and postnatally should be aggressively pursued. Further longitudinal studies involving larger sample size and a longer follow-up period is encouraged to further investigate the issues on foetal or childhood insults that may be the basis for adult diseases.

IDENTIFICATION OF MMP DYSREGULATION IN EARLY CF – EVIDENCE BASED RATIONALE FOR ANTI-PROTEASE THERAPY

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Introduction: Matrix metalloproteinases (MMPs) are a family of enzymes crucial to extracellular matrix modelling and cell migration. Despite knowledge that inflammatory and structural CF lung disease begins in infancy, expression profiles of MMPs and their tissue inhibitors (TIMPs) have not been previously investigated in airways of young children with CF.

Aim: To test the hypothesis that MMP-2 and MMP-9 are present in bronchoalveolar lavage fluid (BALf) from infants with CF and would positively correlate with inflammation severity.

Method: Children with CF ($n = 64$, 0.27–6.50 years) underwent a clinically directed annual surveillance visit including BALf. Total MMP-2, MMP-9, TIMP-2 and TIMP-1 levels in BALf were measured by ELISA. Active/proenzyme ratio of MMP-9 was determined by gelatin zymography. Neutrophil number was measured by differential and total count, IL-8 by ELISA and neutrophil elastase (NE) activity by enzymatic assay. Results presented as mean \pm SD.

Results: BALf were stratified by presence of ≥ 104 cfu/mL infection or presence of detectable free NE activity. There was no significant difference in age between groups (2.88 ± 2.17 years, ANOVA $p = 0.15$). Significantly higher MMP-9/TIMP-1 ratios was associated with infection (73.42 ± 138.30 vs 374.20 ± 1080.00 , Mann-Whitney $p < 0.005$) and free NE activity (51.57 ± 88.89 vs 386.60 ± 1063.00 , Mann-Whitney $p < 0.005$). In contrast, MMP-2/TIMP-2 ratio did not change during infection (8.66 ± 8.95 vs 7.36 ± 9.52 , Mann-Whitney $p = 0.45$) but decreased significantly with free NE (12.74 ± 10.78 vs 3.12 ± 2.20 , Mann-Whitney $p < 0.0001$). Ratio of active/proenzyme MMP-9 was also significantly higher in the presence of free NE activity ($0.46 \pm .22$ vs 1.12 ± 0.73 , Mann-Whitney $p < 0.0001$) but not infection (0.67 ± 0.38 vs 0.86 ± 0.66 , Mann-Whitney $p = 0.60$). Furthermore, the imbalance of MMP and their inhibitors was only seen when NE was present. Across the study cohort, neutrophils per mL of BALf (Spearman $r(64) = 0.76$, $p < 0.0001$) were correlated with total MMP-9.

Conclusion: We report elevated MMP-9/TIMP-1 and decreased MMP-2/TIMP-2 in BALf that were associated with presence of free NE. Elevated MMP-9/TIMP-1 was observed in children as young as 3 months. Correlation with neutrophil number suggests MMP-9 burden is due to infiltrating neutrophils. Significant MMP-9 activation only in the presence of free NE corroborates the recent hypothesis that chronic free NE activates MMPs in vivo. Since MMPs are likely to play a critical role in the abnormal remodelling of CF airways, targeting the effects of free NE in CF could disrupt the pathway that links inflammation and the development of bronchiectasis.

O-L-003

DETERMINANTS OF ANNUAL CHANGE IN PEAK EXPIRATORY FLOW RATE (PEFR) AND PEAK INSPIRATORY FLOW RATE (PIFR) VALUES IN A COHORT OF INDIAN CHILDREN AGED 4–10 YRS

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Aim: Determinants of annual change in peak expiratory flow rate (PEFR) and peak inspiratory flow rate (PIFR) values in a cohort of Indian children aged 4–10 yrs.

Methods: PEFR and PIFR were measured for 2 consecutive years in a cohort of 813 children (467 boys, 356 girls) after obtaining a written informed consent from their parents. Height, weight and age of every child was recorded by trained medical nurse. PEFR was measured by an EU scale peak flow meter [Breathometer Ö, Cipla Ltd, India] and PIFR was measured by Clement Clarke Peak Inspiratory Flow Meter, UK. Best of 3 acceptable readings were used for analysis.

Results: Change in height was the major determinant of change in PEFR whereas change in PIFR did not correlate with height significantly. Change in age and weight did not have any impact on either PEFR or PIFR values.

Conclusion: Increase in height [growth of a child] is a major determinant of increase in their lung functions.

O-L-004

IDENTIFYING EARLY SIGNS AND SYMPTOMS OF IMPENDING ASTHMA EXACERBATIONS IN CHILDREN

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Despite advances in the treatment of asthma, exacerbations remain common. The National Heart Lung and Blood Institute's National Asthma Education and Prevention Program Guidelines recommend early treatment of asthma exacerbation as "key in management", but do not provide specific information or guidance about signs and symptoms that may present before lower respiratory symptoms. We aimed to describe early signs and symptoms of an impending asthma exacerbation in children, and to study how these symptoms vary during a well-period and illness periods.

To collect and study these signs and symptoms we performed focus groups followed by administration of surveys with a 57-symptom inventory (Asthmatic Child Early Signs and Symptoms (ACcESS) inventory) to 200 caregivers of children aged 1–12 years with physician diagnosed persistent asthma recruited from our pediatric asthma clinics. We then recruited caregivers (same inclusion criteria) to perform daily diary cards based on the symptom inventory during a 4-week well-period (ACQ < 1.5) in the summer (n = 19) and a 16-week winter period (n = 27) where there was likelihood of loss of control (≥2 consecutive days of increased LR symptoms).

A wide variety of symptoms were reported as preceding an asthma exacerbation. We categorized these into three main categories: non-respiratory (NR), upper respiratory (UR), and lower respiratory (LR). NR symptoms were further subdivided into changes in eating habits, appearance, activity, and behavior. The most common NR symptoms included decreased activity (31%), decreased appetite (25%), irritability (20%), difficulty falling asleep (19%), and paleness (11%). A total of 25% of caregivers reported runny nose as an early symptom and 68% reported cough. The very first symptom was NR in 25%, UR in 15%, and LR in 60%. Ninety-seven percent of caregivers were able to identify a first symptom, and 89% reported that this first symptom was present always or almost always. There was no difference in symptom reporting or symptom reporting category (NR, UR, LR) according to child's age, gender, ethnicity, race, or use of asthma controller, or the caregiver's age, gender, ethnicity, race, insurance type, income, and education.

During the 4-week well period, there was little symptom variability across all symptom categories. During the 16-week winter period, overall there was a trend for increased likelihood of reporting NR symptoms in the 3 days before loss of control episodes, including changes in behavior, mood, and appearance as compared to period where asthma was controlled. Some NR symptoms were consistently increased over the 3–4 days prior to an episode, with others increased only the day prior to an episode of loss of control. Overall, UR symptoms were not increased during the days prior to a loss of control episode.

In conclusion, caregivers identify a wide variety of signs and symptoms as occurring before an asthma exacerbation. These include non-respiratory symptoms and upper respiratory symptoms, in addition to the typical lower respiratory symptoms of asthma. These symptom patterns are not different by specific parental or child characteristics. The symptoms that were significantly increased before episodes of loss of control were mostly NR in nature. Furthermore, these symptoms do not significantly vary during a well period, and some children may exhibit symptom patterns with recurrent illnesses. A study is currently underway to assess whether augmentation of inhaled corticosteroids triggered by an ACcESS inventory-guided asthma management plan will change asthma morbidity by decreasing severity of asthma exacerbations.

ORAL PRESENTATION – PULMONARY CIRCULATION

O-M-001

REFERENCE VALUES FOR NORMAL PULMONARY ARTERY DIAMETER, RATIO OF PULMONARY ARTERY TO AORTA BY CT SCAN IN KOREAN POPULATION

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Background: The main pulmonary artery diameter (mPA), the aorta diameter (Ao) and the ratio of mPA to Ao (mPA/Ao) are easily imaged in every patient with chest computed tomography (CT). Previous studies have showed they could give us information on the possibility and disease status of diverse cardiopulmonary illness. However, there has been no large population study to determine the normal reference range of these parameters in Korea. We determined the gender-, age-specific distribution of normal reference values for mPA, Ao and mPA/Ao by CT in Korean population.

Methods: A non-contrast, ECG-gated, coronary calcium scoring CT imaging of 2,547 subjects who visited health screening centre in Severance hospital, Seoul, Korea, from January 2011 to December 2012 were used for measurement. Healthy subjects (n = 813) are defined as those without hypertension, diabetes, asthma, obstructive lung disease, ischemic heart disease, smoker, obesity, and abnormal CT finding. We measured the mPA and Ao at the level of bifurcation of main pulmonary artery and calculated the mPA/Ao.

Results: There were 1,023 (40.2%) female and 1,524 (59.8%) male with mean age of 53.1 ± 9.3 years. The mean mPA was 26.6 ± 3.4 mm and mean PA/Ao was 0.84 ± 0.13. mPA is significantly higher in following medical condition: men, obesity, smoker, hypertension, and diabetes mellitus. mPA/Ao is higher in women, obesity, non-smoker, normotensive group, and dyslipidaemic group with statistical significance. mPA/Ao tend to be reduced upon increasing of age in both men and women. In healthy subjects, the 75th percentile value for mean mPA diameter was 28.6 mm in men and 27.5 mm in women, and for mPA/Ao was 0.95, consistent with previous studies.

Conclusion: We established 28.6 mm in men and 27.5 mm in women as a reference value for mean mPA, and 0.95 for mean mPA/Ao in Korean population.

O-M-002

COMPARISON SERUM CA-125 LEVEL IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH AND WITHOUT PULMONARY HYPERTENSION

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Background: Chronic obstructive pulmonary disease (COPD) is a progressive and debilitating disease and is going to be the 3rd most common cause of death worldwide. Pulmonary hypertension (PH) has severely bad influence on prognosis in COPD patients. Hence, early diagnosis of it is important for appropriate therapy. Echocardiography is used for this purpose, which requires cardiologist and expensive equipment which may not be available anywhere. CA-125 a biomarker of ovarian cancer has shown to be associated with left ventricular failure. We aimed to show the relationship between CA-125 levels and PH in patients with COPD.

Methods: Ninety patients with stable COPD were enrolled into the study. Levels of CA-125 were measured from venous blood, and in the same day systolic pulmonary artery pressure (sPAP) was measured by transthoracic echocardiography.

Results: Of 90 Patients 51 had PH and 39 had not. Patients with PH had significantly higher CA-125 levels compared with controls (mean 39.15 U/mL vs. 24.22 U/mL, P < 0.04). Levels of CA-125 were correlated with sPAP (r = 0.17, P = 0.01).

Conclusions: The CA-125 biomarker can be used to identify COPD patients with pulmonary hypertension. Since it is cheap and easily available it can help in centres with less access to echocardiography.

O-M-003

EFFECT OF THROMBOMODULIN ALPHA FOR DISSEMINATED INTRAVASCULAR COAGULATION TREATMENT IN PATIENTS WITH LUNG CANCER

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Background: The mortality rate of disseminated intravascular coagulation (DIC) is higher in patients with lung cancer than in those without. We studied the effect of recombinant soluble thrombomodulin (TM) alpha for DIC treatment in patients with lung cancer.

Methods: Subjects were patients with DIC (n = 52; 39 men, 13 women; mean age, 71.7 years). Twenty-nine patients (21 men, 8 women; mean age, 70.7 years) had lung cancer and 23 patients (18 men, 5 women; mean age, 73.0 years) did not. No significant differences in background characteristics existed between the groups. We then compared the clinical data between surviving patients and fatal cases.

Results: No significant differences in the mortality rate were found between patients with lung cancer (65.5%) and those without (60.9%). The dose of TM alpha correlated negatively, but not significantly, (r = -0.134) with the recovery time from DIC. The dose of TM alpha in surviving patients (419.3 U/kg/day) was higher than in fatal cases (373.8 U/kg/day), but not significantly. The dose of TM alpha in surviving patients with lung cancer (462.5 U/kg/day) was significantly higher than in the other groups (fatal cases with lung cancer, 388.1 U/kg/day, p = 0.05; surviving patients without lung cancer, 370.5 U/kg/day, p < 0.05; fatal cases without lung cancer, 356.1 U/kg/day, p < 0.01). A significant negative correlation was observed between the number of platelets and the recovery time from DIC (r = -0.453, p = 0.05), but the correlations with fibrin/fibrinogen degradation products, the ratio of prothrombin time, and D-dimer levels were not significant. In addition, the relationships between mortality and these parameters, including platelets, were not significant.

Conclusion: The effect of TM alpha showed very little difference between patients with lung cancer and those without. Although 380 U/kg/day of TM alpha is the recommended dose for DIC treatment, the mortality of DIC may be improved by increasing this dose. Moreover, TM alpha should be used before the platelet number is severely decreased. We are continuing to enroll new subjects into our ongoing research and plan to present our final results at the Asian Pacific Society of Respirology 2014.

O-M-004

CLINICAL CONUNDRUM IN PULMONARY EMBOLISM DIAGNOSIS: MANAGEMENT OF IMAGING DISCORDANCE (NEGATIVE CT PULMONARY ANGIOGRAPHY AND HIGH PROBABILITY VENTILATION-PERFUSION SCAN); A CASE SERIES

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Introduction: Diagnosis of pulmonary embolism (PE) is normally achieved through a combination of clinical probability testing, imaging including ventilation-perfusion (V/Q) scan and CTPA (CT pulmonary angiography). However, the literature is limited on the decision making process and outcomes in cases with intermediate and high clinical pre-test probability of PE in the setting of discordant CTPA and V/Q scan results.

Aims: To examine the effects of anticoagulation therapy on V/Q mismatch and pulmonary artery pressures in patients with intermediate and high pre-test clinical probability in setting of negative CTPA and a high probability V/Q scan.

Methods: In our case series, we identified eight cases of PE who were reviewed at our Respiratory Outpatient Clinic between 1st January and 30th June 2014. Four cases had intermediate pre-test probability and four cases had high pre-test probabilities based on Well's Criteria. All cases had a negative CTPA but high probability V/Q scan at diagnosis. D-Dimers, Lower limb dopplers and Trans-thoracic echocardiograms (TTE) were included if available. We report on progress V/Q scan mismatches and right ventricular systolic pressures (RVSP) on TTE after therapeutic anticoagulation therapy.

Results: The high pre-test probability group demonstrated improvements in V/Q mismatches on progress scans. TTE was available in three cases with a median RVSP of 40 (IQR 39–43) mmHg and two cases demonstrated a reduction to a median of 32 (IQR 31–33) mmHg. Three cases in the intermediate pre-test probability group had improvements in V/Q mismatches but non-significant RVSP on initial TTE.

Conclusion: A negative CTPA result in a patient with high, and possibly intermediate clinical pre-test probability for PE warrants further investigation with V/Q scan. In our experience, anticoagulation therapy in the context of a high probability V/Q scan resulted in improvements in V/Q mismatches and RVSP. Further study with a larger series is warranted to develop a diagnostic pathway for patients with high clinical suspicion of PE.

O-M-005

THE CORRELATION BETWEEN CD4 LEVEL AND LEFT VENTRICULAR SYSTOLIC FUNCTION IN HIV/AIDS PATIENTS

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Objective: The research aimed to investigate the correlation between the CD4 level and left ventricular systolic function in HIV/AIDS patients.

Method: The research was an observational study with the cross sectional design conducted in Cardiac Center of Wahidin Sudirohusodo Hospital, Makassar from December 2013 to February 2014 consisting of 42 respondents. The populations were all the HIV/AIDS patients who fulfilled inclusive and exclusive criteria. The respondents were taken using the Consecutive Sampling. The assessment was conducted using questionnaire. The data were analysed using the Spearman's correlation test.

Results: The results of the research indicate that there is significant correlation between the CD4 level and Left Ventricular Systolic Function, dilated Cardiomyopathy incident is indicated by the dilatation of cardiac chambers of HIV/AIDS patients with the value of $p < 0.0001$ with coefficient correlation of $r = 0.747$ and $p < 0.0001$ with coefficient correlation of $r = 0.864$ in which the lower the amount of CD4 the lower the Left Ventricular Systolic Function and the higher the dilated cardiomyopathy incident in HIV/AIDS patients.

ORAL PRESENTATION – RESPIRATORY INFECTIONS (NON-TUBERCULOSIS)

O-N-001

CORRELATION BETWEEN ENDOTRACHEAL ASPIRATE GRAM STAIN AND RESULTS OF BACTERIAL CULTURE AMONG ICU PATIENTS ADMITTED IN A TERTIARY HOSPITAL IN CEBU FROM SEPTEMBER 2009 TO AUGUST 2010: A RETROSPECTIVE STUDY

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Background: Gram stain of endotracheal aspirates (EA) may play a role in the initial antibiotic management. In critically ill patients with suspected ventilator associated respiratory infection (VARI). Various studies done in the past differ regarding the correlation of gram stain to predict final culture result.

Objectives: This study determined the relationship between endotracheal aspirate gram stain and final culture results in intensive care unit patients with suspected ventilator associated pneumonia and to evaluate the utility of gram stain of endotracheal aspirate in decision-making related to empiric antibiotic administration.

Methodology: This is a retrospective analytical study conducted at a 12-bed ICU in a Tertiary Hospital in Cebu City, Philippines. Endotracheal aspirate gram staining was done on intubated patients suspected to have ventilator associated respiratory infection all of which proceeded with bacterial culture. Results of gram staining was compared to that of bacterial culture. Agreement between gram stain and organism was measured using simple K. All analysis were performed using Medcalc 12.3.1.

Results and Discussion: One hundred twenty four patients were included in the study. The most common gram positive organism is Streptococcus species at 9.7% (N = 12). The most common gram negative organism is Klebsiella species at 16.9% (N = 21), followed by Pseudomonas species at 16.1% (N = 20). Of those with negative gram stain, 5.6% (N = 7) had gram positive on culture and 22.6% (N = 28) had gram negative on culture. Of those with gram positive on staining 4.8% (N = 6) has also gram positive on culture, and those with gram negative on staining 14.5% (N = 18) had also gram negative on culture. The study showed the overall agreement between Gram stain class and pathogenic bacteria culture results to be fair (K = 0.37; 95%, CI 0.235–0.506).

Conclusion: Gram stains performed for clinically suspected ventilator acquired respiratory infection fairly predicts the final culture results thus have a limited role in guiding initial empiric antibiotic therapy in such patients.

O-N-002

THE PATHOPHYSIOLOGICAL COMPARISON OF SECONDARY PNEUMOCOCCAL PNEUMONIA AFTER H1N1 PANDEMIC 2009 OR H1N1 NEW CALEDONIA INFLUENZA

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Background: The outbreak of H1N1 pandemic 2009 influenza virus (PDM) caused high morbidity and mortality. The fatal cases were related with bacterial co-infection by *S. pneumoniae*, *S. pyogenes*, and *S. aureus*. There have been only a few studies reported about secondary pneumococcal pneumonia after PDM. In this study, we compared the secondary pneumococcal pneumonia in mice after PDM or H1N1 seasonal influenza virus (NC).

Method: Mice were infected intranasally with PDM or NC, followed 5 days later by nasal infection with *S. pneumoniae* (Sp). At 6, 16, and 48 hours after the pneumococcal infection, lung and blood samples were obtained to examine bacterial and viral titer, cytokines expression, and lung histopathology.

Result: The bacterial density increased similarly in both PDM/Sp co-infected mice (PDM mice) and NC/Sp co-infected mice (NC mice). Compared with NC mice, PDM mice showed higher level of inflammatory cytokines, but lower level of anti-inflammatory cytokines. In the histopathology of the lung tissues of PDM mice, NS1 antigens from H1N1 influenza virus were detected in the alveolar and bronchoalveolar epithelium. In contrast, they were found only in the bronchoalveolar epithelium of NC mice.

Conclusion: Our data indicated that PDM was more invasive in lungs and provoked more severe inflammation in comparison with NC. In contrast, the bacterial load in the lungs after influenza infection was comparable. These results suggested that enhanced inflammation played a critical role to establish severe clinical manifestation of secondary bacterial infection after PDM infection.

INVESTIGATION OF THE ANTIBACTERIAL MECHANISM OF EUGENOL AND CINNAMALDEHYDE ON LEGIONELLA PNEUMOPHILA

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Objective: To investigation the antibacterial mechanism of eugenol and cinnamaldehyde on Legionella pneumophila (Lp).

Methods:

1. Lp was incubated with eugenol and cinnamaldehyde of different concentrations, then the OD260 of the supernatants were determined. The supernatants were analysed by SDS-PAGE electrophoresis, silver staining and Coomassie brilliant blue staining.
2. Integrity of the bacterial envelope was assessed by the fluorescence-based LIVE/DEAD BacLight Bacterial Viability kit.
3. Transmission electron microscope (TEM) was used to observe the morphology changes of Lp treated by the drugs

Results:

1. The OD260 was significantly higher in the Lp solution treated with eugenol at 0.5%, 1%, 5% concentrations than the normal group. There was no significant increase in cinnamaldehyde treated group. Silver staining of Eugenol at 0.5%, 1% concentrations displayed multiple protein bands, the prominent band was 38 kDa, Coomassie blue staining only displayed the 38 kDa band, which illustrated that the 38 kDa molecule was the earliest and most leaked protein when treated by eugenol.
2. The percentage of bacteria with intact envelope was decreased significantly in the eugenol group than the cinnamaldehyde group at the same concentration of 4MIC, 8MIC and 32MIC.
3. The outer membrane of Lp treated with Cinnamaldehyde (1 mg/ml) was still visible by TEM, with high cytoplasmic density. The wavy outer membrane of LP treated with eugenol (1%) disappeared, with thin cytoplasmic, lower density, and visible leakage from damaged cytoplasmic membrane.

Conclusion: Eugenol exerted activity on the envelope of Lp, leading to cell membrane damage, increased permeability, intracytoplasmic material leakage, and resulting in bacterial death. Cinnamaldehyde did not significantly alter the permeability of the envelope of Lp.

O-N-004

LONG-TERM MACROLIDE ANTIBIOTIC THERAPY MAY PREVENT THE DEVELOPMENT OF PNEUMONIA IN THE ELDERLY

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Pneumonia in the elderly is thought to be caused by swallowing dysfunction and an impaired mucociliary transport system. Macrolide antibiotics have immunomodulatory effects, and can ameliorate the effects of decreased mucociliary function. However, the role of macrolide antibiotics for the prevention of aspiration pneumonia remains unclear. Therefore, we evaluated the clinical effects of long-term treatment in elderly people. Fifteen patients aged 65 years and older, who were administered macrolide antibiotics for over six months for the prevention of pneumonia, were retrospectively assessed. We excluded patients with diffuse panbronchiolitis, chronic obstructive pulmonary disease and chronic sinusitis from this study. The frequency of pneumonia that required hospitalization during a period of one year before or after the commencement of long-term macrolide therapy was compared. As a result, no statistically significant decrease in the frequency of hospitalization due to pneumonia was observed in the overall patients. However, 11 patients who had suffered from pneumonia and had required hospitalization one or more times before the administration of macrolide antibiotics had significantly fewer hospitalizations due to pneumonia after the start of the macrolide antibiotic administration [from median, 1 (IQR, 1–3) time to 1 (0–2) time, $p = 0.035$ (Wilcoxon signed-rank test)]. Long-term macrolide antibiotic therapy may prevent the development of pneumonia in elderly patients who are susceptible to developing pneumonia. A further large prospective study is needed to verify this result.

O-N-005

PHARMACOECONOMIC ANALYSIS OF STRATEGIES FOR DIAGNOSIS AND TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN THE FOCUS OF VIRAL ETIOLOGY

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The studies of the recent years significantly expanded and altered the traditional understanding of the etiology of community-acquired pneumonia (CAP) and other complications, paying increasing attention to viral pathogens. New diagnostic technologies and tools of molecular research methods also as therapeutic strategies are quite expensive, so this fact makes it relevant to study feasibility of the use of such strategies for the diagnosis and treatment of patients with CAP. There were proposed probabilistic mathematical models, taking into account costs, diagnostic and therapeutic effectiveness of each strategy. Cost-effectiveness ratio (CER) and incremental cost-effectiveness ratio (ICER) were calculated as the ratio of the costs of strategy to the diagnostic or therapeutic effectiveness of its use. On the basis of proposed models it has been developed computer software which involves univariate and multivariate probabilistic analysis of CER and ICER. As the example of software application it was used own data from clinical research study, conducted during the autumn and winter seasons of 2012–2013. There were analysed clinical samples from 112 patients from 19 to 25 years with CAP, who received or did not receive additional antiviral therapy. It was analysed alternative diagnostic and therapeutic strategies: the use of rapid tests for one pathogen, the use of multiplex PCR for twelve respiratory viruses, among which one could be detected with rapid tests, as well as the use of rapid test and verification of its negative result using multiplex PCR. Multivariate probabilistic analysis towards to the diagnosis of adenoviruses (4.46% of the investigated samples) showed that implementation of multiplex PCR will reduce the cost per unit of diagnostic effectiveness by 24.36% versus the use of rapid tests. Despite the additional costs for the use of antiviral agent, total cost of antimicrobial therapy was significantly lower than in the control group by 15.54%. The results of simulations showed that, despite the relatively high cost, the implementation of multiplex PCR method into the diagnostic strategy of respiratory viruses in patients with CAP is an economically viable solution. It was also shown that the use of antiviral drugs as additional treatment is cost-effective and significantly reduces the incidence of infectious complications, duration of occurrence, duration of antibiotic therapy, and time to achieve positive outcomes in patients with viral and bacterial CAP.

O-N-006

MULTIDRUG RESISTANT GRAM-NEGATIVE BACTERIAL ISOLATES CAUSING NOSOCOMIAL PNEUMONIA IN A TERTIARY CARE HOSPITAL, NEPAL

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Introduction: Nosocomial infection is becoming a leading problem in medical practitioners now-a-days placing an extra burden on individual patients worldwide. Nosocomial pneumonia caused by multidrug resistant (MDR) pathogens is a major threat in the intensive care unit patients in developing country which are increasing numbers in Nepal.

Objective: The aim of this study was to determine the etiology of nosocomial pneumonia caused by multidrug resistant Gram-negative bacterial isolates.

Methods: A total of one hundred Gram-negative bacterial strains isolated from the patients diagnosed of nosocomial pneumonia were studied during 2011–2012 at Tribhuvan University Teaching Hospital (TUTH). Antibiotic sensitivity test was determined by modified Kirby Bauer Disc Diffusion method as described by Clinical and Laboratory Standards Institute (CLSI).

Results: Nosocomial pneumonia were caused by *Acinetobacter calcoaceticus baumannii* (Acb) complex was found to be more predominant (36 %) which was followed by *Klebsiella pneumoniae* (28%) and *Pseudomonas aeruginosa* (17 %). Of the total isolates, eighty seven percent were MDR which is much higher in Acb complex and *Escherichia coli* (100%) each.

Conclusions: The emergence of MDR bacterial strains causing nosocomial pneumonia are increasing in number. The high prevalence of MDR has demanded the special attention to the management of such patients and prevention of dissemination of such strains into hospital.

O-N-008

DYNAMIC CHEST IMAGING EVALUATION IN SEVERE AVIAN INFLUENZA H7N9 VIRUS INFECTED PATIENTS: A RETROSPECTIVE SMALL-SCALE STUDY

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Introduction: As a potential emerging pathogen with significant associated morbidity and mortality, a broader understanding of chest radiographic characteristics associated with human H7N9 infections is needed, especially dynamic chest computed tomography (CT) evaluation and in cured cases.

Methods: Lesion patterns, distributions, and changes at follow-up chest X-ray and/or CT were investigated in patients with H7N9 influenza (n = 11). Clinical courses were divided into 2 groups on the basis of mechanical ventilation therapy (group 1) or not (group 2). The time to progress on image and the time to initial resolution on CT were assessed.

Results: The most common thoracic CT findings were exudative lesions, lobar consolidation with air bronchogram and patchy infiltration. The time to progress on image was days 1–6 days (a median value, 3). For 7 recovering patients, the time to initial resolution on CT was 6–54 days (a median value, 18). Radiologic changes correlate with patient course, and resolution of pneumonia was delayed in group 1. After resolution of illness, the secondary fibrosis and traction like bronchiectasis were main exhibition of chest CT scan in recovering patients.

Conclusions: We have shown that a comparative longitudinal assessment of CT changes in patients with H7N9 with and without a complicated course provided insight into the course of this emerging infection.

O-N-007

ARE THERE ANY DIFFERENCES ON CLINICAL MANIFESTATIONS OF COMMUNITY ACQUIRED PNEUMONIA ACCORDING TO PRESENCE OF NON-TUBERCULOUS MYCOBACTERIUM?

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Background: Nontuberculous mycobacterium (NTM) has been frequently found in patients with chronic lung diseases such as bronchiectasis and post infectious destroyed lung. To get the diagnosis of NTM pulmonary diseases repeated NTM positive culture is needed. Clinical implication of NTM positive sputum culture other than NTM pulmonary diseases is not certain.

Hypothesis: Presence of NTM in sputum negatively influences to the clinical manifestation and prognosis of community acquired pneumonia (CAP).

Methods: Clinical data of admitted patients with community acquired pneumonia from January 2012 to December 2012 were reviewed retrospectively. Positive NTM culture group was defined as at least one positive culture of NTM expectorated during admission period.

Results: Among all 230 patients who admitted with the diagnosis of CAP, there were 23 patients (10%) with positive NTM culture. There was no difference in age (67.6 vs. 66.0) and female sex ratio (61.0% vs. 58.5%) between positive and negative culture group. Bronchiectasis was found on chest CT in 6 (6/16, 37.5%) in NTM positive patients and 35 (35/124, 28.2%) (p > 0.05). Cavitary lesions were infrequently found in both group (2/16 [12.5%] vs 13/124 [10.5%], p > 0.05). Length of hospital stay was mean 11.4 days in NTM positive group and 9.7 day in negative group (p > 0.05). Mortality rate was higher in NTM positive patients (4/23, 7.4%) than in NTM negative patients (16/202, 7.9%) but there was no statistical significance (p = 0.130).

Conclusion: Positive NTM culture in sputum makes no differences on clinical manifestations and prognosis of admitted patients with CAP.

O-N-009

INCREMENTAL PROGNOSTIC PREDICT ABILITY OF CHEST COMPUTED TOMOGRAPHY IN PATIENTS WITH COMMUNITY ONSET PNEUMONIA

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Background: Chest computed tomography (CT) is not generally recommended for routine use in the management of community onset pneumonia (COP). However, chest CT can detect infiltrations and pleural effusions in the patients with negative chest radiography. We hypothesize chest CT has incremental prognostic predict ability for existing model in COP patients.

Method: This study was performed as a sub-analysis of registry sponsored by Adult Pneumonia Study Group Japan (APSG-J). We included 267 COP patients who were admitted to our hospital and received chest CT. We generated two new prognostic scores for our cohort. X-ray modified CURB-65 was defined as follows; original CURB-65 (5 points) + pleural effusion in x-ray (1 point) + infiltrations over two lobes in x-ray (1 point). CT modified CURB-65 was defined as follows: original CURB-65 (5 points) + findings of pleural effusion in CT (1 point) + infiltrations over 4 lung lobes in CT (1 point). We compared the prediction capabilities of original CURB-65, x-ray modified CURB-65 and CT modified CURB-65 for 30-days mortality.

Result: There were no statistically significant differences between the area under the receiver-operating characteristic curves (AUCs) of original CURB 65 (0.64, 95% CI:0.50–0.78) and of x-ray modified CURB 65 (0.65, 95% CI:0.51–0.79, p = 0.46). However, AUC of CT modified CURB 65 (0.76, 95% CI:0.65–0.88) was larger than that of both original CURB-65 (p < 0.001) and x-ray CURB-65 (p < 0.001).

Conclusion: Modified CURB-65 criteria based on chest CT findings improved the prognostic prediction capability of original CURB-65. This suggests that CT findings have incremental prognostic predictability to existing model in patients with COP.

O-N-010

COMMON PRESENTATION OF UNCOMMON INFECTION: A CASE OF PULMONARY ACTINOMYCOSIS

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69 year old patient presented with of shortness of breath, MRC Grade II for 3 months with minimally productive cough with wheezing associated with mild fever, generalized ill health. He denied of allergic predisposition or significant family history. He is current smoker with 45 pack years. Patient had been working as a farmer for 15 years mainly in vegetable and paddy. Clinical examination revealed coarse crepitations in the right mid and upper zones associated bilateral rhonchi and normal other system. Biochemical investigations revealed ESR 26 mm/1st Hr, CRP < 5 mg/dl, FBC. Renal function and liver function tests were within normal range. Mantoux test 6 mm, nebulized sputum for acid fast staining negative. Chest X-ray showed thin wall cavitations, nodules, patchy consolidation with minimal fibrosis in right mid zone. HRCT of the lung revealed Irregular patches of consolidation involving R/middle lobe and anterior segment of the right upper lobe with adjacent pleural thickening, fibrotic areas with bronchiectasis. Soft tissue density materials seen in distal part of right main bronchus and right upper lobe bronchus too. Focal areas of bronchiectasis in L/lingular lobe, no hilar or mediastinal adenopathy. Fibre optic bronchoscopy showed fungating growth infiltrated into the right upper lobe bronchus which has covered with yellow colored thick slough. Histopathology of bronchial biopsy revealed reactive bronchial epithelial cells with scattered lymphocytes, no malignant cells or granuloma seen suggest actinomycosis with moderate to chronic inflammation highly suggestive of Infection. BAL was negative for mycobacteria, other organisms and malignant cells. Patient received treatment with Intravenous C. penicillin double dose 4 Mu 6 hourly for 10 days and followed by oral Coamoxyclav 625 mg three times per day. He improved ill health and constitutional symptoms and currently being followed up in regular clinic with plan of continuation treatment for the period of 6 months.

Discussion: Actinomycosis is a rare cause of pulmonary infection which is frequently under diagnosed. There are no reported cases in Sri Lanka. This country is recognized as intermediate burden for tuberculosis and tendency of misdiagnosis of pulmonary Actinomycosis as cases of negative PTB. It is important to consider these rare possibilities in diagnosis work up in a case of suspected chronic pulmonary infection with negative microbiological proof for common disease like tuberculosis in order to avoid unnecessary treatments and targeting them to appropriate management to prevent morbidity and mortality. These diseases are easily treated if diagnosed early.

O-N-011

PROGNOSTIC FACTORS OF MORTALITY IN PATIENTS WITH DRUG-RESISTANT ACINETOBACTER BAUMANNII VENTILATOR-ASSOCIATED PNEUMONIA

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Background: Ventilator-associated pneumonia (VAP) caused by *A. baumannii* is associated with high mortality in critically ill patients.

Objective: To identify the prognostic factors of 30-day mortality in patients with VAP caused by drug-resistant *A. baumannii* and compare survival outcomes among multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) *A. baumannii* VAP.

Methods: A retrospective cohort study was conducted in medical intensive care unit at Chiang Mai University Hospital, Thailand. All adult patients diagnosed with *A. baumannii* VAP between 2005 and 2011 were eligible. Univariable and multivariable Cox's proportional hazards regression were performed to identify the prognostic factors of 30-day mortality.

Results: A total of 337 patients with microbiologically confirmed *A. baumannii* VAP were included. The proportion of drug-sensitive, MDR, XDR and PDR *A. baumannii* were 9.8%, 21.4%, 65.3% and 3.6%, respectively. The 30-day mortality rates were 21.2%, 31.9%, 56.8% and 66.7%, respectively. The independent prognostic factors were SOFA score >5 (HR = 3.33, 95% CI 1.94–5.72, P < 0.001), presence of septic shock (HR = 2.66, 95% CI 1.71–4.12, P < 0.001), SAPS II > 45 (HR = 1.58, 95% CI 1.01–2.46, P = 0.045) and inappropriateness of initial antibiotic treatment (HR = 1.53, 95% CI 1.08–2.20, P = 0.016).

Conclusion: Drug resistant *A. baumannii*, particularly XDR and PDR, were associated with high mortality. Septic shock, high SAPS II, high SOFA score and inappropriate initial antibiotic treatment were independent prognostic factors for 30-day mortality. For prevention of inappropriate initial antimicrobial therapy, centre with high incidence of drug-resistant *A. baumannii* should develop local empirical antibiotic guideline for VAP to cover this virulent organism.

O-N-012

ANTIBIOTIC USE FOR RESPIRATORY TRACT INFECTIONS IN CHILDRENTIWARI P¹, AHLAWAT R¹, GUPTA G²¹National Institute of Pharmaceutical Education and Research (NIPER), Sec-67, S.A.S. Nagar, Punjab, India, ²Charak Care Clinics, S.A.S. Nagar, Punjab, India

Background: Respiratory tract infection (RTI) is one of the most commonly occurring infections in children. Antibiotics are commonly prescribed for RTIs in children in primary care. According to NICE standard treatment guideline for RTI, URTIs are mostly self-limiting and complications are likely to be rare if antibiotics are withheld. Overuse of antibiotics for treating the RTI leads to irrational use.

Objective: To evaluate the antibiotic utilization for treating respiratory tract infections.

Method: An antibiotic utilization study was carried out in a paediatric outpatient clinic for the period of 8 months, on a pilot basis. The prescriptions of children up to 18 years of age diagnosed with respiratory tract infection were studied and the data was captured from the "Wise-kid" software.

Results: A total of 462 patients were included in the study. The average age of patients was found to be 44 ± 2.4 months. URTI were found to be commonly occurring infection in 430 children (93%), of these patients, only 60 patients (14%) were prescribed an antibiotic. Forty patients were prescribed with Azithromycin followed by prescribing of Amoxicillin, and clarithromycin. In LRTI out of total 32 children diagnosed with LRTI, 25 had actually received an antibiotic. Twelve patients were prescribed with combination of Amoxicillin and 13 patients prescribed with azithromycin.

Conclusion: Use of antibiotics in LRTIs was found to be in accordance with the NICE STG. From these results, it seems that the use of antibiotics in URTI can be further decreased.

Reference:

1. NICE. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. *National Institute of Health and Clinical Excellence*. 2008; 2008:1–122.

O-N-013

HEART RATE VARIABILITY AS A TOOL TO ASSESS THE SEVERITY OF COMMUNITY-ACQUIRED PNEUMONIA IN HOSPITALIZED PATIENTS: PRELIMINARY RESULTS

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Background: Many guidelines recommend various severity scores to assess community-acquired pneumonia (CAP). Growing evidence suggests that alterations in heart rate variability (HRV) correlate with the severity of illness.

Objectives: The aim of this study was to compare the performance characteristics of the severity scores with HRV to predict outcomes in CAP.

Methods: Patients with CAP were recruited. Demographic characteristics, medical illnesses, HRV record and baseline blood tests were recorded. The outcomes of CAP were 30-day mortality and intensive care unit (ICU) admission. Relationships between HRV, low frequency (LF), high frequency (HF) and ratio of LF/HF with these scores were recorded.

Results: Eighty-four episodes of CAP were entered into analysis. Changes in abnormal HRV activity were HRV 21.4%, LF 23.8%, HF 23.8% and LF/HF 25.0%. Most of the ICU patients had low significance of HRV ($p = 0.03$), low LF ($p = 0.04$), and high HF ($p = 0.04$). Patients with low LF and high HF significantly had 33% ICU admission and mortality rates. HRV (0.80) and LF (0.78) had higher areas under the ROC curves than PSI IV + V (0.77) and ATS-IDSA2007 (0.71).

Conclusions: Finally, we found that patients who had a high HF and decreased level of LF, LF/HF ratio, or HRV, required more ICU interventions. Low LF and high HF played a crucial role in mortality in severe CAP. In addition, LF and HRV had better overall discrimination to test the performance of ATS-IDSA2007, CURB65, CRB65, SMART-COP, SMRT-CO, and PSI in predicting outcomes in CAP.

O-N-014

A CONTROL OF RESPIRATORY TRACT INFECTION IN ADULT PATIENTS AFTER CARDIAC SURGERY IN POST SURGICAL ICU. A STUDY OF 300 PATIENT RANDOMLY AND CO-RELATE THE PATIENT RESPIRATORY CULTURE WITH ENVIRONMENT AND OT CULTURETHOSANI RM, THOSANI AR, DOSHI C, SURTI JIGAR, MARIA R
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300 patients from ASA Grade II were selected who were posted for coronary and valvular heart surgery in this study. 195 male and 105 female patients were randomly selected to find out the co-relation between environment and OT culture with respiratory tract infection in developing country. The aim is to screen the patient for direct infection or for indirect infection as hospital acquired. These all patient were treated with proper antibiotic as per culture and sensitivity. In our study there were 3% mortality in patient who required long term ventilation for more than 5 days. These study has cleared that aseptic precaution, proper antibiotics, pre operative screening has more role to prevent the infection in post op ward in the major institute where more than 13 cardiac surgery per day. We also found drastic reduction of infection only by proper hand wash before touching to the patients.

O-N-015

NONTUBERCULOUS MYCOBACTERIA LUNG INFECTION IN BRONCHIECTASIS IN CHINA: PREVALENCE AND CLINICAL CHARACTERISTICSXU J-F, JI X-B, FAN L-C, BAI J-W, LU H-W, LI H-P, XIAO H-P, FEI K
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Rationale: To discuss the prevalence, risk factors and clinical features of NTM lung infection in bronchiectasis patients in China.

Methods: Retrospective analysis of the information of patients diagnosed as bronchiectasis or bronchiectasis with NTM lung infection from January 2009 to December 2012 in the electronic databases of a tertiary specialized hospital. The demographic data, risk factors and clinical characteristics data were concluded and comparatively analysed. Systematic analysis was performed in 192 cases who diagnosed as bronchiectasis with NTM lung infection.

Results: The number of eligible patients with bronchiectasis was 3,857 cases. 431 cases of bronchiectasis had at least one positive culture result of NTM, the separation rate was 11.2%. Patients with ultimate diagnosis of bronchiectasis with NTM lung infection were 192 cases, accounting for 4.98%. The sex ratio of bronchiectasis with NTM lung infection group was 1:2.1. They were mostly from the southern provinces. The percentages of past history of pulmonary tuberculosis in bronchiectasis patients with or without NTM lung infection were significantly different (16.7% vs. 28.8%). The proportion of history of long-term use of immunosuppressive agents in bronchiectasis with NTM lung infection patients (11.5%) was significantly higher than that in bronchiectasis patients (5%). There are no differences on age, smoking history and history of diabetes between two groups. 24.3% of the bronchiectasis with NTM lung infection patients showed CD4 + T/CD8 + T cell ratio decreased. The positive rates of blood tuberculosis antibody test and blood interferon gamma release assay (IGRA/T-SPOT) test in bronchiectasis with NTM lung infection patients were low. The PPD skin test results mainly showed a diameter of less than 10 mm. The separation rate of other bacteria in bronchiectasis with NTM lung infection (14.1%) was lower than that in bronchiectasis patients (24.5%). The CT-scan of bronchiectasis with NTM lung infection showed lung lesions mainly in the above lung fields, with dominant of thin-walled small cavities, small nodules or fibre cord.

Conclusion: 4.98% of bronchiectasis patients combined with NTM lung infection. Women, residents of southern and long-term use of immunosuppressive agents in bronchiectasis patients were prone to accompany NTM lung infection. For susceptible bronchiectasis patients, doctors should take the initiative to screen whether combining NTM lung infection.

O-N-016

ASSOCIATION BETWEEN INTERLEUKIN-6 SERUM LEVEL WITH TREATMENT FAILURE OF COMMUNITY ACQUIRED PNEUMONIA PATIENTS WITH COMORBIDS COPD AND HEART FAILURE

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Background: Treatment failure in community acquired pneumonia is related to lack of response to antibiotic treatment and it also depends on the causal microorganism, the initial severity of the infection, host conditions, and Interleukin-6 (IL-6) serum level. This study aimed to evaluate factors associated with treatment failure in community acquired pneumonia with comorbid COPD and heart failure.

Method: 16 patients of CAP with comorbid COPD and heart failure which is hospitalized in Saiful Anwar Hospital were observed by the host factors (age and smoking status), causal microorganism and measurement of serum IL-6 level that were obtained on day 1, 3, and 7 with ELISA method.

Result: 4 (25%) out of 16 patients had a failure treatment which is called late failure treatment. Based on repeated ANOVA analysis, the average serum IL-6 level on day 1 = 85.83 ± 50.89 pg/ml, day 3 = 42.63 ± 23.11 pg/ml, day 7 = 16.94 ± 11.49 pg/ml. According to contingency coefficient analysis, the age was not significantly contribute to treatment failure ($p = 0.146$), smoking status ($p = 0.368$), and causal microorganism ($p = 0.126$). Sample t-test independent analysis showed that serum IL-6 level day 7 was significantly different ($p = 0.003$). Logistic regression analysis revealed that serum IL-6 level was not significantly influenced ($p > 0.05$).

Conclusion: Serum IL-6 level was decreased with CAP treatment. Statistically, treatment failure was not related with age, smoking status, causal microorganism, and IL-6 level serum.

O-N-017

INVESTIGATION OF THE MOLECULAR REGULATING EFFECT OF PROMOTER-ASSOCIATED SPACER SEQUENCES ON CTX-M EXPRESSION

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Objective: The aim of the project is to explore the modulatory function of the conserved promoters with different spacer sequences upstream of blaCTX-M and investigate the possible key element associated with blaCTX-M high-level expression.

Methods: Five kinds of promoter fragment of blaCTX-M with the different spacer sequences were amplified, sequenced and cloned into a specific expression vector pUA66 carrying green fluorescent protein (GFP) gene. These blaCTX-M, promoters with associated spacers and their recombinant plasmids were: (1) blaCTX-M-14, IS42 and pUA-IS42, (2) blaCTX-M-55, IS45 and pUA-IS45, (3) blaCTX-M-1, IS48 and pUA-IS48, (4) blaCTX-M-3, IS127 and pUA-IS127, and (5) 127 bp sequence of Kluyvera spp. -127 and pUA-127, respectively. Fluorescence microscope, flowcytometry measurement (FCM) and qRT-PCR were applied to analyse the expression of the blaCTX-M gene via GFP reporter at the level of RNA and protein.

Results: The nucleic deletion and point mutation downstream of the conserved promoter were detected in the spacer sequence between the promoters and blaCTX-M gene. IS48 displayed a trend to the highest fluorescence intensity (103) than the other transconjugants. IS42 and IS127 showed very closed fluorescence intensity (102–103). Fluorescence intensity of IS45 was slightly higher than -127 (101), which was the weakest in GFP expression. The relative GFP mRNA copies of IS48 was the highest (49.52 fold than that of -127). IS127, IS42 and IS45 were 44.02, 31.79 and 11 fold higher than that of -127 respectively.

Conclusions: The nucleic deletion and point mutation downstream of the conserved promoter of blaCTX-M may be the key element that implement the pivotal element of expression in blaCTX-M. The phenomena of ceftazidime being efficient hydrolysis by CTX-M-producing strain may be taken into account on blaCTX-M driven by stronger promoter, such as blaCTX-M-15.

O-N-018

COMMUNITY-ACQUIRED PNEUMONIAS IN DIFFERENT AGE GROUPS ON DATA OF THE FAR EAST OF RUSSIA

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Background: Community-acquired pneumonia (CAP) remains one of the leading problem of the modern public health in the Far East of Russia. One of the main epidemiological problems is to define the epidemiological peculiarities of pneumococcal CAP in different age groups. The other epidemiological problem was to determine the main risk factors in different etiology CAP groups. The aim was to define role of *S. pneumoniae* and to determine role of other respiratory pathogens in etiological structure of community-acquired pneumonia.

Methods: Our patients with confirmed CAP (400 patients) were divided on 4 age groups of 1–5 years, 6–15 years, adults (18–54), aged adults (55+). The etiology was established by PCR, then the cultures of *S. pneumoniae* were isolated and studied for antimicrobial agents resistance according to CLSI standards and MLST on Enright M.C.

Results: Pneumococcus was the leading pathogen in all age groups, and it was the most frequent in 1–5 children (42%), 6–15 (30%), 18–54 (35%), >55 years (60%). In some cases it was defined in association with the Chlamydia pneumoniae, Mycoplasma pneumoniae and Haemophilus influenzae. The resistance of pneumococci to macrolides was in all groups, and it was connected with the spread of the *mefE* and *ermB* determinants, and there were only 12 penicillin resistant strains. The isolates were distributed among four major serotypes: 23F, 14, 18C, 6B. MLST (30 isolates) showed the spread of sequence types 90, 189, 240 and some others. The prevalent MLST type in isolated pneumococci in aged patients was Taiwan-19F and in young patients Spain 23F clone.

Conclusions: Pneumococci remains the leading pathogen causing CAP in all age groups, and the epidemiological surveillance with molecular epidemiology study should be the first step for preventive measures and the spread of the pneumococcal vaccines (e.g. Prevnar) among population.

O-N-019

CHARACTERIZATION OF HUMAN METAPNEUMOVIRUS INFECTION OF PRIMARY HUMAN AIRWAY CELLS

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Aims: Human metapneumovirus (HMPV) is a recently discovered respiratory pathogen that presents with similar clinical indications to respiratory syncytial virus (RSV), ranging from mild respiratory symptoms to severe cough, wheezing, bronchiolitis and pneumonia. There is mounting evidence suggesting an association between HMPV infection and asthma exacerbation in both adults and children. Our study examined HMPV infection of primary human bronchial airway cells and assessed cytokine and innate immune responses.

Methods: We infected primary human bronchial epithelial cells, fibroblasts and macrophages with HMPV. Virus replication, production of inflammatory mediators and anti-viral responses were examined by RT-PCR and ELISA.

Results: HMPV can infect human bronchial epithelial cells, fibroblasts and macrophages with robust increases in replication. We observed differences between the cell types with virus replication peaking at 48 hours post infection in epithelial cells, whereas replication was still increasing at 72 hours post infection in fibroblasts and macrophages. Epithelial cells expressed the cytokine MIG, whereas fibroblasts and macrophages released MCP-1 (all $p < 0.05$ versus control). All cell types yielded strong anti-viral responses, expressing IP-10 and RANTES and the interferon-stimulated gene, ISG56 ($P < 0.01$ versus controls).

Conclusions: Our data demonstrate that HMPV infects and replicates in primary human bronchial epithelial cells, fibroblasts and macrophages, and induce a strong inflammatory and anti-viral response. Future studies are looking at these indices in cells obtained from asthmatic patients to identify a mechanism to explain the link between HMPV infection and asthma exacerbation.

ORAL PRESENTATION – RESPIRATORY NEUROBIOLOGY AND SLEEP

O-O-001

FAMILIAL AGGREGATION OF OBSTRUCTIVE SLEEP APNOEA USING CHILDREN PROBANDS – OBESITY MAKES THE DIFFERENCE

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Objective: This study aimed to examine familial aggregation of obstructive sleep apnoea (OSA) using paediatric probands.

Hypothesis: First-degree relatives of children with OSA have more severe OSA than those of children without OSA.

Methods: Children aged between 6 and 18 years who attended our paediatric sleep disorder clinic with symptoms suggestive of OSA were invited to undergo nocturnal polysomnography (PSG). Children with obstructive apnoea hypopnoea index (OAHI) between 1 and 5/h were defined as having mild OSA, while those with OAHI \geq 5/h had moderate-to-severe OSA. Control subjects without habitual snoring were recruited from a concurrent population-based epidemiological study. Parents and siblings of both cases and controls were also invited to undergo nocturnal PSG. Data analysis was performed to examine if first degree relatives of children with OSA had higher OAHI than those of children without OSA using generalized estimating equations. Subgroup analyses were performed to see if childhood OSA had significant association specifically with OSA in fathers, mothers or siblings. Separate analyses were also performed for families of overweight and normal weight children.

Results: Two hundred and twenty-two children were recruited, of whom 32 had moderate-to-severe OSA, 67 had mild OSA and 123 were controls. A total of 398 first-degree relatives participated, of whom 59 were of children with moderate-to-severe OSA, 120 were of children with mild disease and 219 were of healthy controls. We found that OAHI of first-degree relatives of children with moderate-to-severe or mild OSA did not differ significantly to those of controls after adjustment for age and gender ($p > 0.25$). Separate analyses for fathers ($p > 0.65$), mothers ($p > 0.06$) and siblings ($p > 0.3$) all showed negative findings. Subgroup analysis for families of normal weight children also revealed similar negative result ($p > 0.7$). Nevertheless, for families of overweight children, first-degree relatives of children with moderate-to-severe OSA had significantly higher log-transformed OAHI than those of children with milder disease even after adjustment for age, gender and body mass index (adjusted mean OAHI = 4.1/h c.f. 2.2/h, $p = 0.047$).

Conclusions and Implications: First-degree relatives of overweight children with moderate-to-severe OSA had significantly higher OAHI than those of children with milder disease. Similar results could not be obtained from families of normal weight children. This suggests that significant familial aggregation of OSA may only exist in families of overweight children. In contrast, OSA in normal weight children, that is caused by other factors such as adenotonsillar hypertrophy, may not be heritable.

O-O-002

FAMILIAL AGGREGATION OF OBSTRUCTIVE SLEEP APNOEA IN CHILDREN WITHOUT TONSILLAR HYPERTROPHY

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Family studies in adults suggest the presence of familial aggregation in obstructive sleep apnoea. Whether the presence of OSA in either or both parents affect disease occurrence in their offspring is unclear. In this study we aimed to investigate if OSA in either parent is a risk factor for childhood OSA, after controlling for the effect of tonsillar size. A total of 124 trios with a child/adolescent aged 6–18 years as index case were recruited. All cases and their parents underwent in-hospital and home nocturnal polysomnography respectively. Tonsillar size of the index subjects was assessed with the standard Brodsky grading system. Significant interaction was observed by tonsillar size of index subjects and family history of OSA ($p = 0.015$), therefore index cases who had minimal (grade I) or no tonsils (grade 0) and those with prominent tonsils (grade II to IV) were analysed separately.

Within the group of minimal or no tonsils, twenty-three out of a total of 46 index subjects had at least one parent with moderate-to-severe OSA (defined as an obstructive apnoea hypopnoea index (OAHI) of 15/h or more). Compared to those without a parent having moderate-to-severe OSA, subjects whose parent had the disease had a significantly higher OAHI (0.4/h (0–0.8) c.f. 1.2/h (0.3–3.4), $p = 0.036$) as well as a higher prevalence of OSA (defined as an OAHI $> 1/h$, 21.7% c.f. 52.2%, $p = 0.032$), while the two groups had similar age, body size and sex ratio. These findings were not seen in subjects with prominent tonsils. Our results suggest that parental history of OSA is a significant risk factor for the presence of disease in children with minimal tonsillar enlargement.

O-O-003

EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN MALE PATIENTS WITH MODERATE AND SEVERE OBSTRUCTIVE SLEEP APNOEA SYNDROME

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Objective: Brainstem auditory evoked potentials (BAEPs) are the potentials recorded from the ear and vertex in response to a brief auditory stimulation to assess the transduction along auditory pathway up to midbrain. The present study aimed to evaluate the prevalence rate of BAEP abnormalities in male patients with moderate and severe OSAS, and to analyse the possible correlation of BAEP abnormalities with sleep-related parameters.

Methods: Binaural BAEP were performed using MEB 9200 system before overnight polysomnography (PSG). All subjects were divided into three groups: moderate OSAS group (26 male patients), severe OSAS group (27 male patients) and control group (18 age-matched healthy subjects). The BAEP parameters were compared between the control and OSAS patients. The correlation was carried out between BAEP parameters and PSG results in OSAS patients.

Results: In 53 OSAS patients, 9 had BAEP abnormalities. The BAEP latency of wave I was prolonged in moderate OSAS group when compared to control group (1.57 ± 0.15 ms vs. 1.44 ± 0.11 ms; $P < 0.05$). The latencies of wave V and the interpeak latencies of III-V in severe OSAS group were significantly prolonged when compared to moderate OSAS group and control group (wave V: 5.75 ± 0.23 ms vs. 5.59 ± 0.28 ms and 5.63 ± 0.19 ms, III-V: 2.00 ± 0.22 ms vs. 1.89 ± 0.30 ms and 1.89 ± 0.19 ms; $P < 0.05$). Positive correlations between the latency of wave I and apnoea hypopnoea index, oxygen desaturation index and the percent of total sleep time spent under 90% oxygen level were observed in OSAS patients (0.59, 0.58, 0.55; $P < 0.05$).

Conclusions: Moderate and severe OSAS male patients showed BAEP abnormalities. This suggests that OSAS is a risk factor for auditory pathway dysfunction.

O-O-004

O-O-007

5-HT_{1A} RECEPTOR IN RAPHE MAGNUS NUCLEUS MODULATES VENTILATORY LONG-TERM FACILITATION INDUCED BY CHRONIC INTERMITTENT HYPOXIA

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Objective: Intermittent hypoxia can elicit ventilatory long-term facilitation (vLTF), which is a unique form of 5-HT-dependent respiratory plasticity. vLTF data were only collected after ~1 week chronic intermittent hypoxia (CIH), while the influence of 5-HT_{1A} receptor in raphe magnus nucleus (RMg) on the vLTF induced by longer CIH was not investigated. This study aimed to examine the role of 5-HT_{1A} receptor in RMg in the vLTF induced by 4-week CIH.

Methods: The rats were exposed to 4-week CIH (45 s 10% O₂/60 s 21% O₂, 188 s/cycle, 8 h/day), and the rats in control group were subjected to room air in parallel. vLTFs were measured before and on the 1st day, 3rd day, 7th day, 14th day, 21st day and 28th day of CIH in awake rats. As previously described, vLTFs were numerically expressed by the magnitude and duration of enhanced minute ventilation. Thirty minutes before the measurement of the vLTF, 8-OH-DPAT (5-HT_{1A} receptor agonist, 100 nL, 0.1 mM) was microinjected into RMg. In control group, artificial cerebrospinal fluid was injected. The rats were mainly divided into 4 groups: normoxia group, normoxia+8-OH-DPAT group, CIH group, CIH+8-OH-DPAT group.

Results: Compared to normoxia group, minute ventilation was unchanged in normoxia+8-OH-DPAT group, while vLTFs were elicited in all hypoxic rats. Compared to CIH group, the vLTF magnitude was lower in CIH+8-OH-DPAT group (13.25 ± 2.1% above baseline, 60-min duration vs. 10.10 ± 1.7% above baseline, 60-min duration; P < 0.05).

Conclusions: These data suggest that 5-HT acting on 5-HT_{1A} receptor in RMg plays a role in the vLTF response induced by 4-week CIH.

THE OBSTRUCTIVE SLEEP APNOEA AND ISCHEMIC HEART DISEASE STUDY

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Background: Ischemic Heart Disease (IHD) is the leading cause of mortality and morbidity in the world. Recent data suggests that it is a vitally important public health problem even among developing nations. Obstructive Sleep Apnoea (OSA) has been established as one of the important modifiable risk factors for IHD. However, it is often undiagnosed and therefore, untreated. Although studies linking IHD and OSA have been done in western populations, there is a paucity of data from India. This study aims at identifying the association between OSA and IHD among a cohort of patients diagnosed with IHD based on coronary angiography.

Methodology: This study was a prospective observational study conducted among 70 patients undergoing evaluation for IHD at the Department of Cardiology, CMC Vellore. The subjects were chosen by convenience sampling, depending on the willingness of the subjects to undergo sleep study and availability of the testing equipment. Clinical and laboratory data was collected using a standardized proforma. Testing for OSA was performed using a portable screening device- 'Apnea Link'.

Results: The prevalence of OSA and OSAS among the study cohort was 75.7% and 18.6% respectively. The prevalence of metabolic syndrome and syndrome Z among the study cohort was 77.1% and 58.6% respectively. Over half of the patients who were diagnosed with OSA had moderate or severe OSA. Subjects with increased neck circumference, history of snoring and witnessed apnoea had significantly higher risk of OSA (AHI ≥ 5). The severity of OSA showed significant correlation with witnessed apnoea and severity of IHD based on coronary angiography.

Conclusions: This is the first study from South Asia that has attempted to look at the prevalence of OSA in a cohort of patients with angiography proven IHD; and has demonstrated that it is high. There is significant correlation of the severity of OSA with the severity of IHD. If treatment of patients with OSA could favourably modify the prognosis of IHD patients, screening for OSA becomes important. Further studies are needed in larger number of patients to identify the subgroup of IHD patients that should be tested for OSA.

O-O-006

5-HT_{1A} RECEPTOR IN RAPHE DORSAL NUCLEUS MODULATES GENIOGLOSSUS CORTICOMOTOR ACTIVITY DURING ACUTE INTERMITTENT HYPOXIA

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Objective: Raphe dorsal (DRN) 5-HT neurons play an important role in the facilitation of genioglossus corticomotor activity induced by intermittent hypoxia (IH). The increased genioglossus activity has been observed across sleep-wake cycle when the 5-HT_{1A} receptor of DRN descending neurons was suppressed, while the role of 5-HT_{1A} receptor in DRN on genioglossus corticomotor activity during IH was still unknown. In the present study, we evaluated the effect of 5-HT_{1A} receptor in DRN on the transcranial magnetic stimulation (TMS) response of genioglossus corticomotor area during acute IH.

Methods: The rats were divided into 4 groups: normoxia group, IH group, IH+ACSF group, IH+8-OH-DPAT group. Before the treatment of 1-hour IH (45 s 10% O₂/60 s 21% O₂, 188 s/cycle), 8-OH-DPAT (5-HT_{1A} receptor agonist, 100 nL, 0.1 mM) was injected into DRN in IH+8-OH-DPAT group. In IH+ACSF group, artificial cerebrospinal fluid (ACSF) was injected into DRN before 1-hour IH. The rats in normoxia group were subjected to room air in parallel. TMS were measured before and after 1-hour IH in all rats. Comparisons were conducted among the four groups.

Results: Before 1-hour IH, latencies of genioglossus TMS responses have no significant difference among the four groups. Compared to normoxia group, shorter latencies of genioglossus TMS responses were observed followed by 1-hour IH in IH group (4.73 ± 0.60 ms vs. 4.33 ± 0.18 ms; P < 0.05). There were no statistically significances between IH group and IH+ACSF group. Longer latency was found in IH+8-OH-DPAT group when compare to IH group (4.78 ± 0.49 ms vs. 4.33 ± 0.18 ms; P < 0.05).

Conclusions: The results suggest that 5-HT_{1A} receptor in DRN play a role in the inhibition of the genioglossus corticomotor facilitation induced by acute IH.

ORAL PRESENTATION – RESPIRATORY STRUCTURE AND FUNCTION

O-P-001

THE ROLE OF NITRIC OXIDE IN TRACHEOBRONCHIAL CILIARY MOTILITY

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Background: The ciliary beat is an important primary innate defense mechanism, and ciliary dysfunction leads to upper and lower respiratory tract diseases such as chronic bronchitis, bronchiectasis, chronic sinusitis and chronic otitis media in patients with primary ciliary dyskinesia (PCD) from their infancies. In patients with PCD, it is well known that exhaled nitric oxide (NO) levels is inversely correlated with the degree of ciliary beat frequency (CBF). However, the role of NO in ciliary motility is unclear. Therefore, we investigated the role of NO in ciliary motility using triply NOS knockout mice in the present study.

Method: We have determined CBF in 8–12 weeks male wild C57BL/6J and triply (*i/e/n*) NOS knockout mice. Tracheal rings of 1 mm width were quickly removed and mounted on the plate within the medium. Then, CBF were measured on 5 different locations in each mouse by high-speed video camera. Ultrastructure of the cilia was also evaluated using electron microscope.

Results: Mean CBFs were 15.8 ± 3.1 and 14.9 ± 3.1 beats/second in wild-type mice and triply NOS knockout mice, respectively ($P = 0.53$). There were no obvious ultrastructural abnormalities in inner and outer dynein arms, and radial spokes in both wild-type and triply NOS knockout mice.

Conclusion: There were no significant differences between wild-type and triply NOS knockout mice in CBF and ultrastructure of the cilia. We speculate that inflammatory stimulation (i.e. viral and bacterial infections) may reveal the differences of ciliary functions in triply NOS knockout mice, as repeated infections cause disease progression in patients with PCD, therefore, further study of CBF in wild-type and triply NOS knockout mice exposed to lipopolysaccharide is ongoing.

O-P-002

AGE AS THE MAIN PREDICTOR IN CORRELATING BLOOD PRESSURE AND LUNG FUNCTION IN MALAYSIAN POPULATION

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Background: The association between high blood pressure and lung function remains equivocal. An inverse relationship between lung function and blood pressure has been noted in several studies. However, no definite cause has been postulated as the main factor in causing the correlation between the two.

Objectives: To determine the correlation between blood pressure and lung function in the Malaysian adult population, and identify the main predictor of the correlation.

Materials and Methods: Data for this study were derived from the ongoing PURE RUS study, which is a prospective cohort study to track changing lifestyles, risk factors and chronic diseases in urban and rural population in Malaysia. Subjects aged 18–80 years and able to perform spirometry according to the American Thoracic Society criteria were included in this study. Subjects with underlying hypertension, smoker and chronic lung disease were excluded. A total of 1640 subjects fulfilled the criteria and were included in this analysis.

Results: Of the total, 43.5% were males and 56.5% were females. There was a significant negative correlation between lung function and systolic blood pressure (SBP) in both sexes measured by FEV1 ($r = -0.111$, p -value = <0.001) and FVC ($r = -0.104$, p -value = <0.001). There was also a significant negative correlation between age and lung function, seen in single and multiple linear regression (age vs FEV1: β = -0.02 , p -value: <0.001 , β = -0.026 , p -value: <0.001), (age vs FVC: β = -0.019 , p -value <0.001 , β = 0.026 , p -value: <0.001). A significant positive correlation can also be seen between age and systolic blood pressure, with $r = 0.322$, p -value <0.001 . No significant differences in lung function were evident between hypertensive and age-matched normotensive subjects.

Conclusions: Our findings are in line with previous observations showing an inverse correlation between blood pressure and lung function. However, this correlation is probably due to the effect of age rather than the effect of lung function on SBP or vice versa.

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O-P-004

THE RELATIONSHIP BETWEEN COLLAGEN FIBRE ORIENTATION AND ANISOTROPY IN MECHANICAL PROPERTY ON THE HUMAN LUNG

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Background: Respiration gives human lung the periodic mechanical stress. However it remains unclear how the lung maintains its structure against the mechanical stresses by respiratory movements. We have investigated the collagen fibre orientation in the human lung and demonstrated the collagen fibre orientation was closely related with respiratory movements. In this study, we aim to investigate the relationship between the collagen fibre orientation and mechanical property in two dimensions on the human lung

Methods: Sheet lung samples from the coronal and horizontal plates of the human lung were prepared for this study. Collagen fibre orientations on the sheet lung samples were measured by the microwave method. To investigate the mechanical properties, the sheet samples were cut into strips (5 mm × 15 mm) for two dimensions. The mechanical breaking energy at each strip was calculated by stress-strain curves measured using a Tensilon UTM-IIIIL instrument. The distributions of the mechanical breaking energy for two dimensions on the coronal and horizontal plates of the human lung were mapped.

Results: 1) On the horizontal plate the mechanical breaking energy was mainly high in anterior-posterior direction, while on the coronal plate it was mainly high in the perpendicular direction. 2) The mechanical anisotropy in coronal plate was correlated with the anisotropy of the collagen fibre orientation.

Conclusions: Mechanical anisotropy exists in the human lung tissue. The anisotropy in mechanical property of the human lung may be related with collagen fibre orientation.

O-P-005

ACUTE EFFECTS OF HYPERBARIC OXYGEN THERAPY ON RESPIRATORY RATE AND BASIC VITAL FUNCTIONS

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Background: Hyperbaric Oxygen Therapy (HBOT) is based on administration of 100% oxygen to the patients in a pressurized chamber. With this treatment, partial pressure of oxygen in the blood and body tissues is increased. Major urgent HBOT indications are CO poisoning, decompression sickness, and sudden vision/hearing loss. Routine indications are non-healing wounds, osteomyelitis, and radionecrosis. The aim of our study is to demonstrate the effect of HBOT on basic vital functions.

Method: A multi-place HBOT chamber is used in our hospital. Patients are evaluated by Aerospace Medicine specialist and the necessary follow-up and treatments are planned. Basic vital functions and patient data were collected by using two in-device monitor. Two measurements were taken, which are immediately before and after treatment. Calculations and tables were prepared by using the Microsoft Excel program.

Results: 18 patients were included in our study. Mean of pre-treatment values of our patients were calculated as blood pressure (systolic/diastolic): 117.4/75.1 mmHg, heart rate: 89.9, oxygen saturation: %97.2 and respiration rate: 19.2. Mean of post-treatment values of our patients were calculated as blood pressure: 116.8/73.4 mmHg, heart rate: 72.5, saturation: %97.8 and respiration rate: 18.5.

Conclusion: The acute effects of HBOT on basic vital functions have been investigated in our study. Reduction in patients' blood pressures and pulses were determined. Rise in saturation and decline of respiratory rate was noted in the parameters of the respiratory system due to hyperoxic treatment. In order to determine the chronic effects of HBOT, large clinical trials are needed.

ORAL PRESENTATION – TUBERCULOSIS

O-Q-001

CLINICAL BENEFIT OF DELAMANID (OPC-67683) IN THE TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS PATIENTS IN CHINA

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The cure rates are much lower for multidrug-resistant (MDR) tuberculosis (TB) patients. Delamanid (OPC-67683) has been evaluated in phase-II MDR-TB clinical trials. Herein, we reviewed MDR-TB cases in which treatment regimens, with/without delamanid, were administered. Thirty-eight patients were enrolled; 26 received delamanid-containing regimens (treatment group) while 12 received placebo-containing regimens (control group) for 56 days. Data regarding clinical/radio-microbiological characteristics, drug tolerability and treatment outcomes were collected. We found that all patients had isolates resistant to a median of 5 (range 2–7) drugs; 24 (92.3%) patients in treatment group and 11 (91.7%) in control group had cavities. Culture conversion was obtained in 32 pulmonary TB cases (median 74.5 days). At data censure, 30/38 patients successfully completed therapy with documented negative cultures for at least 18 months before the end of treatment. Two patients (5 consecutive negative cultures) are still on treatment. Six patients had poor outcome (3 failures/2 lost/1 death). In 13 patients, adverse events were observed that included mental disorder, QT interval prolongation and increased blood cortisol whereas only 3 patients stopped delamanid treatment because of adverse events. It was therefore concluded that delamanid was well-tolerated, had low rates of discontinuation and could be effective for treating MDR-TB.

O-Q-003

XPERT MTB/RIF TESTING OF POOLED INDUCED SPUTUM

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Some studies have suggested that Xpert MTB/RIF testing may not expedite pulmonary tuberculosis (PTB) treatment nor impact tuberculosis related morbidity in low and high disease burden settings. But this has not been evaluated in intermediate burden settings. We hypothesize that performing the Xpert MTB/RIF test on two induced sputa (IS) pooled together on the same day would improve diagnostic yield and impact treatment in symptomatic patients with active PTB. This is a prospective audit of adult patients suspected of PTB from June 2013 in a university hospital. In patients who were smear negative or unable to expectorate, 2 IS were collected and processed as one for acid fast bacilli, culture and Xpert. The reference standard for diagnosis of PTB was any positive culture. Patients were reviewed over 3 months. We report on the first 115 patients. PTB was diagnosed in 11/115 (9.6%). Positive Xpert in pooled IS detected 5/11 (45%) cases. 3/5 (60%) were smear, culture and Xpert positive. 2/5 (40%) were smear negative, Xpert and culture positive. One smear negative case was rifampicin resistant. Additional 6 cases of PTB were detected from other respiratory specimens. All 11 patients were started on treatment on a positive smear and/or Xpert test the same day. Detection of rifampicin resistance resulted in the use of second line drugs. There were also 5 cases of non-tuberculous mycobacteria of which 4 were smear positive. Among these, 1 patient who had positive smear but indeterminate Xpert test received empirical PTB treatment. We conclude that there is a potential role for Xpert testing of pooled IS to improve diagnostic yield and expedite treatment in nearly half of new PTB cases.

O-Q-004

A CASE-CONTROL COMPARISON OF THE MANTOUX TEST AND A COMMERCIAL INTERFERON GAMMA RELEASE ASSAY (IGRA) IN ADULTS: FIRST REPORT IN A SRI LANKAN SETTING

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The IGRAs are used to screen high risk populations for latent tuberculosis infection (LTBI). In the absence of a gold standard test for diagnosis of LTBI, active tuberculosis (TB) is used as a surrogate marker. IGRAs, which have shown variable test characteristics in different populations have not been evaluated in Sri Lanka. This study evaluated the performance of a commercial IGRA in comparison to the Mantoux test in patients with suspected pulmonary tuberculosis (PTB) and contacts of smear positive cases. Adult patients with no prior history of PTB were prospectively recruited and assigned to case or control groups based on results of sputum smear microscopy and/or mycobacterial culture. Routine investigative workup and IGRA (TSPOT.TB, Oxford Immunotec, Abingdon, UK) was done on all patients and adult contacts of smear positive patients. A total of 149 patients (cases n = 75, controls n = 74) and 27 contacts were included in the analysis. The sensitivity (95% CI), specificity, PPV and NPV of the Mantoux test for active PTB was 70.7% (54–83%), 64.2% (50–76%), 60.4% (45–74%) and 73.9% (58–85%) respectively. For the IGRA, the values were 73.5% (59–85%), 75.4% (62–85%), 72% (57–83%) and 76.8% (63–86%) respectively. Linear logistic models fitted to the data showed that active disease and a positive IGRA result had similar predictors while a positive Mantoux test was not predicted by these variables. Agreement between tests was moderate ($\kappa = 0.4113$). Of the contacts investigated, there was no significant difference between the proportions who were Mantoux positive (50%) vs. IGRA positive (27%). Neither test correlated with duration or proximity of exposure to the smear positive case. A high rate of indeterminate results (23.9%) was seen with the IGRA, mainly due to poor mitogen response ($p < 0.05$). Average cost of kit and consumables for one IGRA was LKR 9200. There was no significant advantage of using the IGRA as a screening test in this population. The higher specificity of the IGRA indicates that it would be a better test for use in diagnosis than the Mantoux, but high cost and high indeterminate result rate makes this test impractical for general use in the local setting. The wide confidence intervals of all estimates show the high variability seen in the test results.

O-Q-006

ANALYSIS OF MEDICAL BURDEN OF TB PATIENTS IN DOTS OF TAIWAN HEALTH INSURANCE

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Background: Under the proposal of day observation therapy (DOTs) in the whole country, pulmonary tuberculosis (TB) has the higher prevalence by the way of the aging community. So the outcome of pulmonary tuberculosis in primary health care institution is worth exploring in depth.

Method: We collected the local data of tuberculosis case management in new cases at the regional hospital from 2007 to 2009. Total case number was 516 patients. We analysed the outcome and trend of medical cost in the different hospital care retrospectively.

Result: The average age of tuberculosis was 61-year-old and average age is 61.66-year-old. The ratio of male/female is 62.6%/37.4%. The rate of abnormal radiology finding in chest is about 95.9%, which is very high. The positive rate of sputum smear is 61.2%. Total negative rate of family history in pulmonary tuberculosis is highly 97.5%. The case of extra-pulmonary lesion is totally 15.1%. The comorbidity of the total case is 55.2%, predominantly in the diabetics and cardiovascular disease. The average length of treatment is 171.8 days and the rate of complications totally is 33.9%, predominantly in the gastroenteral upset. The outcome of cure is totally 59.1% and the outcome of death is 11.8%. The average clinical visit is 7.2 and the length of stay in the hospital is 16.4 days. The average of medical cost in hospitalization is 1.5977.23 NT dollars. In the predictive analysis, the age and the body weight is the independent risk factor of the outcome, especially statistically difference when the age more than 75 and the BW low than 55 kilogram.

Conclusion: The prevalence and cure rate in tuberculosis got low in the past, but we still got low in WHO goal. In the ongoing aging society, the prevalence of the tuberculosis will increase, so we must take more care in the outcome and medical cost to benefit public health.

O-Q-007

COMPARISON OF CHARACTERISTICS OF PATIENTS WITH TUBERCULOSIS DIAGNOSED AND NOT DIAGNOSED BY FIBRE OPTIC BRONCHOSCOPY

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Background: Some patients with pulmonary tuberculosis in whom mycobacteria could not be detected with sputum examination also could not be diagnosed by fibre optic bronchoscopy.

Methods: We retrospectively reviewed 28 patients with tuberculosis who underwent diagnostic fibre optic bronchoscopy from April 2007 to March 2013 in Jichi Medical University Hospital. We defined the diagnosis of tuberculosis as a positive mycobacterium culture or a positive polymerase chain reaction. The patients were divided into two groups: those who were diagnosed by initial fibre optic bronchoscopy (Group A) and those who were not diagnosed by initial fibre optic bronchoscopy but diagnosed by further examination (Group B). We evaluated the clinical background, thoracic computed tomography (CT) findings, and the procedures of bronchoscopic examination in these two groups of patients.

Results: A total of 17 patients and 11 patients comprised Group A and Group B, respectively.

In Group B, 5 patients were diagnosed by operative thoracoscopic lung biopsy, 3 patients were diagnosed by sputum examination after fibre optic bronchoscopy, 1 patient was diagnosed by re-examination of the fibre optic bronchoscopy, and the other 2 patients were diagnosed clinically.

Between the two groups, there were no significant differences in age (53 vs. 53 years-old), BMI (20.6 vs. 20.0), and underlying diseases. The ratio of males to females was significantly higher in group B (52.9% vs. 90.9%, $p < 0.05$), pack year was higher in group B (16.6 vs. 32.2, $p < 0.05$), and the QuantiFERON-TB2G (QFT) positive rate was significantly higher in group A (90% vs. 37.5%, $p < 0.05$). No difference was observed in the following thoracic CT findings: tree-in-bud pattern (53% vs. 55%), consolidation (24% vs. 27%), single nodular lesions (12% vs. 18%), and cavity lesions (12% vs. 18%). However, pulmonary emphysema was significantly more frequent in group B (5.9% vs. 36.4%, $p < 0.05$). There was no difference in the inspection procedure: bronchial brushing (94% vs. 100%), transbronchial lung biopsy (TBLB) (71% vs. 82%), and bronchial washing (88% vs. 100%). However, tissue culture using TBLB specimens was performed in only 4 patients of Group A, and those results were all positive.

Conclusion: Patients with tuberculosis who have negative QFT results, a heavy smoking history, or pulmonary emphysema were difficult to diagnose by an initial fibre optic bronchoscopy. Tissue culture using TBLB specimens may be useful for diagnosis of pulmonary tuberculosis.

O-Q-008

CLINICAL AND BRONCHOSCOPIC CHARACTERISTICS OF PATIENTS DIAGNOSED WITH ENDOBRONCHIAL TUBERCULOSIS (EBTB) AT SELAYANG HOSPITAL, SELANGOR MALAYSIA

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Background: Endobronchial tuberculosis (EBTB) is defined as a tuberculous infection of the tracheobronchial tree with microbial and histopathological evidence, with or without parenchymal involvement. In this study, we observed the clinical aspects and bronchoscopic findings of 17 patients who were diagnosed with EBTB.

Methods: From 2011 to 2013, 17 patients were diagnosed as having EBTB based on the histopathological examination of endobronchial biopsy and/or positive AFB stain/culture on microbiological examination of bronchial alveolar lavage (BAL) specimens were included in our study. Demographics data, radiological, microbiological and histopathological findings were recorded. Endobronchial lesions were classified according to Chung classification.

Results: EBTB was found to be more common in females (M : F, 1/3) with a mean age of 43 years old (range: 16–74 years). About 47% of the patients have had underlying comorbid disease (type 2 diabetes, HIV, Systemic Lupus Erythematosus (SLE) on steroid therapy and post transplanted kidney on immunosuppressive drugs). Most common symptoms were cough (15 cases, 88%), fever (8 cases, 47%), weight loss (5 cases, 29%), haemoptysis (2 cases, 12%) and dyspnoea (1 case, 6%). Most common chest radiograph findings revealed consolidations (14 cases, 82%), cavitary lesions (4 cases, 24%), pleural effusion (1 case, 6%) and lung mass (1 case, 6%). Most common endobronchial lesions observed bronchoscopically were active caseous lesions (Type 1, in 8 cases, 47%), Oedematous hyperaemic lesions (Type 2) was seen in 3 cases (18%), tumorous lesions (Type 4) in 2 cases (12%), granular lesions (Type 5) in 2 cases (12%), ulcerative lesion (Type 6) in 1 case (6%) and fibrostenotic lesions (Type 3) in 1 case (6%). Most common histopathological examination (HPE) of biopsy specimens were caseating granulomatous inflammation in 8 cases (47%), granulomatous inflammation in 7 cases (41%) and chronic inflammation in 2 cases (12%). The bronchial alveolar lavage (BAL) specimens grew *Mycobacterium tuberculosis* in 65% of all cases.

Conclusions: EBTB is more common in female and younger patients below 50 years of age. In this study, the most common bronchoscopic subtype of EBTB was the active caseous lesion subtype and most of the cases showed good clinical response with antituberculosis treatment. After initiating antituberculosis, bronchoscopy was only repeated in 5 patients and all 5 showed a complete resolution of endobronchial lesion.

O-Q-009

AUDIT OF TUBERCULOSIS TREATMENT INTERRUPTERS IN KANDY DISTRICT, SRI LANKA

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Objective: To investigate the factors associated with interruption of tuberculosis treatment in Kandy district, Sri Lanka.

Methodology: A descriptive cross-sectional survey. Sample was selected from tuberculosis (TB) patients who commenced treatment in Kandy District registered in respiratory unit 2 between June and December 2013. This included all TB patients over 15 years ($n = 351$) including pulmonary ($n = 237$) and extra pulmonary ($n = 114$) cases. Treatment interrupters were defined as those who failed to take treatment for more than seven days but less than 2 months. Data was collected using an interviewer administered questionnaire.

Results: The sample included 30 treatment interrupters (8.5% of total) with mean age 48 years (18–76). 19 (63.3%) were male. There were 22 (73.3%) pulmonary TB, 6 (20%) extra-pulmonary and 2 (6.6%) disseminated cases. Of the pulmonary TB cases 17 were sputum smear positive and 5 negative. 28 (93.3%) were new cases and 2 (6.6%) retreatment. Interruption had been during the intensive phase in 17 (56.6%) and in the continuation phase in 13 (43.3%). Among the sample 18 (60%) did not have underlying diseases, 5 (16.6%) had hypertension, 3 (10%) had chronic renal failure, 2 (6.6%) had diabetes mellitus and chronic obstructive pulmonary diseases whereas 1 (3.3%) had ischemic heart disease. 10 (33.3%) had no formal education and 8 (26.6%) had only primary level schooling. 11 patients were educated up to secondary level. 16 (53.3%) patients were employed and 14 (46.6%) unemployed. 5 (16.6%) had a low monthly income (<Rs5000), 18 (60%) had an income of Rs5000-25000 and 7 (23.3%) had an average income of more than Rs25000. Majority of treatment interrupters 14 (46.6%) had poor family support, 12 (40%) had average family support and 4 (13.3%) had good family support. 18 (60%) patients were given self administered therapy and 14 (46.6%) DOTS. Reasons provided for treatment interruption included symptomatic improvement after treatment 9 (30%), minor side effects of drugs 5 (16.6%), unawareness regarding disease 5 (16.6%), financial reasons 2 (6.6%), substance abuse 2 (6.6%), stigma regarding disease 2 (6.6%) and family commitments 1 (3.3%). Difficult access to DOTS centre was not a factor.

Conclusion: In comparison to WHO default rate, there was a higher percentage of interrupters in our sample. The majority were new smear positive pulmonary cases in the intensive phase with a higher risk of morbidity and infectivity. A larger percentage had minimal or no formal education, poor family support and were prescribed self administered treatment. Major reasons provided for treatment interruption were related to poor health education rather than financial or logistical. Therefore a good health education programme and adhering to DOTS may aid in minimizing interruption.

O-Q-010

PROSPECTIVE STUDY: IL-10 AND IL-17 PLASMA LEVELS DURING ORAL ANTITUBERCULOSIS TREATMENT WITH SPUTUM CONVERSION AND SUCCESSFUL TREATMENT IN ACTIVE LUNG TUBERCULOSIS PATIENT

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Background: Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. *Mycobacterium tuberculosis* infection remains one of the world's major cause of illness and mortality with an estimated 1.4 million deaths in 2010. Sputum smear acid fast bacilli at 2nd months and 6th months are used for evaluation of conversion and cured in individual patients. This study aims to determine differences of IL-10 and IL-17 levels in patients with sputum smear positive pulmonary tuberculosis before OAT, 2nd and 6th months are associated with sputum conversion and therapeutic treatment.

Method: 22 new cases patients with pulmonary TB sputum smear positive in Dr. Saiful Anwar Malang general hospitals, Indonesia were included in a prospective observational cohort study. IL-10 and IL-17 levels were measured by ELISA kits before OAT, 2nd month and 6th month OAT treatment.

Results: Showed IL-10 levels were higher in TB patients before treatment and gradually decreased then increased the 6th month. Fluctuations of IL-10 level was not significant with TB treatment ($r = 0.25$, $p\text{-value} = 0.212$). IL-17 levels in patients with TB was decreased until the end of treatment, and IL-17 levels before treatment was not significantly different with 2nd month treatment ($p = 0.143$) but significantly different in 6th month treatment ($p < 0.001$). Changes in IL-10 and IL-17 levels was not associated with sputum conversion at the end of treatment.

Conclusion: Changes of IL-17 levels was associated with successful treatment, and changes the of IL-10 and IL-17 levels were not associated with sputum conversion. In this study IL-10 and IL-17 level can not be use as biomarkers of sputum conversion and monitor successful treatment.

O-Q-011

THE PROFILE OF MATRIX METALLOPROTEINASE-9 (MMP-9) SERUM LEVELS AND ITS CORRELATION WITH DISEASE SEVERITY IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Background: There is a hypothesis that extracellular matrix degradation and the formation of cavities in pulmonary tuberculosis (TB) may be mediated by inflammatory mechanisms. As a protease, MMP-9 is capable to degrade type IV collagen which is the main component of basement membrane in lung. Levels of MMP-9 was found higher in pulmonary disease with or without a cavity. Local and circulating inflammatory cells is able to synthesize MMP-9. One of the *Mycobacterium tuberculosis* components, Lipoarabinomannan is capable of inducing the activity of MMP-9. One study found a correlation between MMP-9 serum level and disease severity define by radiographic lesions in patients with pulmonary TB.

Objectives: To determine the profile of MMP-9 serum level and its relationship with disease severity in patients with pulmonary TB.

Methods: We conducted an analytical observational study with cross-sectional from February until October 2011, and enrolled subjects with new cases of positive smear pulmonary TB, age ≥ 15 years, in the RS DR. Wahidin Sudirohusodo Makassar. On population, we conducted anamnesis, physical examination, sputum acid fast bacilli smears and chest X-ray examination. Subjects who meets inclusion criterias evaluated for MMP-9 serum levels and the degree of radiographic lesions were classified in order to determine disease severity of pulmonary TB.

Results: Total of 66 subjects were collected, aged between 16–70 years, consisted of 41 males (62.1%) and 25 women (37.9%). The lowest level of serum MMP-9 was 123.4 ng/ml, the highest 2000 ng/ml with a mean 1038 ± 580.4 ng/ml. Although not statistically significant, mean levels of MMP-9 was found higher in women (1205.7 ng/ml) than men (937.1 ng/ml), and BMI categories of underweight (1074.8 ng/ml) than obese plus normal category (990.1 ng/ml). In addition, there was a tendency that the older age, the lower levels of serum MMP-9. The mean levels of MMP-9 serum in the the extensive lesion (1379.9 ng/ml) was significantly higher than the moderate lesions (717.9 ng/ml) with $p < 0.001$.

Conclusion: There is a correlation between the MMP-9 serum levels with disease severity. Levels of serum MMP-9 was found higher in the extensive lesions on radiographic findings of new cases of positive smear pulmonary TB patients. Although not statistically significant, mean levels of MMP-9 serum were higher in female subjects and underweight BMI category, and there is a tendency that the older the age, the lower the levels of serum MMP-9.

O-Q-012

THE EFFECT OF ETHANOL EXTRACT PROPOLIS (EEP) ON THE LEVEL OF IFN- γ AND SUPEROXIDE DISMUTASE (SOD) ACTIVITIES IN PATIENTS WITH MDR TUBERCULOSIS

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Background: Multidrug Resistant Tuberculosis (MDR TB) is a form of TB in which the mycobacteria cannot be killed by at least two the most effective anti TB drugs, that is, rifampicin and isoniazid. The attention to MDR-TB has been increasing because its morbidity and mortality are extremely high. Interferon gamma (IFN- γ) is one of the most important cytokines in the pathogenesis of pulmonary tuberculosis. The level of IFN- γ in TB patients declines. In TB patients, severe oxidative stress resulting from poor dietary intake, free radicals burst produced by activated-macrophages, poor immune status, etc, has been reported. Oxidative stress is the result of the predominance of oxidants over anti-oxidants. Superoxide Dismutase (SOD), the anti-oxidant, activity is decreased in TB. Ethanol Extract Propolis (EEP) – the resinous substance produced by honeybees – has been known to have natural immunomodulation and anti-oxidative activities. The aim of this research is to investigate the effect of EEP supplementation on the level of IFN- γ and SOD activities in the patients with MDR TB treated with anti-MDR TB.

Methods: This is an experimental study using simple randomized controlled trial pre-test – post-test control group design that was conducted at Dr. Soetomo Hospital, Surabaya. The total of 28 MDR-TB patients were divided into 2 groups: the experimental group was treated with ATD MDR TB + 500 mg EEP 2 times daily and the control group was treated only with ATD MDR TB.

Result: The level of IFN- γ between pre-treatment (39.4 ± 4.5 pg/mL) and post-treatment (46.1 ± 8.9 pg/mL) were increase significantly in the experimental group ($p < 0.05$) compared with control group ($p > 0.05$). SOD activity between pre-treatment (0.306 ± 0.483 U/mL) and post-treatment (1.033 ± 1.048 U/mL) were increase significantly in the experimental group ($p < 0.05$), whereas the control group were decrease significantly between pre-treatment (0.824 ± 0.643 U/mL) and post treatment (0.388 ± 0.443 U/mL), $p < 0.05$. The level of IFN- γ in the experimental group (6.7 ± 5.8 pg/mL) was significantly high compared with the control group (-1.8 ± 3.1 pg/mL), $p < 0.05$. SOD activity in the experimental group (0.728 ± 0.921 U/mL) was significantly high compared with the control group (-0.436 ± 0.589 U/mL), $p < 0.05$.

Conclusion: The addition of EEP can increase the level of IFN- γ and SOD activity in the patients with MDR-TB treated anti MDR-TB drugs.

O-Q-013

TUBERCULOSIS IN INDONESIAN HAEMODIALYSIS PATIENTS: A SINGLE CENTRE EXPERIENCE

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Introduction: Data on the incidence and prevalence of tuberculosis (TB) in haemodialysis (HD) patients varies and depends on the study region. Diagnosis of TB may be complicated and difficult in HD patients because of atypical clinical presentation and non-specific symptoms. This study aimed to investigate HD patients with TB during a five-year period in Rasyida Dialysis Clinic, Medan.

Method: A total of 654 patients undergoing HD for at least three months in our unit between 2009 and 2013 were evaluated retrospectively. The diagnosis of TB was established by combining clinical, radiological and microbiological findings. Choice of anti-TB drugs used, the results of therapy and patient outcome were noted.

Results: Out of 654 patients studied, 20 (3%) were diagnosed with TB, 4 of whom were diagnosed by microbiological assessment and 16 by clinical and radiological findings. Mean age at diagnosis was 48.7 ± 12.7 years and the male/female ratio was 12/8. No patient had had a history of TB. The mean duration of dialysis therapy and the duration of dialysis till the diagnosis of tuberculosis were 75.8 ± 59.4 and 61.4 ± 49.8 months. Pulmonary TB constituted 100%. Of these patients, one case (5%) had multisystem involvement (spondylitis and pulmonary TB). All patients were treated with rifampicin or levofloxacin and isoniazid. Treatment ended with a cure in 10 (50%), ongoing in 3 (15%) patients and 7 (35%) patients died during the study.

Conclusion: The frequency of TB in our HD patients was similar to those reported by others. The demographic and clinical parameters were quite similar to the average dialysis population compared with previous reports, which might be related to the same characteristics of patients from developing countries. Early diagnostic and therapeutic considerations will help in improving the outcome of TB among HD patients.

O-Q-014

TREATMENT OUTCOMES AMONG PULMONARY AND EXTRA PULMONARY TUBERCULOSIS PATIENTS IN MALAYSIA

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Background: Pulmonary tuberculosis (PTB) is the most prevalent type of tuberculosis (TB) while extra-pulmonary tuberculosis (EPTB) is quite rare but requires longer duration of therapy.

Objective: The aim of the present study was to evaluate the difference between pulmonary and extra pulmonary tuberculosis patients in terms of treatment outcomes.

Methodology: A multi centre retrospective study design was adopted from January 2006 to March 2009 in four states of Malaysia (Penang, Sabah, Sarawak and Selangor) in order to collect data of TB patients. All adult patients diagnosed with TB were included, whereas patients with missing records were excluded. A validated data collection form was used to note patient demographic and clinical data. All the data was analysed by using SPSS version 20.0. All relevant ethical considerations were obtained.

Results: Out of 9337 TB patients, the majority 7781 (83.3%) had PTB, 1556 (16.7%) had EPTB. The mean age and weight of patients was 41.61 ± 16.57 years and 41.75 ± 10.11 kg respectively. Overall PTB prevalence was high while lymphadenitis TB, pleural TB and meningitis TB were the most common among EPTB patients. Gender ($p < 0.001$), race ($p < 0.001$), area of residence ($p = 0.008$), smear type ($p < 0.001$) and marital status ($p < 0.001$) had a significant difference with type of TB. A total of 7240 (77.5%) patients were successfully treated out of which 6181 (85.3%) were of PTB, 1059 (14.7%) were of EPTB. Male gender (OR = 0.73, 95% CI 0.65–0.82, $P < 0.001$) married individuals (OR = 1.24, 95% CI 0.65–0.82, $P < 0.001$) and presence of co-morbidity (OR = 1.31, 95% CI 1.17–1.46, $P < 0.001$) had significant difference with PTB group. The treatment success rate was 1.934 times higher in the PTB patients (95% CI 1.10–1.40, $P < 0.001$) as compared to EPTB patients.

Conclusion: Although, the prevalence of PTB is high but still the treatment successful rate is quite favourable as compared to EPTB and PTB along with EPTB patients.

O-Q-015

CHARACTERISTICS AND PROBLEMS OF FOREIGN TUBERCULOSIS TREATED IN OUR HOSPITAL

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Background: National Center for Global Health and Medicine (NCGM) is a tertiary care hospital with 700 beds, including a 40-bed tuberculosis (TB) ward, located in Shinjuku, Tokyo, Japan. While the incidence of TB in Japanese has decreased (16.9 in 2013), the number of patients with TB from abroad is increasing.

Objective: To investigate the current situation of foreigners' tuberculosis in our centre, and to propose effective measures on imported tuberculosis in urban setting.

Methods: A retrospective study of tuberculosis patients undergoing medical treatment in NCGM in January 2010 to December 2013. The total number of foreigners' active pulmonary TB was 116. Of them, 66 were hospitalized (mostly smear-positive) and 50 outpatient (all smear-negative). We also investigated 674 Japanese TB patients who were hospitalized during the same period as a control.

Results: The rate of foreigners with active pulmonary tuberculosis was elevated rapidly, from 7.3% (13 cases in 178 cases) in 2011 to 14.2% (28 cases in 196 cases) in 2013. The number of immigrants from Southeast and West Asian countries has increased rapidly in 2013. Many patients were diagnosed with tuberculosis in more than six months after arriving in Japan. Rifampicin resistance (4.5% vs 0.74%; $p = 0.027$) and Multiple drug resistance (4.5% vs 0.29%; $p = 0.012$) were higher in foreign population. Compared to the Japanese, foreigners' TB patients were much younger (median age of 29.0 vs 62.0), with fewer diabetics (3 vs 157; $p < 0.001$), and more HIV positive (6 vs 13; $p = 0.006$). No difference in chest X-ray findings was observed.

Discussion: As a result of globalization, a lot of Japanese language schools accept foreign students from Southeast and West Asian countries. Since the number of active TB diagnosed in the first six months of their entry was elevated, early detection is urgent. In urban areas, the risk of developing tuberculosis outbreaks in young population is high because the more opportunity to contact the people in an unspecified number is growing. To ensure early detection of imported tuberculosis is very much important for preventing the spread of resistance and for continued decline in incidence rate.

O-Q-016

TWO YEAR FOLLOW UP STUDY OF TB PATIENTS PUT ON DOTS FROM SOUTH INDIAVENUGOPAL K¹, SREELATHA PR², NISHA RS³¹General Hospital, Alappuzha, India, ²Department of Pediatrics, MCH Vandanam, India, ³Department of Community Medicine, MCH Vandanam, India

Background: DOTS being implemented (intermittent therapy) all over India since 1994. India is one of the high TB burden countries with poor resources. Detection rate in India is far behind the expected which is more evident in South India. This is because of doubt of the doctors about the effectiveness of intermittent regimen. There is no reported study of long term follow up of DOTS therapy. So the present study is to evaluate the long term follow up and relapse of DOTS for various forms of TB.

Aim of the Study: To evaluate the relapse rate and effectiveness of intermittent regimen for various forms of tuberculosis.

Material and Method: All tuberculosis patients registered in 2009 I & II Quarter of the entire Districts were given call letter for review on particular day in respective TB Units. They were interviewed as per questionnaire prepared at District TB Centre by the trained doctors from Community Medicine Department. Those with suspected TB were arranged sputum examination.

Observation: Of the 886 patients registered and invited 322 reported for study (36.34%) of which 253 (79%) were pulmonary (160 were positive and 93, negative) and 69 (21.43%) were extra pulmonary with following distribution. Lymph node – 31 (9%), plural effusion – 16, intestine – 7, bone & joint – 4, neuro – 5, miliary – 2, thyroid – 1, pericardium – 1, genito urinary – 1. Of the reported patients 194 were asymptomatic and 126 has minor symptoms. Of the 30 under went sputum examination, 2 (0.62%) were positive. There was no extra pulmonary case with suggestive symptom of relapse.

Conclusion: Intermittent regimen is highly effective to all forms of tuberculosis with insignificant relapse.

O-Q-017

THE PROFILE OF INTERLEUKIN (IL)-12P70 AND IL-12P40 SERUM LEVEL AMONG ACTIVE TUBERCULOSIS PATIENTS, LATENT WITH POSITIVE INTERFERON GAMMA RELEASE ASSAY (IGRA), CONTACT WITH NEGATIVE IGRA

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Background: Close to one-third of the world's population is infected with Mycobacterium tuberculosis (Mtb) resulting in almost 3 million deaths per year. Cell-mediated immune responses are critical to host defense, with interleukin (IL)-12 induction of interferon- γ (IFN- γ) production providing their primary pathway by which bacterial growth is controlled. Recently, it has been proved, the importance of IL-12p70 in the CD4 T cell response to Mtb. However, IL-12p40, a subunit of IL-12p70 and IL-23, has been shown to inhibit IL-12p70 activity and IFN- γ .

Objective: The aim of this study was to evaluate the profile of IL-12p70 and IL-12p40 serum level among active lung TB patients, latent with positive IGRA, and contact with negative IGRA.

Methods: We analysed serum level of IL-12p70 and IL-12p40 among three groups of samples, i.e active lung TB patients (n = 30), latent with positive IGRA test (n = 30), and the contact with negative IGRA test (n = 28). ELISA method was used to determine the serum level of IL-12p70 and IL-12p40 in each of sample groups.

Results: From 88 subjects, we found 46.6% male, 53.4% female, aged between 12–76 years (mean 39 + 16 years, median 36 years). Level of serum IL-12p70 varied between 0–69 pg/mL (mean 2.42 + 11 pg/mL). Level of serum IL-12p40 varied between 110–1941 (mean 403.45 + 280.63 pg/mL). Obese was found in 21.6% subjects, and 78.4% non-obese. Diabetes mellitus was found in 8% subjects, and 92% without DM. There was a significant difference in level of serum IL-12p40, highest in active lung TB patients (519.97 pg/mL), and lowest in contact with negative IGRA test (290.64 pg/mL), with $p = 0.017$. Among subjects aged < 36 years, there was no significant difference in level of serum IL-12p70 and IL-12p40 based on groups ($p > 0.05$). Among subjects aged > 36 years, there was a significant difference in level of serum IL-12p40, highest in active lung TB patients (573.25 pg/mL), and lowest in contact with negative IGRA test (257.22 pg/mL), $p = 0.047$. Among subjects without DM, there was a significant difference in level of serum IL-12p40, highest in active lung TB patients (401.88 pg/mL), and lowest in contact with negative IGRA test (290.64 pg/mL), $p = 0.041$.

Conclusion: These data show that in active lung TB patients, latent with positive IGRA, and contact with negative IGRA, the level of serum IL-12p70 is much lower than IL-12p40. There is a significant difference of IL-12p40 serum level among 3 groups based on age > 36 years and without DM.

O-Q-018

A STUDY ON INOCULUM DENSITY AND REPRODUCIBILITY OF DRUG SUSCEPTIBILITY TESTING BY DAC (DISC AGAROSE CHANNEL)KIM H¹, LEE E-H¹, CHOI J², KIM H¹, JUNG H¹, YOO J², PARK KO², RYOO S¹, JUNG Y-G²¹Korean Institute of Tuberculosis, Osong, Cheong Ju, Chung Buk, 363-954, Republic of Korea, ²QuantaMatrix Inc., Seoul National University, Seoul 151-742, Republic of Korea

The bacterial density of the inoculum is critical to the correct performance of DST (drug susceptibility testing) because variations in inoculum size can affect interpretation of diagnostic results. Recently, microfluidic cell culture devices have been applied in drug screening assays, which was suitable for long-term observation of the cytotoxic effect and evaluation of the drug activity. In tuberculosis, it has been reported such experiments could apply to drug susceptibility of mycobacteria using 3D agarose system. In this report, we evaluated the bacterial activity of 1st-line drugs, rifampin, isoniazid, ethambutol, and streptomycin for TB using DAC system. DST results were not influenced by variety of bacterial density. To validate DAC system is not affected by inoculum density, DST was performed in this system. Lowenstein-Jensen (L-J) medium and MGIT 960 DST system were used as gold standard. The cell density of tuberculosis used for this experiment was from 103 to 107 cells. Neither L-J nor MGIT DST system can report the results in higher density. But DAC system was possible to estimate reproducible result in broad inoculum density. This device could easily performing DST without a strict preparation of the inoculum volumes. IE is not observed even at inoculum higher than 107 mycobacteria per ml. Therefore, DAC system will achieve in the accurate prediction of microbiological efficacy against anti-tuberculosis drugs.

O-Q-019

O-Q-021

COMPARATIVE ANALYSIS OF DU REGION IN THE MYCOBACTERIUM BOVIS BCG-KOREA STRAIN

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The Bacille Calmette-Guérin (BCG) vaccine has been used to protect against tuberculosis. Currently, BCG vaccine strains used in different countries and vaccination programs demonstrate clear variations in their genomes and immune protective properties. In 2011, Korean Institute of Tuberculosis (KIT) established the BCG-Korea, daughter strains from M. bovis Pasteur1173P2 strain. According to our previous report, we performed the comparison analysis of the genome sequence of the BCG-Korea and BCG-Pasteur strains and discovered that DU1 and DU2, two tandem chromosomal duplication, have been largely rearranged. While DU1 existed as single copy, DU2 was contained as three copies in the genomic segment of BCG-Korea, compared with the BCG-Pasteur strain. These reasons why BCG strains harbouring DU1 and DU2 had rearranged the genomic segment, and the role of DU region diversity in BCG vaccine efficacy or immunogenicity effect, are yet unknown. The aim of this study was to characterize the proteomic profile on the region of DU1 and DU2 in BCG-Korea and BCG-Pasteur by using a SWATH-based mass spectrometric approach (Sequential Window Acquisition of all Theoretical mass spectra) and to understand the physical and functional relationships between proteins, by using the EMFAS software program (Ensoltek, Inc., Daejeon, South Korea) which uses homology searches in the NCBI/UniProt databases and non-homology-based function annotations (genome context analysis). In total, 792 proteins (about 22%) were identified by SWATH and 22 of them contained in the DU1 and DU2 region, were investigated. We reported the relationship of differential expressed proteins in BCG-Korea DU1 and DU2 region compared to BCG-Pasteur and studied their functions by EMFAS software. The identified proteins and their functional linkage networks are useful for better understanding of the cellular biology of BCG-Korea and BCG-Pasteur, and hopefully would assist in the design of better anti-TB vaccine and drugs.

O-Q-020

CORRELATION BETWEEN POSITIVITY OF ACID FAST BACILLI (AFB) AND LEVEL OF INTERFERON- γ (IFN- γ) AMONG TUBERCULOSIS PATIENTS IN MAKASSAR

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Background: Tuberculosis (TB) is still an important health problem throughout the world. Interferon- γ (IFN- γ), a cytokine of T helper-1 cells (Th1), plays an important role in eliminating M. tuberculosis. Disturbance or decrease in Th1 cell activity and IFN- γ will affect the immune system against pulmonary TB (PTB). The aim of this study was to determine the correlation of acid fast bacilli (AFB) positivity and levels of IFN- γ among PTB patients in Makassar.

Method: This study design was a descriptive analytics with cross-sectional approach, conducted in June 2013 until March 2014. Subjects were new cases of PTB patients, male and female, either outpatient or inpatient at the hospital Dr. Wahidin Sudirohusodo Makassar.

Result: We had 50 subjects aged 17 to 76 years with a mean of 41 + 15 years, consisting of 32 (64%) males and 18 (36%) females. Distribution of AFB positivity are positive three in 22 (44%) subjects, positive two in 17 (34%) subjects, positive one in 7 (14%) subjects, and negative in 4 (8%) subjects, consecutively. In terms of the levels of IFN- γ , the lowest is 0.06 pg/mL, the highest is 0.29 pg/mL, with a mean of 0.99 + 0.47 pg/mL. Based on the positivity of AFB groups, the mean of IFN- γ levels are, 0.12 + 0.06 pg/mL in positive three group, 0.08 + 0.01 pg/mL in positive two group, 0.08 + 0.02 pg/mL in positive one group, and 0.09 + 0.01 pg/mL in negative group, with $p = 0.000$.

Conclusion: From this study, the most commonly found sputum smear of AFB in PTB patients is positive three 44%. We also found a significant correlation ($p < 0.001$) between positivity of AFB and levels of IFN- γ , whereby the mean levels of IFN- γ was highest in PTB patients with AFB positive three.

A CROSS SECTIONAL STUDY OF PENGAWAS MINUM OBAT (PMO) IN GOING HAND IN HAND WITH TUBERCULOSIS PATIENTS IN JAKARTA RESPIRATORY CENTER (JRC) – THE INDONESIAN ASSOCIATION AGAINST TUBERCULOSIS

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Tuberculosis (TB) is an infectious disease that is the second most deadly disease in the world. Indonesia has the third largest population affected by TB, which accounts for 10% of TB cases worldwide and is considered the third most deadly disease in Indonesia. TB treatment regimen is a 6 months long process with an intensive phase, followed by a continuous phase. Compliance to this treatment regimen and regular consumption of medication is crucial to the treatment. Adherence in consuming anti-TB drugs regularly is considered the most important success factor in treating TB. World Health Organization (WHO) designed Directly Observed Therapy, Short-course (DOTS) as a strategy to eradicate TB by increasing the effectiveness of TB treatment through preventing irregular consumption of TB drugs. Pengawas Minum Obat (PMO) is one of the DOTS strategy applied in Indonesia that involves appointing someone to support to TB patients, motivating, educating and reminding them to take their medication regularly. In most cases in Indonesia, family members assume the role of PMO due to the lack of health care workers. This research aims to study the factors which influence the role of PMO in the treatment of TB patients. This is a cross sectional study involving 22 cured TB patients from Jakarta Respiratory Center. Data were collected through medical records and interview. Data analysis is done by Chi-square analysis. The result showed that there is no relationship between the education level of PMO ($p = 0.318$), occupation of PMO ($p = 0.631$) and duration of treatment ($p = 0.597$) with the role of PMO in supervising the TB patients. Ideally, TB patients prefer family members as PMO for practical reasons and the psychological support they can give. The results of this study is revealing of the PMO system in Indonesia. Considering many aspects of public health in Indonesia, such as unevenly distributed primary healthcare and low ratio of healthcare workers to population, Indonesia had set a feasible and applicable supervision and patient support system, which called Pengawas Minum Obat (PMO). This study concluded statistically there are no relation between the role of PMO with their education, occupation and patients' duration of medication. Most of the PMO are coming from family members who have strong psychological bond with the patients; hence, they had motivation to help the patients and going hand in hand to fight the disease.

O-Q-022

CLINICAL EXPERIENCE WITH IMMUNOTHERAPY REGIMENS IN TB PATIENTS

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There are many factors triggering clinical disease in a small proportion of individuals latently infected with *M. tuberculosis*. In our view the major role is played by the host's immune response, especially self-destructive, inflammatory immune response. However, immune correlates associated with TB treatment outcome are still unknown. TB chemotherapy has bactericidal or bacteriostatic effects, but immunopathological changes need to be corrected by immunotherapy. Various attempts have been made to find optimal immune interventions, but many have failed. Over past few years we have conducted nearly thirty clinical studies of adjunct immunotherapies, i.e., Ukrainian herbal immunomodulator, Immunoxel (Dzherelo), and oral therapeutic vaccines, V5 and V7, involving more than 2,000 patients. All three regimens resulted in shorter time to sputum clearance and were equally effective against drug-sensitive TB, MDR-TB and TB-HIV. The immune response that strongly correlated with protective immunity was of anti-inflammatory nature, which can be, for example, measured by two unsophisticated tests, i.e., erythrocyte sedimentation rate and leukocyte counts. Fever reduction and body weight gain are additional parameters, which correlate with positive outcome. These simple biomarkers combined with immunological tests evaluating anti-inflammatory cytokines and Th1/Th2 balance can provide reliable correlates of immune protection. Thus, immune interventions, which are effective, must possess similar if not identical property in terms of anti-inflammatory effect in order to produce clinical improvements we have observed in our trials, the details of which will be presented.

O-Q-023

SMOKING AND ALCOHOL CONSUMPTION AS RISK FACTORS OF PULMONARY TUBERCULOSIS DEVELOPMENT IN MEDAN, INDONESIA

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Background: Many studies showed that smoking and alcohol consumptions can decrease the subject's immunity and associated with the risk of pulmonary tuberculosis (PTB) development.

Objective: The aim of this study was to know the association between smoking and alcohol consumption with the development of pulmonary tuberculosis.

Method: A case-control study was conducted in Medan, Indonesia, with 76 PTB patients and 76 healthy normal control. Sex, age and ethnic were matched. Cases were PTB patients with positive Acid Fast Bacilli taken from sputum; positive HIV, having Diabetes Mellitus, other severe disease and immunosuppressive drug consumption were excluded. Controls were healthy normal individual with no PTB symptoms and normal chest X-ray. Smoking and alcohol consuming were self reported. Smoking status was differentiated into smoking and not smoking. Alcohol status was differentiated into consuming and not consuming alcohol.

Results: From 152 subjects, 30.3% were females and 69.7% were males in cases group and the same number in controls group. In the cases group, 22.4% were smoking-only, 1.3% were alcohol consuming-only, 43.4% were smoking and alcohol consuming, and 32.9% were not smoking and not alcohol consuming. In the control cases, 21.1% were smoking-only, 3.9% were alcohol consuming-only, 7.9% were smoking and alcohol consuming, and 67.1% were not smoking and not alcohol consuming. There was a significant association between smoking (without excluding smoking person who also alcohol consuming) and PTB disease development (OR 4.72, 95% CI: 2.38–9.37). There was also a significant association between alcohol consuming (without excluding alcohol consuming person who also smoking) and PTB disease development (OR 6.026, 95% CI: 2.63–13.82). A logistic regression test was done with the non-smoking and non-alcohol-consuming group as a comparison factor. The odds ratio for smoking-only group was 2.17, 95% CI: 0.94–4.99, OR for alcohol-consuming-only group was 0.68, 95% CI: 0.07–6.87, and OR for smoking and alcohol group was 11.22, 95% CI: 4.16–30.28.

Conclusion: Smoking and alcohol consumption are risk factors of pulmonary tuberculosis development. This information is important in TB control and policies strategy in TB programme.

O-Q-024

MAGNETIC BEAD PROTOCOL DENOTED COGENT RESULTS FOR CULTURING MYCOBACTERIUM TUBERCULOSIS FROM SPUTUM SPECIMENS

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Background: With an estimated 1.3 million deaths in 2013, pulmonary tuberculosis is the second leading cause of death due to infectious diseases worldwide. The DAC (Disc agarose channel) system immobilizes bacteria by using agarose in a microfluidic culture chamber so that single cell growth can be tracked by microscopy. Recently, magnetic beads have been developed to bind specifically to mycobacteria, including both nontuberculosis mycobacteria (NTM) and *M. tuberculosis*. These beads were favourably evaluated for increasing the sensitivity of culture examination of sputum.

Methods: Prior to inoculation, all specimens were dispatched into two aliquots and decontaminated using the 4% N-acetyl-L-cysteine(NALC)-NaOH method. One aliquot was centrifuged according to our standard protocol, and the second aliquot was treated with the magnetic bead protocol according the supplier recommendations (Tb-Beads; Microsens Medtech Ltd, London, United Kingdom). Decontaminated sputum specimens were then inoculated and incubated at 37°C in DAC.

Results: In a total of 33 H37Rv spiking sputa samples, a magnetic bead protocol and a standard centrifugation protocol yielded about same time to detection (TTD) in all samples in 7 ± 2 days in DAC. According to cfu count in Middlebrook 7H11 medium, 15 samples were similar on the standard centrifugation protocol and the magnetic bead protocol. 18 samples showed 2–4 times more colony count at magnetic bead protocol than the standard centrifugation protocol.

Conclusions: The magnetic bead protocol is a technically nondemanding protocol which offers a suitable alternative to the standard centrifugation protocol for the pre-inoculation steps with sputum specimens for culturing *M. tuberculosis*. It could be easily implemented in laboratories in both developed and developing countries.

POSTER PRESENTATION – ASTHMA

P-A-001

AIRWAY EXPOSURE TO STAPHYLOCOCCUS AUREUS PARTICLES PROMOTES DEVELOPMENT OF ANTIGEN-SPECIFIC TH2-TYPE IMMUNITY TO INHALED ANTIGENS THROUGH PRODUCTION OF THYMIC STROMAL LYMPHOPOIETIN (TSLP)

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Rationale: While Th2-type CD4⁺ T cells play important roles in allergic asthma, the immunological mechanisms involved in development of Th2 immunity in the airways are not fully understood. Human airways and skin are often colonized with *Staphylococcus aureus* (*S.aureus*), and cutaneous *S. aureus* is implicated in development of atopic dermatitis. Thymic stromal lymphopoietin (TSLP) is highly expressed by bronchial epithelial cells in patients with asthma. In this study, we tested the hypothesis that airway exposure to *S. aureus* facilitates Th2-type immune responses in the airway.

Methods: *S. aureus* particles were administered intranasally (i.n.) to airways of naïve Balb/c mice or TSLP receptor deficient mice (TSLPRKO). Alternatively, *S. aureus* particles were administered together with endotoxin-free ovalbumin (OVA) (i.e. chronic exposure) on days 0 and 7, and mice were then exposed to OVA alone i.n. on days 21, 22, and 23. Bronchoalveolar lavage (BAL) samples and lungs were collected and analyzed for cell differentials and cytokine levels.

Results: Airway administration of *S. aureus* particles to naïve mice increased lung levels of TSLP and IL-17 and BAL levels of IL-1b and IL-6 in BAL within 6 hours. In the chronic model, airway exposure to OVA alone did not sensitize naïve mice. In contrast, naïve mice treated with both *S. aureus* particles and OVA developed OVA-specific Th2- and Th17-type immune responses and, when exposed to OVA alone, they developed airway eosinophilia and neutrophilia, peribronchial hypertrophy, and increased BAL levels of IL-5, IL-13 and IL-17. Importantly, the airway Th2, but not Th17, response to OVA was significantly inhibited in TSLPR KO mice.

Conclusions: Airway exposure to *S. aureus* promotes development of Th2-type immune responses to inhaled antigens through production of TSLP. Prevention of *S.aureus* colonization or inhibition of TSLP may be effective in the treatment of patients with allergic asthma.

P-A-002

ROLE OF EPIDERMAL GROWTH FACTOR RECEPTOR IN METHACHOLINE-INDUCED AIRWAY HYPERRESPONSIVENESS IN RATS IN VIVO

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Background: Increased expression of epidermal growth factor receptor (EGFR) in airway epithelium is recognized in patients with asthma, and is related to the induction of goblet cell hyperplasia. However, it is not well elucidated whether EGFR signaling also plays a role in the development of airway hyperresponsiveness (AHR) in asthma.

Purpose: To examine the effect of a selective EGFR tyrosine kinase inhibitor AG1478 on methacholine induced-AHR in ovalbumin (OVA)-sensitized and challenged rats.

Methods: Specific pathogen-free male Brown-Norway rats were sensitized by an intraperitoneal injection with 1 mg OVA and 200µg Al(OH)₃ in 1 mL of sterile saline on days 0 and 7. The rats were then exposed to aerosolized OVA (1% in PBS) or sterile saline for 30 min on days 14, 15 and 16. To evaluate the involvement of EGFR signaling in the development of AHR, a selective EGFR tyrosine kinase inhibitor AG1478 (3 mg/kg; intratracheal instillation) or vehicle was administered every 48 h from days 17 to 38. The AHR against methacholine (1.0 to 30 mg/ml for 3 min) was evaluated using non-invasive whole-body plethysmography. The enhanced pause (Penh) ratio was recorded, and was presented as a relative percentage increase of Penh. The expression of MUC5AC and EGFR, and inflammatory cell recruitment in bronchoalveolar lavage fluids were also determined. All outcome measurements were made on days 14 (before OVA challenge), 17, 24, 31 and 38.

Results: A marked goblet cell hyperplasia, an extensive inflammatory cell infiltration (eosinophilia and neutrophilia) and an increased immunoreactivity of both MUC5AC and EGFR in airway epithelium were seen on day 17, and the increases in the Penh value in response to methacholine inhalation were seen on day 24 in OVA-sensitized and challenged rats. The spontaneous resolution in goblet cell hyperplasia and inflammatory cell infiltration were observed by day 38, whereas the increases in Penh value persisted until day 38. Intratracheal instillation of AG1478 facilitated the resolution of airway goblet cell hyperplasia, and also induced a significant decrease in Penh value ($p < 0.05$, significantly different from OVA-sensitized and challenged rats).

Conclusions: These results indicate that the EGFR signaling may play a role not only in the induction of goblet cell hyperplasia, but also in the development of AHR in a rat model of asthma and that the inhibition of EGFR signaling pathway can be a promising candidate for the treatment of asthma.

P-A-003

EFFECT OF ROFLUMILAST ON AIRWAY REMODELING IN A MURINE MODEL OF CHRONIC ASTHMA

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Background: Asthma is characterized by airway inflammation and remodeling. Roflumilast is a selective phosphodiesterase-4 (PDE4) inhibitor that has anti-inflammatory effect in chronic obstructive pulmonary disease (COPD). However, little is known regarding the effect of roflumilast in chronic asthma. This study is aimed to evaluate the effects of roflumilast on airway inflammation and remodelling in a murine model of chronic asthma.

Methods: Female BALB/c mice, 6 weeks of age, were used. We developed a mouse model of airway remodeling in which ovalbumin (OVA)-sensitized mice were repeatedly exposed to intranasal OVA administration twice a week for 3 months. Roflumilast was administered orally starting on the 38th day and 5 days a week thereafter for 3 months during the intranasal OVA challenge. A lung fibroblast cell line was used in the proliferation assay.

Results: Compared with control mice, mice chronically exposed to OVA developed sustained eosinophilic airway inflammation, airway hyperresponsiveness (AHR), and exhibited features of airway remodeling. Administration of roflumilast significantly inhibited eosinophilic inflammation and AHR. The levels of interleukin (IL)-4, IL-5, and IL-13 in the bronchoalveolar lavage (BAL) fluids were significantly lower in the roflumilast group. The level of hydroxyproline was also significantly lower in the roflumilast group. In vitro, roflumilast significantly inhibited stem cell factor (SCF) induced cell proliferation of fibroblasts.

Conclusion: These results suggest that roflumilast administration modulates the airway inflammation, AHR, and airway remodeling associated with chronic allergen challenge.

P-A-004

P-A-006

THE EFFECT OF INHALATION DURATION ON LUNG DEPOSITION WITH A PRESSURIZED METERED-DOSE INHALER (PMDI)

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Rationale: Although the guidance for using a pMDI is to inhale 'slow and deeply', many patients inhale fast over a short duration. The ERS/ISAM Task Force suggested 'slowly' equates to inhaling over 4–5 seconds (s) for adults¹, a much clearer instruction. This study therefore examined the influence of inhalation time on total lung deposition (TLD) using Functional Respiratory Imaging (FRI).

Methods: Three-dimensional airway models of 6 asthma patients (mean FEV₁ 83%), treated with an ICS/LABA combination, were included. The lung deposition characteristics of an HFA-based pMDI (MMAD ~3.0 µm; fine particle fraction (FPF) ~40%) were assessed using FRI. Simulations were performed on 3 different inhalation profiles matched for the same inspiratory volume (3 L) with durations of 1s, 3s and 5s and actuation at start of inhalation.

Results: For the 1s, 3s and 5s profiles, the TLD values were 22.81 ± 3.71%, 36.13 ± 2.51% and 41.61 ± 3.11% of nominal dose respectively, and were predicted using a concave down quadratic model (R² = 0.87, p < 0.001). The central to peripheral deposition ratios were 1.58, 0.81 and 0.57 respectively.

Conclusions: A 5 s inhalation led to highest TLD with greatest peripheral deposition. Increased deposition with longer times mainly reflected increased peripheral deposition, central deposition was less affected by flow rate. These data support ERS/ISAM guidance for inhaling over 4–5 sec to optimize deposition, although similar TLD were achieved with 3s. These data also suggest that high FPF pMDIs can achieve reasonable deposition even with short, fast inhalations.

This study was funded by Mundipharma International.

Reference:

¹ Laube B.L. et al. *ERJ* 2011; **37**(6):1308–417.

P-A-005

ANALYSIS OF T CELL-DEPENDENT BRONCHOCONSTRICTION

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Background: Helper T (Th) cells have been implicated in asthma. To investigate a role of Th cells in airflow limitation, T cell-transfer model was analyzed for immediate and late phase asthmatic responses after antigen challenge.

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

Results: When unprimed mice were transferred with Th clones, T5-1, T6-2, T6-4, and T6-7, Penh values were significantly increased 6 hr after OVA challenge. In contrast, mice transferred with other Th clones, BF7, T6-1, or T6-10 did not show any change. Airflow limitation was confirmed by a direct measurement of airway resistance under anaesthetized, restrained, and intubated conditions. The airflow limitation was also induced by the challenge with T cell epitope peptide, OVA323-339. Contractile activity of BSMCs was detectable in the supernatants of T6-2 stimulated with immobilized anti-CD3.

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

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RHINOVIRUS EXACERBATES HOUSE-DUST-MITE INDUCED LUNG DISEASE IN ADULT MICE

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Human rhinovirus is a key viral trigger for asthma exacerbations. To date, murine studies investigating rhinovirus-induced exacerbation of allergic airways disease have employed systemic sensitization/intranasal challenge with ovalbumin. In this study, we combined human-rhinovirus infection with a clinically relevant mouse model of aero-allergen exposure using house-dust-mite in an attempt to more accurately understand the links between human-rhinovirus infection and exacerbations of asthma. Adult BALB/c mice were intranasally exposed to low-dose house-dust-mite (or vehicle) daily for 10 days. On day 9, mice were inoculated with human-rhinovirus-1B (or UV-inactivated human-rhinovirus-1B). Forty-eight hours after inoculation, we assessed bronchoalveolar cellular inflammation, levels of relevant cytokines/serum antibodies, lung function and responsiveness/sensitivity to methacholine. House-dust-mite exposure did not result in a classical TH₂-driven response, but was more representative of noneosinophilic asthma. However, there were significant effects of house-dust-mite exposure on most of the parameters measured including increased cellular inflammation (primarily macrophages and neutrophils), increased total IgE and house-dust-mite-specific IgG1 and increased responsiveness/sensitivity to methacholine. There were limited effects of human-rhinovirus-1B infection alone, and the combination of the two insults resulted in additive increases in neutrophil levels and lung parenchymal responses to methacholine (tissue elastance). We conclude that acute rhinovirus infection exacerbates house-dust-mite-induced lung disease in adult mice. The similarity of our results using the naturally occurring allergen house-dust-mite, to previous studies using ovalbumin, suggests that the exacerbation of allergic airways disease by rhinovirus infection could act via multiple or conserved mechanisms.

P-A-007

EFFECT OF RESVERATROL ON AIRWAY REMODELING IN CHRONIC ASTHMA MODEL

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Objectives: Asthma is characterized by airway inflammation and remodeling. Resveratrol, a natural polyphenol, is found in various fruits and vegetables and is abundant in grapes. Little is known regarding the effect of resveratrol in chronic asthma. This study is aimed to evaluate anti-remodeling effect of resveratrol in chronic asthma model.

Methods: Female BALB/c mice, 8–10 weeks of age, were used. We developed a mouse model of airway remodeling in which ovalbumin (OVA)-sensitized mice were repeatedly exposed to intranasal OVA administration twice a week for 3 months. Mice were treated with resveratrol during the OVA challenge. A lung fibroblast cell line was used in proliferation assay.

Results: Compared with control mice, the mice chronically exposed to OVA developed sustained eosinophilic airway inflammation, airway hyperresponsiveness (AHR), and exhibited features of airway remodeling, including thickening of the peribronchial smooth muscle layer. Administration of resveratrol significantly inhibited eosinophilic inflammation and AHR. The level of Th₂ cytokine is significantly lower in resveratrol group. The level of hydroxyproline and smooth muscle area were also significantly lower in resveratrol group. In vitro, resveratrol significantly inhibited cell proliferation of fibroblast.

Conclusion: These results suggest that resveratrol administration can prevent airway inflammation, AHR, and airway remodeling associated with chronic allergen challenge.

P-A-008

TRANSFORMING GROWTH FACTOR-BETA INDUCES THE PRODUCTION OF NEUROTROPHINS IN LUNG FIBROBLASTS VIA SMAD PATHWAY

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Background: Neurotrophins (NTs), such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), are growth factors which induce survival, development, and function of neurons. Recently, these NTs are considered to be contributors to pathological processes in respiratory diseases, such as asthma and pulmonary fibrosis by inducing proliferation of mesenchymal cells, and are reported to be abundant in the sputum of patients with severe asthma. However, little is known about the origin and production process of these NTs. Transforming growth factor-beta (TGF-beta) is a key fibrogenic and immunomodulatory factor in the pathogenesis of severe asthma, particularly in the process of airway remodeling, and elevated levels of TGF-beta have been reported in the asthmatic airway. We hypothesized that NTs might be induced by TGF-beta in fibroblasts and play important roles in the pathogenesis of asthma.

Methods: The activation of neurotrophin signaling in the asthmatic tissues was evaluated using the Gene Set Enrichment Analysis (GSEA) of open-access microarray database. The expression of BDNF and NGF in the WI-38 human fetal lung fibroblasts was evaluated with qPCR. The downstream signaling pathway was explored by Western blotting of phospho-Smad2/Smad3 and siRNA-mediated knockdown of Smad4.

Results: GSEA of microarray data (GSE23611), which compared gene expression between asthmatic tissue (n = 19) and normal tissue (n = 13), revealed that the neurotrophin signaling pathway was significantly enhanced in asthmatic patients (p = 0.049). In both 2 microarray data (GSE1724 and GSE17518) which defined the comprehensive target genes of TGF-beta in lung fibroblasts, TGF-beta 1 clearly upregulated the expression of BDNF/NGF, and these two genes could be novel targets of TGF-beta. This effect was validated by qPCR in WI-38 cells. In the downstream of TGF-beta signaling pathway, Smad2/Smad3 was phosphorylated 30 min after stimulation of TGF-beta 1. Furthermore, knockdown of Smad4, which forms complex with Smad2 and Smad3 and regulates transcription of target genes, diminished the upregulated expression of BDNF/NGF by TGF-beta.

Conclusion: In lung fibroblasts, NTs, such as BDNF and NGF, are induced by TGF-beta in Smad-dependent manner. NTs might play important roles in the pathogenesis of asthma, in cooperation with TGF-beta.

P-A-009

ONCE-DAILY TIOTROPIUM RESPIMAT® IS WELL TOLERATED AND EFFICACIOUS OVER 52 WEEKS IN JAPANESE PATIENTS WITH SYMPTOMATIC ASTHMA RECEIVING INHALED CORTICOSTEROIDS (ICS) ± LONG-ACTING B2-AGONIST (LABA): A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Rationale: Tiotropium, a once-daily long-acting anticholinergic bronchodilator, improved lung function and reduced severe exacerbations in patients with severe symptomatic asthma, despite ICS / LABA (Kerstjens et al. NEJM 2012;367:1198–207). The present study evaluated long-term safety and efficacy of tiotropium (delivered via Respimat® [tiotropium Respimat®]) in Japanese patients with moderate to severe symptomatic asthma, despite ICS ± LABA.

Methods: In this randomized, double-blind, placebo-controlled, Phase III trial across 54 Japanese centres (NCT01340209), patients were randomized to receive evening tiotropium Respimat® 5 µg, 2.5 µg, or placebo, for 52 weeks. Eligible patients: age 18–75 years; never smoked/ex-smokers (≥1 year; <10 pack-years); ≥12-week history of asthma at enrollment; initial asthma diagnosis before age 40; seven-question Asthma Control Questionnaire mean score ≥1.5; forced expiratory volume in 1 second (FEV1) reversibility ≥12% and ≥200 mL (15–30 minutes after 400 µg salbutamol); maintenance treatment with medium-dose ICS ± LABA for ≥4 weeks before screening. Primary endpoint: long-term safety. Secondary endpoints included: trough FEV1; in-clinic peak expiratory flow rate (PEFR) using spirometry.

Results: 285 patients randomized, 264 completed treatment. Mean age was 44.5 years, 61.8% were female. The incidence of adverse events (AEs) was similar across treatment groups; most AEs were mild to moderate in intensity. Drug-related AEs occurred in 10 (8.8%), 6 (5.3%), and 3 (5.3%) patients in the tiotropium Respimat® 5 µg, 2.5 µg, and placebo groups, respectively. Serious AEs were less frequent with tiotropium Respimat® 5 µg (n = 4, 3.5%) and 2.5 µg (n = 4, 3.5%) versus placebo (n = 9, 15.8%). Adjusted mean trough FEV1 response was significantly higher with tiotropium Respimat® 5 µg versus placebo at Weeks 12, 36, and 52 (Week 52 difference: 0.112 L [95% confidence interval (CI): 0.018, 0.207; p = 0.0203]); no significant difference with tiotropium Respimat® 2.5 µg (Week 52 difference: 0.012 L, p = 0.7971). At Weeks 24 and 52, adjusted mean in-clinic PEFR was significantly higher with tiotropium Respimat® 5 µg versus placebo (difference: 28.981 L/min [95% CI: 5.047, 52.916; p = 0.0177] and 34.176 L/min [95% CI: 9.919, 58.432; p = 0.0058], respectively); no significant difference with tiotropium Respimat® 2.5 µg (p = 0.2302 and p = 0.9677, respectively).

Conclusions: Long-term tiotropium Respimat® treatment for 52 weeks has a safety profile comparable with that of placebo in Japanese patients with moderate to severe symptomatic asthma, despite ICS ± LABA. Improvements in trough FEV1 and trough PEFR with tiotropium Respimat® 5 µg versus placebo at Week 52 support the 5 µg dose as optimal for long-term therapy in this population.

P-A-010

P-A-011

ROLE OF ADRB2 AND TRPM8 GENETIC POLYMORPHISMS IN DETERMINING TREATMENT EFFECTS ON COLD AIRWAY HYPERRESPONSIVENESS AND ASTHMA CONTROL

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Background: Cold airway hyperresponsiveness (CAH) is common in bronchial asthma (BA) and complicates clinical course of the disease in cold climate conditions. The aim of the present study was to assess the influence of single nucleotide polymorphisms (SNP) ADRB2:c.46A>G (rs1042713) and TRPM8:c.750G>C (rs11562975) on changes in CAH and BA control after 6-months of maintenance therapy.

Methods: 60 mild-to-moderate asthmatics (mean age 39 ± 1.32) with uncontrolled disease (14.4 ± 0.42 ACT points) were enrolled in the study. Examination included lung function testing before and 3-minutes after isocapnic (5% CO₂) cold air (-20°C) hyperventilation challenge, asthma control assessment with Asthma Control Test (ACT) questionnaire and SNPs genotyping. CAH presence was determined as ≥10% fall in FEV₁ (ΔFEV₁). All the methods were performed twice: at the beginning of cold season and after 6 months. The patients received maintenance therapy with inhaled corticosteroids (beclomethasone or budesonide) and long acting β₂-agonist (formoterol) in medium daily doses.

Results: Three possible genotypes for each SNP were observed; however, TRPM8 750CC genotype was excluded from the analysis due to its rarity. Previously reported associations with CAH were confirmed for the ADRB2 SNP (p = 0.001) but not for the TRPM8:c.750G>C SNP, due to relatively small sample size. ΔFEV₁ differed significantly between ADRB2 46AA and 46GG genotype carriers (-13.65 ± 3.28% vs. -3.64 ± 1.19% respectively, p = 0.001) and in lesser extent, between TRPM8 750GG and 750GC genotypes (-6.93 ± 1.13% vs. -13.17 ± 3.68% respectively, p = 0.04). By the end of the treatment course, response to cold air decreased in all subjects except for ADRB2 46GG carriers and no significant differences in ΔFEV₁ were observed (-6.85 ± 1.99% vs. -2.95 ± 1.02% for ADRB2 46AA and 46GG genotypes, respectively, p > 0.05; -4.23 ± 0.70% vs. -5.73 ± 2.10% for TRPM8 750GG and 750GC genotypes, respectively, p > 0.05). Significant positive dynamics in BA control was registered independently of genotype after 6 months of maintenance therapy. However, it was less evident in ADRB2 46AA carriers who had lower control level in comparison to 46GG homozygous subjects after the treatment (17.07 ± 1.07 vs. 20.0 ± 0.54, respectively; p = 0.025). TRPM8 SNP did not seem to affect the treatment efficacy in our population sample.

Conclusions: Thus, collected data suggest relatively unfavourable prognosis for ADRB2 46AA carriers in terms of CAH and BA control. The studied TRPM8 SNP also predisposes to CAH, however, it is not so important in determining the treatment response as its effects on changes in ΔFEV₁ and ACT score have not been shown.

ADENOSINE METABOLISM IN BRONCHIAL ASTHMA: ROLE OF ADA, ADA1, ADA2 AND 5'-NT IN SERUM, LYMPHOCYTES AND ERYTHROCYTES

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Background: Adenosine deaminase (ADA) and 5'-nucleotidase (5'-NT) play crucial role in adenosine metabolism in healthy individuals. However, adenosine metabolism and role of ADA and 5'-NT in regulating adenosine level inside the cell as well as in serum of bronchial asthma patients and correlating these changes with severity of asthma is not known clearly.

Methods: Blood (10 ml) was collected and serum, lymphocytes and erythrocytes separated, followed by determination of adenosine levels and assay of activities of ADA, its isoenzymes (ADA1, ADA2) and 5'-NT in serum and lysates of lymphocytes and erythrocytes in 45 patients of bronchial asthma classified into three groups viz. mild persistent, moderate persistent and severe persistent and 15 healthy control.

Results: In bronchial asthma patients, adenosine levels in serum, lymphocytes and erythrocytes were found to be raised significantly as compared to healthy controls (p < 0.0001). A significant reciprocal correlation existed between adenosine levels in serum, lymphocytes and erythrocytes of asthma patients and FEV₁ (% of predicted). The 5'-nucleotidase activity in serum and lymphocytes was raised significantly in moderate and severe persistent groups and a significant inverse correlation existed between 5'-nucleotidase activity and FEV₁ whereas in erythrocytes it was raised only in severe persistent group and FEV₁ (% of predicted) had no correlation with the 5'-nucleotidase activity. The activities of ADA, ADA1 and ADA2 were decreased significantly in serum and lymphocytes of moderate and severe persistent asthmatics (p < 0.0001) and a significant positive correlation existed between ADA and FEV₁ (% of predicted). In erythrocytes, the ADA activity increased in mild persistent group but remains unchanged in moderate and severe persistent group in comparison to healthy control.

Conclusion: The present study provides evidence in favour of adenosine for its role as a crucial inflammatory mediator in asthma and suggests that adenosine levels tend to increase in serum, lymphocytes and erythrocytes with the severity of bronchial asthma. The balance between ADA and 5'-NT determines the levels of adenosine in serum and lymphocytes which may result in pathogenesis of bronchial asthma, or vice versa.

P-A-012

INFLUENCE OF GENE POLYMORPHISM ON AIR POLLUTANTS-INDUCED AIRWAY OXIDATIVE STRESS AMONG ASTHMATIC PATIENTS

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Background: An anti-oxidative enzyme, Glutathione-S-transferase (GST) P1, is known as the most prevalent isoform of the mammalian cytosolic GSTs and GST P1 has an A to G polymorphism at position rs6591256 in the gene. This may change its enzymatic activities, and affect the relationship between airway oxidative stress and gene polymorphism. Thus, a relationship between gene polymorphism of GST P1 and hydrogen peroxide (H₂O₂) in exhaled breath condensate (EBC) was investigated.

Methods: Totally 111 adult patients with asthma were recruited in our study under an informed consent from each patient with an institutional approval. Their DNA was extracted from whole blood, and gene polymorphism of GST P1 was determined, using PCR with specific primer sets. EBC was collected in a R-tube method, and H₂O₂ concentration was measured, using d-ROMs test (DIACRON®, Grosseto, Italia). Blood test and respiratory function test were also investigated. In addition, average data on atmospheric concentrations of nitrogen dioxide (NO₂), nitrogen oxides (NO_x), and particulate matter less than 2.5 micron in aerodynamic diameter (PM_{2.5}) on the previous day and on the previous month of collection of EBC were obtained from websites of the local public sectors.

Results: Seventy-nine patients had AA type of GST P1 polymorphism, thirty-two AG, and none GG. Atmospheric concentration of NO₂ on the previous month and H₂O₂ concentration in EBC were significantly correlated in patients with AA type ($p = 0.03$, $R^2 = 0.0894$, $95\%C.I. = 0.0694$ to 1.609). There is no significant correlation between them in patients with AG type. H₂O₂ levels in EBC were not significantly correlated either with NO₂ levels of the previous day, and NO_x levels, as well as PM_{2.5}, of the previous day and month.

Conclusion and Discussion: Our result indicated that oxidative stress in EBC was enhanced in patients with asthma carrying AA type, who were exposed to air pollutants. This implied that GST P1 polymorphism modifies asthmatic symptoms in association with air pollution.

P-A-013

EVALUATION OF THE RELATIONSHIP BETWEEN FRACTION OF EXHALED NITRIC OXIDE (FeNO) AND ADHERENCE TO MEDICATION IN ASTHMA PATIENTS USING ADHERENCE STARTS WITH KNOWLEDGE-20 (ASK-20)

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Background and Aim of the Study: The fraction of exhaled nitric oxide (FeNO) is one of the reliable bio-marker to monitor eosinophilic airway inflammation in asthma. Although FeNO increase indicate exacerbation of airway inflammation, there are patients have high FeNO with no symptoms. Under-treatment, complications and poor adherence to medication are the factors that would increase FeNO. Previous studies showed about 50% of asthmatic patients have poor adherence. Therefore evaluate adherence to medication may give better understanding of asthma control. We used Adherence Starts with Knowledge-20 (ASK-20) to evaluate adherence and its relationship with FeNO. ASK-20 is a questionnaire consists of 20 questions representing multiple factors that affect patient's adherence to medication.

Methods: We conducted a prospective observational study in NCGM outpatient clinic from February to July 2014. Patients diagnosed as bronchial asthma on steroid inhaler as a controller were asked to fill out ASK-20. To exclude undertreated patients, patients of under 20 in ACT were excluded. We evaluated their medication step, FeNO levels, respiratory function test results and complications. Patients were divided into two groups by FeNO amount of ≥ 38 ppb or below. We used Total Barrier Count (TBC) to assess individual adherence to medication, which is a total number of barriers of ASK-20.

Results: A total of 185 patients were enrolled in this study (aging from 20 to 84 years, mean age 58 years, male/female 93/92). Fifty nine percent of patients did not inhale steroids as prescribed, which indicated their poor medication adherence. Do not know whether reaching health goals (38%), taking medicines more than once a day is inconvenient (29%) were the popular barriers. TBC was correlated with self-reported percentage of inhaled steroids (Pearson coefficient: 0.39), however there was no relationship between TBC and FeNO (Pearson coefficient: 0.05). The level of FeNO was higher in patients with complications such as allergic rhinitis, sinusitis, ABPA and CEP compared with those without complications (FeNO 35.1 ppb vs 27.3 ppb, P value 0.04). FeNO level of the patients without complication had no co relationship with TBC, but male sex and smoking showed co relationship with TBC.

Conclusions: TBC is correlated with adherence to medication in asthmatic patients, but FeNO and ASK-20 has no co relationship with the patients with the score of ≥ 20 in ACT and patients with no complication. This indicates that poor medication adherence is not the only cause that would affect level of FeNO in asthmatic patients.

P-A-014

LOW DOSE OF COMBINED BUDESONIDE/FORMOTEROL (BUD/FM) IS BETTER THAN MEDIUM DOSE OF BUD MONOTHERAPY IN STEPPING DOWN FROM MEDIUM DOSE OF BUD/FM IN CONTROLLED ASTHMATIC PATIENTS

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Background: Asthma guidelines recommend management approach based on control for asthmatics to maintain good controlled state and to find lowest controlling step of therapy. However there is little evidence on the optimal timing, sequence, and magnitude of treatment reductions in asthma. When asthma is controlled with a combination of inhaled glucocorticoid (ICS) and long-acting β_2 -agonist (LABA), it is hard to select stepping down of ICS or LABA. In controlled asthmatics with medium dose of BUD/FM, we investigated which stepping down was better by reducing to low dose of BUD/FM or by discontinuing LABA and maintaining medium dose of ICS monotherapy.

Methods: We performed a prospective, randomized, controlled, two-arm parallel group study. 16 asthmatic patients who were fully controlled with medium dose of BUD/FM (320/9 μg) DPI twice a day for 12 weeks and Asthma Control Questionnaire-5 (ACQ-5) <1.0 were randomly assigned to 12 weeks of open-label treatment with either low dose 160/4.5 μg of BUD/FM DPI twice a day ($n = 8$) or medium dose 320 μg BUD DPI twice a day ($n = 8$). The primary outcome was the change in ACQ-5 between at baseline and at 12 weeks after stepping down. We also evaluated pulmonary function test (PFT), peak expiratory flow (PEF) values and adverse events. Additionally, with continuing the step down therapy, we observed the exacerbation and incidence of step up therapy for additional 8 months.

Results: There was no significant difference in ACQ-5 at baseline period between two groups and at 12 weeks after stepping down (low dose of BUD/FM; 0.0 ± 0.0 vs. medium dose of BUD monotherapy; 0.3 ± 0.6 , $P = 0.269$). In addition, there were no differences in PFT, PEF and adverse events between the two groups. After 12 weeks, five of 8 patients assigned medium dose of BUD monotherapy had to step up to medium dose of BUD/FM because of poor control of asthma. In contrast, only one of 8 patients assigned low dose of BUD/FM had to step up to medium dose of BUD/FM.

Conclusions: In controlled asthmatics by medium dose of BUD/FM, there were no significant differences in between stepping down with low dose of BUD/FM and that with medium dose of BUD monotherapy during 12 weeks. However, there were more exacerbations in the group of medium dose of BUD monotherapy within 8 months and the therapy was stepped up. Thus, in the step down therapy from medium dose of BUD/FM, reducing to low dose of BUD/FM was recommended.

P-A-015

AIRWAY OBSTRUCTION AND LUNG DIFFUSING CAPACITY IN PATIENTS WITH CONCOMITANT OBSTRUCTIVE SLEEP APNEOA AND BRONCHIAL ASTHMA

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Now, it is well established that bronchial asthma (BA) and obstructive sleep apnea (OSA) frequently coexist and mutually worsen and complicate each other in numerous ways. Previously reported data suggested the excessive body weight as the main cause of changes in lung carbon monoxide (CO) diffusion and airway patency. The aim of the present study was to assess lung function and diffusing capacity for CO in non-obese patients with concomitant BA and OSA.

Methods: 54 BA patients (mean age 39.6 ± 1.48) with Body-Mass Index (BMI) <30 were enrolled in the study. OSA was assessed by overnight cardiorespiratory monitoring. In addition, each patient underwent whole body plethysmography and lung CO diffusing capacity measurement to determine airway resistance (Raw) and diffusion parameters (TLCO, KCO).

Results: Out of 54 asthmatics 15% who had OSA (Apnea-Hypopnea Index (AHI) ≥ 5) were distributed to Group I, while the rest were allocated to Group II. Mean BMI was 24.3 ± 0.45 . BMI did not differ significantly between the patients in Group I and Group II. KCO was found to be relatively increased in asthmatics with OSA (97 (88; 101) vs. 74 (67; 98), $p = 0.01$). Expiratory, inspiratory and total Raw parameters were negatively correlated with mean overnight oxygen saturation ($r = -0.27$, $r = -0.49$, $r = -0.37$, respectively, $p < 0.01$). Positive correlations were revealed for TLCO and KCO with AHI ($r = 0.29$ and $r = 0.28$, respectively, $p < 0.05$).

Conclusions: Despite the fact we failed to demonstrate difference in airway resistance depending on the presence of OSA, we found diffusion of CO was significantly higher in OSA what may suggest its link with BA-associated changes in lung parenchyma. Another finding consisted in influence of airway resistance on overnight blood oxygenation. Persistently increased airway tone predisposes affected subjects to hypoxia, thereby promoting longer and more profound desaturation episodes. Thus, the results of the present study indicate the presence of bilateral mechanisms of interaction between OSA and BA that are not related to obesity.

P-A-016

LONG-ACTING ANTICHOLINERGIC AGENTS IN PATIENTS WITH UNCONTROLLED ASTHMA: A SYSTEMATIC REVIEW & META-ANALYSIS

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Background: A novel effective treatment is necessary for severe asthma.

Objectives: Here, we reviewed clinical trials that examined the role of tiotropium in patients with poorly controlled asthma despite inhaled corticosteroid use with or without long-acting β_2 -agonists.

Methods: A computerized search was performed through electronic databases (MEDLINE, EMBASE, and Cochrane Central Register) as well as a manual search for the references listed in relevant review articles. Randomized controlled trials of at least a 4-week treatment duration and published in English were included.

Results: Five studies involving 1,635 patients were finally analyzed. Compared with placebo or a double dose of inhaled corticosteroids, the addition of tiotropium increased mean trough and peak forced expiratory volume in 1 second by 96.52 mL (95% confidence interval [CI] 70.59–122.45) and 102.59 mL (95% CI 42.35–162.83), respectively. The mean differences in morning peak expiratory flow were 19.24 L/min (95% CI 11.83–26.64). Tiotropium also reduced the risk of severe acute exacerbation (relative risk, 0.90; 95% CI 0.88–0.99) and improved Asthma Quality of Life Questionnaire score significantly by 0.10 (95% CI 0.04–0.16). There were no differences in serious adverse events.

Conclusion: The addition of tiotropium can be beneficial for patients with poorly controlled asthma.

P-A-017

INFLUENCE OF OM-85 BV ON HBD-1 AND IMMUNOGLOBULIN IN CHILDREN WITH ASTHMA AND RECURRENT RESPIRATORY TRACT INFECTION

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Objective: To observe the clinical benefit of OM-85 BV (OM-85 Broncho-Vaxom) in children with asthma who have recurrent respiratory tract infection, and the effect of OM-85 BV on human β -defensins 1 (hBD-1) and immunoglobulin levels.

Methods: Sixty-two children with asthma and recurrent respiratory infection treated between 2011 January and December were divided into two groups by randomized, double blind method, a treatment group and a control group. With inhaling corticosteroids, the treatment group was given OM-85 BV, and the control group was given a placebo. Clinical benefit and adverse reactions were observed. Serum levels of hBD-1, IgA, IgG, IgM and urea and alanine aminotransferase (ALT) were measured before treatment, at 6 months and 12 months after treatment.

Results: Compared with the control group and before treatment, the frequency of respiratory tract infection was reduced in the treatment group at 6 months and 12 months after treatment ($P < 0.05$), and serum levels of hBD-1, IgA and IgG in the treatment group increased significantly ($P < 0.05$). There was no significant difference in serum levels of urea, ALT and IgM between the control and treatment groups ($P > 0.05$). Mild adverse reactions occurred in 3 cases in the two groups, 2 cases of abdominal pain and 1 case of constipation.

Conclusions: OM-85 BV can improve serum levels of hBD-1, IgA and IgG, reduce the number of acute respiratory tract infection and cause mild adverse reactions, suggesting its satisfactory therapeutic effect and safety in the treatment of children with asthma who have recurrent respiratory tract infection.

P-A-019

ASSOCIATIONS OF ASTHMA CONTROL AND SERUM LEVELS OF INTERLEUKIN 33 IN ATOPIC ASTHMA

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Background: Atopic asthma is a chronic inflammatory disease of the airways that based on an allergic reaction involving many cells and interleukin 33. Elements including Th-2 cells play an important role in the pathogenesis of atopic asthma. Activation of Th-2 cell by IL-33 as a result of inhalation of allergens will affect dendritic cells in the airways to activate Th0 cells which then would activate Th2 cells release cytokines such as IL-4, IL-5, IL-13. These cytokines then will increase the amount IgE and then stimulates the cells to release mediators such as histamine, leukotrienes, prostaglandins and quinine. The Mediators causes the onset of clinical symptoms of asthma. In addition to affecting IgE, Th2 cells also play a role in airway remodeling in asthma through the activation of IL-13. The degree of asthma control directly reflects the effectiveness of treatment Interventions.

Objective: To Assess the relationship the degree of control the disease and serum levels of interleukin 33 in atopic asthma.

Methods: Observational study with cross sectional approach in patients with atopic asthma were treated at Hasanuddin University Hospital from January to June 2014. The diagnosis of atopic asthma determined by clinical symptoms and skin Prick test. Examination of serum levels of interleukin 33 using Quantikine IL-33 D3300 (R & D Systems) by ELISA.

Results: There were 60 subject involved in the study with 40 subject atopic asthma and 20 non asthma. The mean ages of the subject was 31.7 ± 9.0 years. The mean serum levels of IL-33 was 1735,1 and the mean ACT score was 20.6. The mean serum levels of IL-33 in atopic asthma (1864.6) was significantly higher than non-asthmatic controls (1476.2) ($P < 0.01$). The mean serum levels of IL-33 in subjects aged <30 years old was significantly higher in atopic asthma (1924.2) compared to controls (1451.5) ($P < 0.01$), while the subjects >30 years old the difference was not significant. The mean serum levels of IL-33 was higher in uncontrolled asthma (1809) compared asthma control (1673.3) but not significant ($P > 0.05$).

Conclusion: There were relationship between atopic asthma with serum levels of IL-33, but there were no association with the degree of asthma control.

P-A-018

ASSOCIATION BETWEEN SERUM MAGNESIUM LEVEL AND SEVERITY OF ASTHMA EXACERBATION

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Background: Magnesium is competitor calcium in contraction of smooth muscle. This process play important role in patients with bronchial asthma. Low magnesium level has been associated with poor control of asthma. The understanding of magnesium role in asthma patients could give new perspective of asthma management in the future. The aim of this study is to determine association between serum magnesium level and severity of asthma exacerbation.

Methods: In this cross sectional study, we collected data prospectively; including demographic data, history of asthma and atopy, comorbid, asthma control test scores, history of asthma in family, grade of asthma exacerbation, and serum magnesium level at the time of exacerbation. Data were analyzed using nonparametric Kruskal Wallis test, p value of $<0,05$ is considered as significant.

Result: We found total 60 study subjects: 21 patients with mild exacerbation, 17 patients with moderate exacerbation, and 22 patients with severe exacerbation. Hypomagnesium was found in 16 (76,2%) patient with mild exacerbation, 8 (47,1%) patients with moderate exacerbation and 22 (81,8%) patients with severe exacerbation (Confident interval 95%; $p = 0,000$). The mean of serum magnesium level was getting lower with severity grade of asthma exacerbation ($1,6890 \pm 0,48427$; $1,9059 \pm 0,35789$; $1,6227 \pm 0,43854$; respectively, Confident interval 95%; $p = 0,047$).

Conclusion: Patient with asthma exacerbation tend to have low serum magnesium level.

P-A-020

P-A-022

IN VITRO LUNG DEPOSITION OF FLUTICASONE PROPIONATE/FORMOTEROL (FP/FORM) PRESSURIZED METERED DOSE INHALER (PMDI) WITH DIFFERENT INHALATION PROFILES

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Rationale: When assessing simulated deposition of pMDIs, it is normal to use a Sinusoidal Inhalation (SI) profile, similar to tidal inhalation. However, in real-life some patients with a pMDI inhale rapidly straightaway, with peak flow near the start of manoeuvre, a Rapid Inhalation (RI) profile. This study examined the influence of inhalation profile on lung deposition with fluticasone propionate/formoterol (FP/FORM) pMDI using Functional Respiratory Imaging (FRI).

Methods: 3D airway models of 6 asthma patients (mean FEV1 83%), treated with an ICS/LABA combination, were included. Total lung (TLD), central (C) and peripheral (P) airway deposition of FP/FORM were assessed using FRI. Simulations were performed with both SI and RI profiles, which were matched for the average flow rate (30 L/min and 60 L/min) and duration of inhalation (3s); actuation was timed with the start of inhalation.

Results: TLD and C/P ratios for both SI and RI profiles at 30 and 60 L/min are shown in the table.

TLD	30 L/min	60 L/min
SI	43.96 ± 2.63%	42.38 ± 2.92%
RI	39.73 ± 3.09%	36.13 ± 2.51%
C/P ratios	30 L/min	60 L/min
SI	0.38	0.46
RI	0.64	0.81

Conclusions: In vitro lung deposition was high with both profiles and both flow rates. Both SI and RI profiles resulted in mostly peripheral deposition although this was higher with SI profile, which may be more optimal for pMDIs. These data predict FP/FORM may provide high levels of lung deposition (~40% and above) of nominal dose with both RI and SI profiles, when used optimally, with deposition throughout central and peripheral airways.

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P-A-021

MESENCHYMAL STEM CELLS SUPPRESS ACTIVATION OF OVA LOADED DENDRITIC CELLS DERIVED FROM BONE MARROW OF ACUTE ASTHMA MOUSE MODEL

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Background: Besides the high differentiation potential, mesenchymal stem cells (MSCs) have immunosuppressive activity on both the adaptive and natural immune system. In this study, we aimed to investigate *in vitro* effect of bone marrow derived mesenchymal stem cells (BM-MSCs) both on the activation of dendritic cells (DCs) generated from mouse (m) model of acute asthma and proliferation of lung lymphocytes.

Methods: mBM-MSCs were isolated from Balb/C mice and characterized. To generate murine models of acute asthma, mice were i.p. sensitized with OVA and exposed to aerosolized OVA. After last nebulization, BM-DCs were generated *in vitro* from monocytes induced with granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin-4 (IL-4). Lung lymphocytes were also isolated from murine models of acute asthma and marked with CFSE. Ovalbumin (OVA)-loaded DCs and lymphocytes were cultured with/without MSCs for 3 days and flow cytometric analysis was evaluated.

Results: Numbers of goblet cell were significantly increased in ovalbumine-treated mice of both distal ($p < 0.001$) and proximal ($p < 0.01$) airways compared to PBS group. BM-DCs generated from murine models of acute asthma were characterized according to expression of CD11c⁺-CD11b⁺ (%78,3 ± 4,2) and CD11c⁺-B220⁻ (%60,5 ± 5,4) markers. On the third day of cell cultures, the presence of MSCs (%12,81 ± 0,8) suppressed proliferation of lung lymphocytes cultured with OVA-induced DCs (%16,25 ± 0,5).

Conclusions: Our results showed that mBM-MSCs generated from Balb/C mice inhibited proliferation of lung lymphocytes obtained from acute asthma model by suppressing the function of DCs. The results reported here provided evidence that mBM-MSCs may be an alternative strategy to treatment of asthma.

AWARENESS AND USAGE OF INHALERS AMONG PATIENTS WITH ASTHMA: FINDINGS FROM REALISE ASIA

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Background/Aim: A recent patient survey (REALISE) noted that despite the availability of effective treatments, asthma control remains low in Europe. Contributing factors include poor treatment adherence. We present here data from a similar survey in Asia, looking at impact of awareness and usage of inhalers on asthma control.

Methods: Patients were recruited via validated consumer panels across 8 countries in Asia. A total of 2,467 patients with asthma completed the online survey (46% females, mean age 34 years).

Results: Majority (88%) of respondents were taking some form of medication for their asthma: 54% used a reliever inhaler, 25% on controller inhaler, and 36% on oral medication. 35% of all respondents reported that they had to use their reliever inhaler ≥3 times in the past 7 days. Of the respondents who had a reliever inhaler, their average use was 2.8 times in the past week. Among those who reported having a controller inhaler, only 14% used it daily, 43% said they used it on some days, and 7% never used it at all. Over 40% cited that they did not see the need to take daily medication. Nearly half (48%) of the patients mentioned that inhaler use is a real nuisance, and 47% disagreed that they need to take their controller inhaler regularly to control their asthma. Among those who cited they have inhalers, only 39% and 35% were able to correctly classify their inhalers as controller and reliever respectively. Looking at GINA-defined level of control, a statistically significant larger proportion of respondents who named their controller inhaler correctly were well-controlled (14%), than those who answered incorrectly (6%; $p = 0.05$). The same pattern was seen for those who correctly classified their reliever inhaler (16%) versus those who were incorrect (7%; $p = 0.05$). Patients who correctly identified their inhalers were also significantly more likely to use it daily compared to those who were not able to do so (30% vs 17%; $p = 0.05$). By the same token, significantly more patients who incorrectly named their controller inhaler used it on irregular basis (e.g. only on some days) compared those who are able to do so (53% vs 36%; $p = 0.05$).

Conclusion: Asian patients with asthma are not always able to correctly identify their medications. This emphasizes the need for health care professionals to take time to explain to patients the difference between controller and reliever medications, since such awareness is associated with better adherence and level of asthma control.

P-A-023

PREFERRED SOURCES OF INFORMATION ON ASTHMA: DATA FROM MULTINATIONAL SURVEY OF PATIENTS IN ASIA

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Background/Aim: Provision of suitable asthma information to patients, their family and other carers is an important component of holistic management. A large multinational survey in Europe (REALISE) showed that health care professionals and online sources are two most important sources of disease information favoured by patients with asthma. We describe here the preferred sources of information from a similar survey of patients in Asia.

Methods: Using validated consumer panels across 8 countries in Asia, patients diagnosed with asthma (age 18–50 years, ≥ 2 prescriptions for asthma in past two years) were recruited for this online survey. All patients had used social media.

Results: Over 90% of respondents report they had at least a reasonable knowledge about asthma and how to manage it, with 72% claiming that they know how to manage without the help of physicians. However, only 18% of patients are considered well-controlled using GINA-defined criteria. More than 81% still actively look for information about their asthma at least once a year and 33% even doing such at least once a week. Topics which patients most frequently seek are those relating to asthma exacerbations: how to prevent, what are the triggers, and what they should do in an event of asthma attack. Respiratory specialists are the most preferred sources of information (57%) followed by online sources such as search engines (52%), or specific disease or health websites (39%), and primary care physicians (38%). Over 90% of patients consider physicians (specialists or general practitioners alike) as trustworthy sources of information. Although $>70\%$ of patients consider internet information (i.e. disease or health websites, search engines) as trustworthy, only 33% would recommend them to friends. In general, social media (such as Facebook, Twitter, and YouTube) are not considered as trustworthy information sources as compared to medical professionals.

Conclusion: Patients with asthma in Asia prefer physicians (respiratory specialists and primary care physicians) and internet (disease or health websites, search engines) as sources of information about asthma. To better impact asthma outcomes, health care professionals should leverage on this information-seeking attitude of patients and lead them to effective guided asthma self-management.

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P-A-024

POLYMORPHISMS OF ALOX15 GENE IN JAPANESE PATIENTS WITH ASPIRIN-EXACERBATED RESPIRATORY DISEASE (AERD)

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AERD is known to represent acute asthmatic attacks by means of ingestion of aspirin and other non-steroidal anti-inflammatory drug (NSAID). Individuals with AERD are more commonly found in middle-aged female, and their asthmatic symptoms tend to be chronic, perennial and severe. AERD has been attributed to abnormalities of the arachidonic acid metabolism. However, the pathophysiologic mechanisms underlying the development of this specific asthma phenotype have not yet been fully understood. In this study, we examined the ALOX15 gene polymorphisms in a Japanese adult population.

Methods: DNA specimens were obtained from the following three groups: 50 patients with AERD, 50 patients with aspirin-tolerant asthma (ATA), and 50 normal controls.

Allelic discrimination assay for single nucleotide polymorphisms (SNPs) relating to the ALOX15 gene expression was carried out by using previously described SNPs detective system, sequence-specific thermal-elution chromatography.

Results: The frequencies of the GG genotype of ALOX15(rs2664593) were higher than those of the GC/CC genotype in AERD patients compared to ATA patients and controls ($P = 0.042$ and $P = 0.008$, respectively). In female AERD patients, but not in males, frequencies of the GG genotype were higher than those of the GC/CC genotype of ALOX15 compared to female controls ($P = 0.003$). Comparison of the clinical characteristics in AERD patients according to the ALOX15 gene polymorphisms showed that the level of total serum IgE, the total count of peripheral eosinophils and the prevalence of atopy were not different between the polymorphisms.

Conclusions: We were the first to analyze ALOX15 gene polymorphism in Japanese patients with AERD, and showed that ALOX15 gene polymorphism in Japanese patients with AERD is different from that in the patients with ATA.

P-A-025

P-A-026

CLINICAL, PHYSIOLOGICAL, RADIOLOGICAL AND IMMUNOLOGICAL ABNORMALITIES IN ELDERLY ASTHMATICS WITH FIXED OBSTRUCTIVE AIRFLOW OBSTRUCTION IN RAMATHIBODI HOSPITAL

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Introduction: Elderly with asthma suffer from poor outcomes and unable to clinically distinguish from COPD patients. Immunological senescence and age related physical changes are potential problems. Since asthma COPD overlap syndrome (ACOS) is recognized in practice and mentioned in GINA 2014. We hypothesized whether asthma with fixed obstructive airflow limitation have persistent eosinophilic inflammation and atopic nature as well as airway remodeling in the presence of aging.

Material and Methods: Cross sectional study in asthmatics older than 60 years having post bronchodilator FEV1/FVC ratio <0.7 and post bronchodilator FEV1 < 80% predicted performed in 2013. Serum total and specific IgE were measured using ELISA (ImmunoCap, Sweden). Exhaled nitric oxide (FeNO) concentration was measured using electrochemical technique (NoBREATH, UK). Lung volumes were measured using body plethysmography. DLCO was measured using single breath technique. High resolution computed topography (HRCT) of chest was performed.

Results: There were 25 older asthma patients enrolled. Female were 21 cases. Mean age was 69 ± 6 years. BMI was 24 ± 4 kg/m². Mean duration of being diagnosed asthma was 14 (2–60) years. Tobacco smoking was less than 10 years duration. Mean ACT score was 21.2 ± 3.4. All of them were treated with either ICS or ICS-LABA. However, 20% of cases were treated with LAMA. Mean post BD FEV1 was 67 ± 10% predicted and FEV1/FVC ratio was 0.6 ± 0.1. Mean TLC was 92 ± 13% predicted and RV/TLC ratio was 43 ± 5%. DLCO was 79 ± 16% predicted and KCO was 109 ± 22%. VA/TLC ratio was 0.85 ± 0.1. Bronchiectasis detected from HRCT was noted in 28%. Centrilobular nodules and bronchiolectasis (tree-in-bud pattern) was noted in one-third. Mean serum total IgE was 263.4 (24–1530) IU/ml. Serum specific IgE to mixed respiratory allergen was positive in 40% of cases. Mean FeNO was 62.6 ± 33.1 (16–142) ppb.

Conclusions: Despite of having fixed obstructive defect detecting by using spirometry. The elderly with asthma have their physiological abnormalities consistent with air trapping as well as small airway dysfunction with preserved pulmonary gas exchange. The associated bronchiectasis is commonly observed from imaging studies. Atopy is not uncommon despite of being senile. High exhaled nitric oxide concentration representing eosinophilic airway inflammation is noted in these subjects.

CORRELATION OF BODY MASS INDEX (BMI) WITH ASTHMA CONTROL TEST (ACT) AMONG ADULT ASTHMA PATIENTS

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Background: Obesity and asthma are significant health problems in Malaysia. Obesity can make asthma more difficult to control by reducing beneficial effects of asthma medications. Various studies reported obesity as a risk factor that affects asthma control independent of spirometric readings and airway inflammation. ACT is important parameter to monitor the control of asthma, as BMI is for obesity. This study was conducted to determine the correlation of BMI with ACT.

Methods: In this correlational study thirty three asthma patients were enrolled by the convenient sampling method from Respiratory Specialist Clinics, Universiti Teknologi MARA (UiTM) Selayang, and Sungai Buloh; both located in Selangor, Malaysia. Patients' demographics data and BMI values were taken from patients' records. The validated Malay version of Asthma Control Test (ACT) was used to assess the control of asthma. The extracted data from the patient-completed ACT questionnaires and values of BMI were analyzed for Pearson's Product Moment Correlation (r) by using Statistical Package for Social Sciences (SPSS)®.

Results: A total of 12 (36.4%) patients were obese (BMI ≥ 30); 15 (45.5%) patients were overweight (BMI = 25.0–29.9); and 6 (18.2%) patients had a normal BMI (18.5–24.9). A significant and moderately negative correlation was found between BMI and asthma control test ($r = -0.347$, $p < 0.05$). The correlation findings of the current study were consistent with the findings reported in literature previously i.e. consistent negative relationship between obesity and asthma control.

Conclusion: Obesity negatively influenced the control of asthma. For the optimal management of asthma especially in obese patients, additional research should be conducted with greater sample size and multiple study sites. Furthermore, the impact of obesity on development and clinical expression of asthma need to be explored thoroughly for better management of asthma.

P-A-027

DEFICIENCY OF FCγRII ON MESENCHYMAL STEM CELLS ATTENUATES MSC SUPPRESSIVE FUNCTIONS

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Objective: Discuss the difference function to asthma and dendritic cells between FcγmR deficient and wide type mesenchymal stem cells, and find the reason.

Methods: 1. Co-cultured DC different MSCs stimulating with LPS: (1) detecting the CD11c, I-Ab and CD86 using Flow Cytometry; (2) ELISA for IL-12 of the supernatant; (3) mixed lymphocyte culture with different DC, and then detected the proliferation of T cells.

2. Analyzing MSCs: (1) extracted mRNA from different MSCs, did reverse transcription and Q-PCR; (2) extracted protein from different MSCs, did Western-Blot; (3) ELISA for PGE2 of the supernatant.

3. Grouped and made acute asthma models: NC (naïve control group), AC (asthma control group), T1 (asthma mice treated with wide type MSCs group) and T2 (asthma mice treated with Fcγ-deficient MSCs group);

4. Detected serum IgE, bronchoalveolar lavage fluid (BALF) cells, BALF IL-4, BALF IL-13, BALF IL-10, BALF PGE2; lung pathology (using HE).

Results: MSCs express high level of Fcγr2bII; Fcγr2bII 2B-/- MSC is less effective in suppressing DC maturation; Fcγr2bII deficient MSC is less potent in suppressing antigen-specific T cell response; Fcγr2bII deficient MSCs produce less amount of PGE2. AC-IgE was higher than NC-IgE ($p < 0.001$), T1-IgE and T2-IgE were lower than AC-IgE ($p < 0.05$), and T1-IgE was lower than T2-IgE ($p < 0.1$); BALF cells: AC was higher than NC ($p < 0.001$), T1 and T2 were lower than AC ($p < 0.05$), and T1 was lower than T2 ($p < 0.05$). BALF IL-4 and IL-13: AC was higher than NC ($p < 0.001$), T1 and T2 were lower than AC ($p < 0.05$), and T1 was lower than T2 ($p < 0.05$). BALF IL-10: AC-IL-10 was higher than NC-IL-10 ($p < 0.001$), T1-IL-10 and T2-IL-10 were higher than AC ($p < 0.05$), and T1-IL-10 was higher than T2-IL-10 ($p < 0.05$). BALF PGE2: T1-PGE2 and T2-PGE2 were higher than AC-PGE2 ($p < 0.001$), and T1-PGE2 was higher than T2-PGE2 ($p < 0.05$). HE staining: NC normal, AC the worst, T1 and T2 better than AC, and T1 better than T2.

Conclusion: MSCs could suppress the maturation of DC then suppressing the proliferation of T cells, and could improve the condition of asthma mice. Wide type MSCs produced higher level of COX-2 and PGE2 than Fcγr2bII deficient ones, and the suppressive function of DC, T cells and the ability to improve asthma condition of wt-MSCs were stronger than Fcγr2bII deficient ones.

P-A-028

PREVALENCE AND EFFECT OF METABOLIC SYNDROME (MS) ON SEVERITY AND CONTROL OF BRONCHIAL ASTHMA: AN OBSERVATIONAL STUDY IN INDIAN SCENARIO

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Background: Asthma is a recognized cause of chronic morbidity in both children and adults. Recently metabolic syndrome (MS) has been recognized as a significant co-morbidity in asthmatics, though the exact data from Indian population is lacking.

Objectives: To determine the prevalence of MS in Indian adult bronchial asthma patients and to compare asthma severity, control and pulmonary functions amongst those with MS and those without it.

Methods: This cross-sectional study included 100 patients with bronchial asthma between 18–65 years of age. All patients were evaluated for presence of MS as per International Diabetes Federation (IDF) 2006 criteria on clinical and laboratory parameters (abdominal girth, blood pressure, fasting blood glucose, HDL and triglycerides levels). A detailed history, clinical examination and pulmonary function testing using spirometry was undertaken for assessment of asthma control and severity (based on GINA guidelines 2012) and compared between those with MS and those without it using standard statistical methods.

Results: Thirty six males (36%) and 64 females (64%) asthmatics with a mean age of 37.41 ± 11.55 years were examined. Of these, MS was present in 38 patients comprising 14 males and 24 females (38.8% and 37.5% of total, respectively). 79% asthmatics were found to be obese (based on BMI), 23% were diabetic and 17% had hypertension. On spirometry, no significant difference was observed in mean FEV1 and mean post-bronchodilator percentage change in FEV1 between asthmatics with MS ($1.86 \pm 0.56/L$ and $26.68 \pm 20.44/L$) and those without MS ($2.00 \pm 0.60/L$ and $24.44 \pm 20.4/L$) (p -value 0.24 and 0.56 respectively). However, on asthma control test, only 5.3% asthmatics with MS had well controlled asthma compared to 67.7% asthmatics without MS. Most asthmatics with MS had partly controlled (50%) or uncontrolled asthma (44.7%) compared to those without MS (27.4% and 4.8%, respectively) (p -value 0.000). Further, asthmatics with MS had mild persistent asthma in 36.8%, moderate persistent in 50% and severe persistent in 13.2% while corresponding values for asthmatics without MS were 35.5%, 6.5% and 0%.

Conclusion: The prevalence of metabolic syndrome was high among the asthmatics studied. We also recorded worse asthma control and more severe asthma in those with MS. Hence it is recommended to screen all patients with asthma for components of metabolic syndrome and institute early measures to improve overall outcome of asthma management.

P-A-029

MANAGEMENT OF PATIENTS WITH ASTHMA REQUIRING ICU ADMISSION USING NON-INVASIVE VENTILATION: A PILOT STUDY

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Background: Non-invasive ventilation continues to be used in clinical practice for acute respiratory distress caused by asthma, despite the lack of large randomized trials supporting its use. It has been shown that Non-Invasive Ventilation (NIV) augments the use of bronchodilators; however the exact role of NIV in preventing further escalation of care, complications, and prolonged length of stay is unclear. This study aims to describe the use of NIV among patients admitted to a metropolitan Australian Intensive Care Unit (ICU) with an admission diagnosis of asthma.

Methods: A retrospective investigation was conducted of an opportunistic sample of 21 patients admitted to Frankston Hospital with a primary diagnosis of asthma between 2011 and 2013. Information retrieved from patients' Digital Medical Records included demographic information, management in ED and ICU, and length of hospital and ICU admission.

Results: 11 of the 21 patients (52.4%) were active smokers at the time of admission. Prior to hospital admission 3 patients (14.3%) took short acting beta agonist relievers only, while nearly half (47.6%) were managed with the combination of an inhaled reliever and steroid prophylaxis. 47.6% had previous ICU admissions for asthma. Of the 21 patients studied, 71% received only NIV in ED; 9.5% were intubated in ED and 19% received only high flow supplemental oxygen while in ED. 8 out of the 21 patients (38%) were intubated during their ICU stay, while 7 patients (33%) received only NIV. 62.5% of patients that were intubated in ICU had previously received NIV but required mechanical ventilation due to BiPAP failure. Average hospital LOS was 8 days for intubated patients, and was 6 days for patients receiving only NIV in ICU. Average hospital LOS was 3 days for patients that did not require ventilatory support whilst in ICU. Among patients that were intubated 3 developed complications whilst in ICU (pneumonia, acute kidney injury, hyperkalaemia), while only one patient receiving NIV in ICU developed any in-hospital complications (pneumonia).

Conclusion: NIV appears to be a first line therapy for the majority of patients with severe asthma requiring ICU admission, and the use of this therapy for management of severe asthma warrants further investigation. Larger sample sizes are required to identify the influence of interventions such as NIV on outcomes for patients with severe asthma requiring ICU admission.

- More patients in Malaysia are well-controlled (28%)
- Indonesia has lowest number of well-controlled (9%) and highest uncontrolled asthma (62%)

Steroid and antibiotic use: 73% required >1 course of oral steroids, and 76% required >1 course of antibiotics in the past 12 months for worsening of asthma

- China has the highest number of courses of oral steroids (3.3x) and Philippines, the least (1.4x)
- China has highest proportion of patients who had antibiotics (85%), while Taiwan, the least (59%)

Inhaler use:

- 76% own a reliever inhaler, of which 32% used it >3x in the past week, with Indonesia having highest average frequency (3.7x).
- Among those who use a controller inhaler, only 14% takes it daily. China and Hong Kong report higher proportion of patients (59% and 51% respectively) who use their controller inhaler on some days, but not on others.
- Almost half (48%) of patients find using their inhaler a real nuisance, highest noted in Korea (58%)

Consultation:

- Patients in China (81%) and Taiwan (61%) see respiratory specialists for asthma, while SG (75%) and HK (59%) mainly see family physicians/general practitioners.
- Top reasons for consults are regular asthma review (39%) and worsening of symptoms (29%).
- Malaysia and Philippines had the least proportion of patients who ignore physicians' instructions on when and how often to take inhaler medication (25% and 23% respectively).

Conclusion: Differences in patient perceptions and levels of asthma control exist among countries in the Asia-Pacific region. Such differences could be considered in identifying unmet needs in each of the countries, and when embarking on country or regional programmes aimed at improving asthma care in this part of the world.

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P-A-031

DIFFERENCES IN PATIENT-PERCEPTIONS AND LEVELS OF ASTHMA CONTROL ACROSS 8 ASIAN COUNTRIES: DATA FROM THE REALISE ASIA SURVEY

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Background/Aim: A recent survey in Europe (REALISE) provided insights into their attitudes of patients to asthma. We report here results from a similar survey, showing differences in patient-perceptions and asthma control across 8 countries in Asia.

Methods: Online surveys were conducted in patients with asthma (aged 18–50 years, >2 prescriptions for asthma in the past two years), recruited via validated consumer panels. 2,467 patients completed the survey, split across: Mainland China (n = 800), Hong Kong (n = 200), Indonesia (n = 166), Korea (n = 500), Malaysia (n = 151), the Philippines (n = 150), Singapore (n = 200), and Taiwan (n = 300).

Results: For several parameters, results were similar across the countries. Significant differences compared to over-all rates are summarized below:

Asthma control: 18% are well-controlled, 32% partly controlled, and 50% uncontrolled as per GINA-defined criteria

P-A-032

NITRIC OXIDE (NO) SPUTUM LEVEL IN ASTHMA EXACERBATION PATIENT

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Background: Diagnose of asthma is based on clinical symptoms, degree of airflow limitation and airflow hyperactivity. Degree of airflow limitation can be detected by lung function examination using spirometry, and bronchial hyperactivity can be detected by administration of stimulant such as histamine and meticholin. Patients with mild asthma often show normal value on FEV1 and bronchial challenge test on meticholin or histamine only assess bronchial hyperactivity but difficult to assess the degree of inflammation. To evaluate airflow inflammation and examination which can describe the current inflammation condition and NO sputum measurement suggested as non invasive examination to assess airflow inflammation on asthma.

Methods: This research was conducted in emergency department Dr Soetomo hospital with total sample 36 subject consist of 18 asthma exacerbation patients and 18 normal peoples as control. Respondents male and female 15–55 years old who meet the include and exclude criteria. Sample collected using consecutive sampling and statistics analyzed using SPSS 17. The difference was conclude when the value of statistic test less than 0.05.

Results: In this study, a significant increase in level of NO in asthma exacerbations than those of normal ($1130 \pm 179 \mu\text{mol/L}$ vs $684 \pm 214 \mu\text{mol/L}$, $p < 0,001$) and there is a statistically significant positive correlation NO sputum level with asthma exacerbation ($r = 0,783$; $p = 0,001$). On lung function measurement PEF value on asthma exacerbation significant lower than those normal ($165,94 \pm 63,02 \text{ L/mnt}$ vs $454,44 \pm 54,03 \text{ L/mnt}$; $p < 0,001$). There is negative correlation between asthma exacerbation with PEF ($r = -0,870$; $p < 0,001$). This research looks at the relationship between NO sputum level with PEF value measurement. Statistical analyses showed increasing NO sputum level were negatively correlated with PEF value ($r = -0,726$; $p < 0,001$). Which means the higher level of NO sputum PEF value getting lower and the other way the higher PEF level NO sputum level getting lower. In this research the cut off point is determined using the ROC curve methods and cut off point obtained NO sputum level is $900 \mu\text{mol/L}$ with a sensitivity of 100% and specificity of 80%.

Conclusion: Generally, NO sputum examination can be used as a inflammatory biomarker in asthma exacerbations with cut off point NO sputum level is $900 \mu\text{mol/L}$.

P-A-033

INHALED CORTICOSTEROID USE AND RISK OF DIABETES MELLITUS

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Background and Aims: Inhaled corticosteroid (ICS) is the basis in treatment of asthma and chronic obstructive pulmonary disease (COPD). ICS use was revealed to increase the risk of glaucoma, cataracts, but the risk of diabetes mellitus (DM) and ICS use has not been completely studied. We conducted a meta-analysis for the relationship between ICS use in asthma or COPD and the risk of new onset DM.

Methods: The relevant published studies were identified using a search of PubMed, Embase. The effect sizes of DM risk with ICS use were calculated by risk ratio (RR). The effect sizes were combined using a random-effects model.

Results: With unadjusted data, ICS use was significantly associated with DM risk ($RR = 1.179$; $p < 0.001$). However, with adjusted data, ICS use seemed to be associated with DM, but there were no statistical significance ($RR = 1.096$; $p = 0.174$). DM event rate in ICS use patient was 29% (95% CI: 0.011–0.076; $p < 0.001$).

Conclusions: ICS use in COPD and asthma may increase the DM risk. Thus, ICS use patients should be screened for the DM.

P-A-034

EFFECT OF YOGA PRACTICE & DIAPHRAGMATIC BREATHING EXERCISES IN BRONCHIAL ASTHMA: A PROSPECTIVE STUDY FROM INDIA

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Introduction: Effect complementary and alternative therapies (CAT) are being studied in Asthma management, locally in various countries with reports of varying effects. CAT includes a variety of breathing and relaxation exercises including Yoga, Buteyko Breathing Technique diaphragmatic breathing, progressive relaxation etc. If these can facilitate easy disease control, they can be utilized in bringing down the cost of Asthma treatment, a major issue in resource limited countries like ours, and troublesome adverse effect.

Aim: 1. Compare the effect of 2 CATs i.e YOGA practice Training (YPT) and Diaphragmatic Breathing Exercises (DBE) in asthma treatment. 2. Compare the effect of each to conventional treatment alone.

Materials and Methods: Prospective, case-control study conducted in an allergy clinic at Alappuzha. Patients with persistent asthma aged 25–65 years were randomly grouped into 3. A) Receiving conventional therapy alone; B) Above+YPT; C) Above+DBE. Disease control was assessed by spirometry, Mini Asthma Quality of Life Questionnaire, Asthma Control Test and β -agonist use during the first week of study and end of third month. Statistical analysis was by 2 way ANOVA technique.

Result: Total of 60 patients, 20 in each group studied. No significant difference in FEV1 among 3 groups; statistically significant improvement in quality of life (QOL) among groups B & C, with reduction in β -agonist use.

Conclusion: YPT is useful in improving QOL among asthmatics. It may be useful for reducing β -agonist use.

P-A-035

P-A-036

REAL-WORLD SWITCHING EFFECTS OF DIFFERENT INHALED CORTICOSTEROID/LONG-ACTING BETA-AGONIST COMBINED INHALERS IN THE TREATMENT OF ASTHMA

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Background: Current development of treatment modalities in treating bronchial asthma reduces mortality of asthma and improves quality of life of asthmatic patients. There are several inhaled corticosteroid/long-acting beta-agonist (ICS/LABA) combinations currently used to treat asthmatic patients, however, the clinical differences between these two ICS/LABA combinations have not been fully investigated. Therefore, we evaluated the switching effects of two ICS/LABA combinations (fluticasone propionate/salmeterol combined Discus inhaler; FP/SM, budesonide/formoterol Turbuhaler inhaler; BUD/FM) in a real-world setting.

Patients and Methods: Asthmatic patients over 20 year-old treated with FP/SM or BUD/FM for more than two months with persisting asthmatic symptoms (scores of Asthma Control Test; ACT less than 25 or scores of Asthma Control Questionnaire 5; ACQ5 more than 0) were enrolled. FP/SM (250/50 µg bid) was switched to BUD/FM (160/4.5 µg two inhalations bid) and FP/SM (500/50 µg bid) was also switched to BUD/FM (160/4.5 µg four inhalations bid). Conversely, BUD/FM (160/4.5 µg two inhalations bid) was switched to FP/SM (250/50 µg bid) and BUD/FM (160/4.5 µg four inhalations bid) was switched to FP/SM (500/50 µg bid). The spirometric analysis including the values of the peak expiratory flow (PEF) and forced expiratory volume in one second (FEV1) at the time of 0, 4, 12 and 24 weeks after switching from FP/SM to BUD/FM or from BUD/FM to FP/SM, and the scores of the asthma control test (ACT) and asthma control questionnaire-5 item version (ACQ5) were also evaluated.

Results: Sixty patients (35 and 25 patients had received medium- and high-dose ICS/LABA, respectively) were switched from FP/SM to BUD/FM, and 20 patients (10 and 10 patients had received medium- and high-dose ICS/LABA, respectively) were eligible for an evaluation after switching from BUD/FM to FP/SM. In patients switched from FP/SM to BUD, ACT and ACQ5 were significantly improved four and eight weeks after the switch to ICS/LABA treatments, and the spirometric analysis also revealed significant improvements of the values of the PEF and FEV1 after switching from FP/SM to BUD/FM. In patients switched from BUD/FM to FP/SM, asthmatic symptoms (ACT and ACQ) and the values of spirometric analysis were not significantly changed, except for FEV1 that showed significant improvement after switching ICS/LABA, but one patient dropped out because of an exacerbation of asthmatic symptom.

Discussion: Switching of ICS/LABA combined inhalers can be an alternative treatment for asthma in symptomatic asthmatic patients.

EFFECT OF ADJUSTING THE COMBINATION OF BUDESONIDE/FORMOTEROL

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Background: One of the characteristics of the combination of budesonide/formoterol (BFC) is that the dose can be adjusted in a single inhaler, according to the asthma symptoms. We analyzed the relationship between asthma symptoms, including peak expiratory flow rate (PEFR) and adjustment of the dose by the patient.

Material and Methods: Subjects were patients with asthma who used BFC for their asthma (male: female = 10:10; mean age, 60 years). We explained to the patients that BFC dose could be increased to a maximum of 8 times of inhalation per day, according to asthma symptoms. Patients measured PEFR every morning and evening, and they noted PEFRs in their asthma diary as well as their symptoms and the dose of drugs. The mean observation period was 245 days. The personal best PEFR in the observation period was 100%. The study was approved by the ethics committee of Dokkyo Medical University (No. 22072).

Results: In the observation period, 11 patients did not increase their dose of BFC (fixed group), and 9 patients increased their dose when they had asthma symptoms (variable group). PEFR was decreased to less than 80% of the personal best for 5.78 days per month in the fixed group and 0.35 days per month in the variable group. The relationship between PEFR at the dose be increased (X) and days taken for when the dose be increased to when PEFR recovered to greater than mean PEFR at no symptom (Y) was $Y = -0.006X + 0.9085$ ($r = -0.73$, $p < 0.0001$). To keep no symptom, BFC should be increased before PEFR is decreased to 90% of personal best. It will take 18 days to recover, if BFC is increased in the time when PEFR is decreased to 80% of personal best.

Conclusion: For increasing BFC when patients have asthma symptoms, exacerbation of asthma recovered earlier in the variable group than in the fixed group. When mild asthma symptoms, such as cough or sputum are present, or PEFR is decreased to 90% of personal best, BFC should be increased. We are continuing to enroll new subjects in our on-going study. We will present the final results at APSR 2014.

P-A-037

A MULTI-CENTRE NON-INTERVENTIONAL STUDY OF THE ASTHMA CONTROL LEVEL ACHIEVED BY BUDESONIDE/FORMOTEROL IN CLINICAL PRACTICE

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Objective: To determine the asthma control rate achieved by budesonide/formoterol (B/F) combination therapy under clinical practice in Chinese asthma patients according to Global Initiative For Asthma 2011 (GINA) definition and Asthma Control Test (ACT) score.

Methods: This study is of a multi-centre, cross-sectional design. Patients were enrolled if they were ≥ 18 years old, outpatients with a clinical diagnosis of asthma 6 months, have received B/F for ≥ 3 months and the same maintenance dose of B/F for ≥ 4 weeks before enrollment, and had not been given any other asthma maintenance medication in the past 3 months.

Results: A total of 628 patients from 27 sites were recruited, 617 patients were in FAS who used B/F for a mean of 15.4 months. The mean (SD) age of patients was 44.2 (13.8) years with a mean (SD) asthma history of 7.2 (9.7) years; 66.1% of patients were female. 85.7% of the patients was at least middle school in education. Regarding the history of smoking, 87.8% of patients had never smoked, 10 (1.6%) are current smokers, and 65 (10.5%) had previously smoked. Among all patients, 516 (83.6%) patients used B/F as maintenance and reliever therapy (SMART®), whilst the remaining 16.4% of patients used short-acting β_2 -agonists (SABA) as reliever. Controlled and partly control asthma was achieved in 59.6% and 33.5% of patients, respectively, according to GINA definition. While well-controlled asthma (ACT score ≥ 20) was achieved in 83.1% of patients. During the last week before visit, 88% of patients experienced daytime symptoms ≤ 2 , only 15.2% of the all patients used as-needed medications, the mean(SD) use of relief medication of the whole population is 0.4 (1.41) inhalations/week, 91.2% of patients did not experience any limitation of daily activities, and only 7.6% of patients had nocturnal symptoms or night awakening. Logistic analysis indicated that the factors associated with control level were age, gender, course of disease, and educational background.

Conclusion: With no less than 3 months treatment with B/F, well-controlled asthma was achieved in 83.1% (ACT score ≥ 20) while the controlled and partly controlled asthma was achieved in 93.2% of patients according to GINA definition. B/F combination therapy is effective at managing asthma in clinical practice in China.

P-A-038

RELATIONSHIP OF ASTHMA CONTROL WITH STIGMATIZATION DEGREE, SELF ESTEEM AND KNOWLEDGE OF ASTHMA AMONG ADULT ASTHMA PATIENTS

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Background: A complex cycle of interrelated psychological and psychosocial health factors is emerging and making asthma self-management harder to address effectively. Stigmatization degree, self-esteem and asthma knowledge influence asthmatic patients' self-management and asthma control. This study was undertaken to assess the relationship of asthma control with degree of stigmatization, self-esteem and level of knowledge of asthma among Malaysian adult asthmatic patients.

Methods: A correlational descriptive study was conducted using a convenience sample of thirty adult asthmatic patients from Respiratory Specialist Clinics, Universiti Teknologi MARA (UiTM) Selayang and Sungai Buloh; both situated in Selangor, Malaysia. The self-administered questionnaire was adopted and adapted with approval from the corresponding authors and translated into Malay language using previously established international translation guidelines. The extracted data from the completed questionnaires were analyzed for Pearson's Product Moment Correlation (r) by using Statistical Package for Social Sciences (SPSS)®.

Results: In present study, asthma patients showed moderate level of stigmatization degree 64.1 ± 7.81 (64.1/110), moderate self esteem 29.56 ± 3.65 (29.56/40), good level of knowledge 19 ± 2.87 (19/25) and ACT score 17.96 ± 4.76 (17.96/25). The score of asthma control test showed a significant strong positive correlation ($r = 0.477$) with self-esteem of asthma patients, whereas the correlations were weak and negative with stigmatization degree ($r = -0.193$) and knowledge ($r = -0.208$) of asthmatic patients. The findings of the present study were consistent with the findings reported in literature previously.

Conclusion: For better asthma management, psychological and psychosocial factors associated with asthma should be thoroughly explored by correlating with asthma control of the patients. The results of this study lend themselves to further investigation with bigger sample size and different population.

P-A-039

THE EFFECTS OF A SELF-MANAGEMENT PROGRAMME ON ASTHMA CONTROL SCORES AND LUNG FUNCTION OF ASTHMATIC THAI PATIENTS

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Asthma is one of the most common health problems. Patients that are unable to control their asthma exhibit an increased risk of recurrent exacerbations and hospitalization or death. Self-management of asthmatic patients would assist them in controlling the disease. The purpose of this quasi-research was to evaluate the effects of an asthma self-management programme among asthmatic patients. A total of 40 individuals participated in the control group, while 39 participants were in the intervention group. Those in the intervention group participated in a 9-week self-management programme consisting of asthma education, teaching a self-management method, skills training (inhaler use, avoidance/removal of asthma triggers, peak expiratory flow monitoring, and exercise with an elastic band), and home visits. The asthma control scores and lung function were measured after the intervention. Data were collected by using the asthma control test (ACT) and assessment of lung function with a spirometer. Data were analyzed by using descriptive statistics, independent sample t-tests, and paired sample t-tests. The results revealed that the intervention group had significant improvements in the asthma control scores and lung function than at baseline and over those in the control group ($p < .05$, and $p < .05$ respectively). These results confirmed that the asthma self-management programme could lead to improvements in asthma control scores and lung function in asthmatic patients. However, the lung function was not clinically different. The results suggest that the programme developed in this study could be used in asthma clinics. Further study should be carried out to test the effect of the programme on lung function in a longer time frame.

P-A-040

P-A-042

PEAK INSPIRATORY FLOW RATE MEASUREMENT BY USING INCHECK DIAL® FOR THE DIFFERENT INHALER DEVICES IN THE ELDERLY WITH OBSTRUCTIVE AIRWAY DISEASES

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Introduction: Inhaler device problem is common cause of treatment failure in the elderly with asthma and associated with poor drug delivery in COPD patients. Since dry powder inhaler requires optimal peak inspiratory flow rate (PIFR), the lower flow rate generation are not uncommon in elderly. Patient lung function and intrinsic inhaler resistance are crucial factors for determining PIFR.

Materials and Methods: Prospective study was conducted by using Incheck Dial® devices (Clement, USA) for measuring PIFR in chest clinic from January to December 2013. Individual mean PIFR (L/min) values for each device were obtained from three measurements.

Results: Total 138 patients diagnosed obstructive lung diseases with mean age 59.5 (15.6) years (15–90) were assessed their PIFR for all three inhalers during stable phase of diseases. Total 71 patients (51%) having age over 60 years. Mean measured PIFR was not different between younger than 60 years (115.0 ± 15.1 L/min, 95% CI: 111.8–118.8) and older patients (115.4 ± 13.2 L/min, 95% CI: 112.1–118.7) for pMDI ($p = 0.86$). Regarding different DPI, PIFR generated from the older (72.5 ± 18.8 L/min 95% CI: 67.7–77.3) was significantly lower than younger group (82.4 ± 21.1 L/min 95% CI: 76.2–88.6) for using turbuhaler ($p = 0.01$). PIFR generated from accuhaler was not significant difference between older (93.8 ± 22.9 L/min 95% CI: 87.8–99.7) and younger than 60 years patients (99.4 ± 24.2 L/min 95% CI: 106.5–101.3) respectively ($p = 0.86$).

Conclusions: The lower generated PIFR from turbuhaler was noted in older patients with obstructive lung diseases when compared to younger patients. In contrast to accuhaler, there was no significant difference between two groups. Despite lower PIFR generated, their means of both DPIs were above 60 L/min as optimal PIFR for drug delivery.

CLINICAL FEATURES AND ASSOCIATION WITH AIR POLLUTION IN PATIENTS WITH SEVERE ASTHMA

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Introduction: The prevalence of bronchial asthma (BA) is increasing in many countries including Japan. Severe asthma is a serious socio-medical problem, because it is difficult to be controlled with high medical expenses. Therefore, it is necessary to elucidate the mechanism and contributing factors of severe asthma. Recently, it is reported that air pollution adversely affects respiratory diseases including asthma. The aim of this study is to clarify clinical features of severe asthma, and examine relationship between air pollution and severity of BA.

Methods: We analyzed patients who attended our hospital due to BA from January 2012 to June 2014. First, we classified patients into two groups (mild-moderate group and severe group) according to the Japanese Asthma Prevention and Management Guideline 2012, Japan (JGL 2012) for adults. Next, we examined characteristics of clinical history, laboratory findings including fractional exhaled nitric oxide (FeNO), numbers of emergency visits and admissions, and the distance to the residence from main road.

Results: Totally 108 patients (61 women, mean age: 55.2 ± 16.9 , 15 current smokers, 31 ex-smokers and 62 never smokers) were included in this study. There were 73 patients with mild-moderate group and 35 patients with severe group. In severe group, the frequency of emergency visits and admissions were higher than mild-moderate group (2.3 ± 5.1 times/year vs. 0.3 ± 1.2 times/year; $p < 0.0001$ and 0.37 ± 0.77 times/year vs. 0.05 ± 0.23 times/year; $p = 0.0057$, respectively). In severe group, white blood cells (WBC) and blood neutrophils were higher than mild-moderate group ($7929 \pm 2732/\mu\text{l}$ vs. $6303 \pm 1631/\mu\text{l}$; $p = 0.0023$ and $5424 \pm 2532/\mu\text{l}$ vs. $3819 \pm 1346/\mu\text{l}$; $p = 0.0011$, respectively). Although forced expiratory volume in one second (FEV1) and FEV1% were not significant different between two groups, FeNO levels of severe asthma were lower (28.2 ± 25.5 ppb vs. 40.6 ± 31.8 ppb; $p = 0.0355$). More interestingly, the distance from main road in severe group is shorter than mild-moderate group (139.1 ± 148.9 m vs. 222.6 ± 188.1 m; $p = 0.0262$).

Conclusions: High levels of WBC and blood neutrophils in severe group may suggest the possibility of neutrophilic inflammation. The patients of severe group lived nearer from main road than those with mild-moderate group. These results suggested that traffic-related air pollution might be an aggravation factor of BA.

P-A-041

SENSITIVITY OF TUBERCULIN TEST IN ADULT ASTHMATIC PATIENTS

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T helper (Th) lymphocytes have the most critical role in development of asthma and atopy. The aim of this study is to investigate tuberculin reaction that forms with Th1 type immun response in asthmatic patients with dominant Th2 immun response. The study includes 30 nonatopic asthma patients, 18 atopic asthma patients with positive family history and positivity of at least one standard aeroallergen in prick test and 33 healthy voluntary control subjects. Tuberculin tests were applied with Mantoux method and diameter of the induration was measured in millimeters after 72 hours. Tuberculin dermal test results showed that the diameters were 7.42 ± 5.66 mm in asthmatic patients whereas, it was found to be 16.51 ± 5.66 mm in nonasthmatic patients. The difference was significant ($p < 0.05$). There was no significant difference between the atopic and nonatopic asthma patients' tuberculin positivity. Our findings suggest that probability of allergic diseases should be taken into account during the evaluation of tuberculin dermal tests' results.

P-A-043

ASTHMA GUIDELINE ADHERENCE, EFFECT OF GUIDELINE ADHERED PHARMACOTHERAPY ON PATIENT LUNG FUNCTION

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Objective: To evaluate doctor's adherence to asthma clinical practice guideline (GINA 2011) on management and treatment of asthma at respiratory clinic of Hospital Pulau Pinang, Malaysia, and to evaluate the effect of guideline adhered pharmacotherapy on lung function (FEV1) on patient follow up.

Method: This was a cross sectional study conducted at respiratory clinic of Hospital Pulau Pinang, Malaysia. Prescriptions written by 6 doctors to 180 established asthma patients, a total of 30 prescriptions per doctor were noted on patient 1st visit along with patient demographics, clinical data and lung function assessment (FEV1). Prescription written were categorized as "adhered" or "non-adhered" to CPG (GINA 2011) based on pharmacotherapy prescribed in response to patient asthma control. Forced expiratory volume (FEV1) was measured on patient first and second visit, and difference in lung function values was noted. SPSS 20 was used for data analysis.

Results: Of the total 180 patients enrolled for current study, 143 (79%) patients received guideline (GINA 2011) adhered pharmacotherapy. Majority of patients (n = 133, 73.9%) asthma control was categorized as "partial controlled", 14 (7.8%) patients asthma control were categorized as "controlled" whereas 33 (18.3%) patients asthma control were categorized as "uncontrolled". Patient gender (p 0.015) and smoking status (p 0.04) had a statistical significant association with asthma control. The lung function (FEV1) values of patients at second visit (Mean = 1.59) had improved mean values as compared to lung function values at first visit (Mean = 1.24). Paired sample t test (p < 0.001) indicate a positive significant difference in lung function values at patient 2nd visit.

Conclusion: Majority of patients received guideline adhered pharmacotherapy and their asthma control was categorized as "partial controlled". Improvement of patient lung function indicated positive impact of guideline adhered pharmacotherapy.

P-A-045

THE EFFICACY AND SAFETY OF PRONE POSITIONING IN ADULTS PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME; A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Prone positioning for acute respiratory distress syndrome (ARDS) had no impact on mortality despite significant improvement of oxygenation. Recent trial showed mortality reduction associated with prone positioning for severe ARDS. We performed to evaluate the effect of prone positioning for effects of mortality of ARDS patients by duration of prone position and protective lung strategy.

Methods: We extensively searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials to identify randomized controlled trials about prone positioning in acute respiratory failure of adults for meta-analysis.

Results: Eight trials met our inclusion criteria, including 916 patients randomized to prone ventilation and 847 patients to supine ventilation. The pooled risk ratio (RR) for mortality of ARDS patients was 0.82 (95% confidential interval (CI), 0.73–0.82), but, heterogeneity was high between prone and supine ventilated patients. In subgroup analysis, mortalities with lung protective ventilation (RR 0.65, 95% CI 0.53–0.80) and longer duration of prone positioning over 12 hours (RR 0.70, 95% CI 0.59–0.85) were reduced when prone position. The prone positioning has not increased in the incidence of cardiac event (RR 1.01, 95% CI 0.87–1.17) and ventilator associated pneumonia (RR 0.88, 95% CI 0.71–1.09), but, increased pressure sore (RR 1.23, 95% CI 1.06–1.42) and endotracheal dislocation (RR 1.33, 95% CI 1.02–1.74).

Conclusions: Prone positioning have tendency of reducing mortality from ARDS, especially when used with lung protective strategy and longer duration prone positioning. Prone positioning for ARDS patients should be considered before use of other invasive procedure because life threatening complications are not much. However, heterogeneity is high on this analysis, further large randomized control designed study for severe ARDS with lung protective strategy and longer duration of prone position should be needed.

P-A-044

COMPARISON OF THREE ASTHMA CONTROL QUESTIONNAIRES AND PEAK EXPIRATORY FLOW VARIABILITY

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Background: There are many instruments for assessing the level of asthma control in clinical practice, including Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), Asthma Treatment Assessment Questionnaire (ATAQ), Asthma Control Scoring System (ACSS) and Siriraj Asthma Control Questionnaire (SACQ). However, the relationship among those instruments has not been evaluated systematically.

Objective: To prospectively clarify the relationship among ACT scores, ACQ scores, SACQ scores and peak flow variability.

Methods: The study included 36 patients who underwent routine check-up by asthma specialists. All patients had been received peak flow meter to record their PEF values in the morning before using any bronchodilators at home for 2 weeks. The patients were follow-up one month after participating in the programme in order to fill the ACT questionnaire, ACQ questionnaire, SACQ questionnaire, and underwent measurement FEV1 before and after salbutamol. PEF variability was also analyzed in patients undergoing PEF monitoring.

Results: The ACQ scores (r = .547, p = .001) and the ACT scores (r = .387, p = .02) significantly were correlated with PEF variability. However, the SACQ scores was not related to PEF variability (r = .245, p = .149). Among those three questionnaires, the ACT scores was significantly correlated with the ACQ scores (r = .356, p = .033) but not with the SACQ scores (r = .246, p = .148). However, the ACQ scores was significantly correlated with the SACQ scores (r = .370, p = .026).

Conclusion: ACQ and ACT should be simplified as the tools to assess the current level of asthma control and correlated with PEF variability.

POSTER PRESENTATION – BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES

P-B-003

P-B-001

TBNA THROUGH A GUIDE SHEATH (GS-TBNA) FOR PERIPHERAL PULMONARY LESIONS THAT CANNOT BE PRECISELY DETECTED BY RADIAL EBUS

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Background: Endobronchial ultrasonography using a guide sheath (EBUS-GS) has resulted to better diagnostic outcome for peripheral pulmonary lesions (PPLs), although the yield is not satisfactory for lesions that cannot be precisely located by EBUS. We aimed to evaluate whether the addition of a new technique, transbronchial needle aspiration (TBNA) through a GS (GS-TBNA), can increase the yield for these cases.

Methods: This was a retrospective review of cases that were difficult to locate during EBUS-GS for PPL diagnosis. From September 2012 to March 2014, there were 160 PPLs that had either an "adjacent to" (n = 113) or "invisible" (n = 47) EBUS-GS location prior to transbronchial sampling by brush and forceps. The patients were divided into two groups according to the use of additional GS-TBNA for sampling: TBNA group (n = 64) and non-TBNA group (n = 96). Diagnostic yields were compared and multivariate analyses were performed to determine the factors associated with increased diagnostic yield.

Results: There was a tendency for a higher diagnostic yield in the TBNA group compared to the non-TBNA group (60.9% versus 51%, p = 0.26). The complication rate was not significantly different between the TBNA group and the non-TBNA group (1.6% versus 2.1%, respectively, p = 0.65). For PPLs that had an "invisible" EBUS probe location, the diagnostic yield was significantly higher in the TBNA group than in the non-TBNA group (57.1% versus 12.1%, p = 0.003). Multivariate analysis showed that additional GS-TBNA significantly affected the diagnostic yield in "invisible" cases (odds ratio 9.67, p = 0.003).

Conclusion: GS-TBNA is a safe technique for PPL diagnosis and may be useful especially when the EBUS probe cannot precisely reach the lesion.

A NEW TECHNIQUE OF ENDOBRONCHIAL ULTRASONOGRAPHY WITH A GUIDE SHEATH (EBUS-GS) – GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (TBNA), A PRELIMINARY REPORT

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Background: For some cases of peripheral pulmonary lesions (PPLs) that cannot be diagnosed by EBUS-GS transbronchial biopsy (TBB), the addition of TBNA through a guide sheath can potentially increase diagnostic yields. However, when using a thin GS (SG-200C, Olympus), this technique is not reproducible because the diameter of the TBNA needle (NA-1C-1, Olympus) is larger than the GS.

Purpose: The aim was to evaluate the utility of EBUS-GS-guided TBNA for PPLs.

Method: This was a retrospective review of 31 patients (17 male, 14 female) with a median age of 74 years (range 51–93), who underwent EBUS-GS-guided TBNA under fluoroscopy for PPLs at our hospital from June 2013 to July 2014. The bronchoscope 1T260 (Olympus) was used with a thick GS (SG-201C, Olympus) and radial EBUS probe. After locating the target with EBUS, the probe was removed and the GS was left indwelled in the lesion. Then, TBB through the GS with addition of TBNA was performed. Preliminarily, the insertion port of the GS was cut by 8 cm to adapt the length of the needle during sampling.

Result: As of this time, we have a final diagnosis in 26 out of the 31 cases. Bronchoscopy was diagnostic in 88.5% (23/26). In 3 cases, one of which was not detected by EBUS, the diagnosis was established from the TBNA sample alone. There were no significant complications such as haemorrhage and pneumothorax after TBNA.

Conclusion: TBNA through an indwelling guide sheath appears to be useful, especially for cases which are difficult to diagnose by usual EBUS-GS TBB. This new technique has an excellent potential to diagnose the difficult lesion by current bronchoscopy technique.

P-B-002

A NEW MIDDLE-RANGE DIAMETER BRONCHOSCOPE WITH LARGE CHANNEL FOR TRANSBRONCHIAL SAMPLING OF PERIPHERAL PULMONARY LESIONS

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Background: Although the diagnostic yield of guided bronchoscopy for peripheral pulmonary lesions (PPLs) has improved to 70%, it is still low compared to transthoracic needle aspiration. We produced a new bronchoscope with middle-range diameter and large channel (Olympus, Japan), and evaluated its diagnostic efficacy for PPLs.

Patients and Methods: This was a retrospective study on 70 consecutive patients with PPLs who underwent diagnostic bronchoscopy using the new bronchoscope combined with endobronchial ultrasound with a guide sheath (EBUS-GS) at the National Cancer Center Hospital from September 2013 to November 2013. Diagnostic performance of the procedure was analyzed and compared among 3 groups of PPLs: "peripheral-small" lesions (≤ 30 mm and adjacent to visceral pleura), "central-small" lesions (≤ 30 mm and not adjacent to the visceral pleura), and "large" lesions (> 30 mm).

Results: Sixty (85.7%) patients had malignant diseases. Diagnosis was established by bronchoscopy in 61 of 70 patients (87.1%); the respective yields for "central-small" and "large" lesions were significantly higher than that for "peripheral-small" lesions (96.3%, 94.4%, 72%, p = 0.0026). This diagnostic accuracy was achieved regardless of other clinical and procedural factors such as, lesion size, feature (GGO or solid), EBUS-probe location (within or outside), or operator skill. There were no major post-procedural complications.

Conclusions: A new middle-range diameter bronchoscope with large channel combined with EBUS-GS can enhance the efficacy of transbronchial sampling to its maximal potential to diagnose PPLs safely and accurately, particularly for patients who have tumours away from the visceral pleura.

P-B-004

EFFICACY AND ACCURACY OF FLUOROSCOPIC THORACOGRAPHY ON THE IDENTIFICATION OF LEAKAGE SITE ON THE LUNG IN PATIENTS WITH SPONTANEOUS PNEUMOTHORAX WHO HAVE CONTINUOUS AIR LEAKAGE

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Background: To identify the location of air leakage on the affected lung in patients with intractable pneumothorax and continuous air leakage is considered beneficial to compose a therapeutic plan. Contrast thoracography under fluoroscopy (TG) is the only procedure to detect air leakage point in real time, but its efficacy remains unknown.

Methods: From April 2011 to March 2013, 65 patients with pneumothorax who had continuous air leakage were underwent TG. Among them, 34 patients (52%) subsequently underwent thoracoscopic surgery because of persistent air leakage and gave us an opportunity to correlate TG findings with those of thoracoscopic findings during operation. We retrospectively reviewed their medical records to examine the accuracy and efficacy of TG to identify the location of leakage.

Results: The mean age was 38 year-old (range, 15–83). Fifteen patients had left-sided pneumothorax whereas 19 patients had right-sided. Pneumothorax was the first episode in 31 of 34 patients whereas the remaining three were recurrence. Twenty-five patients had primary spontaneous pneumothorax, six had COPD, two had secondary spontaneous pneumothorax caused by nontuberculous mycobacterium infection (NTM) and one suffered from catamenial pneumothorax. TG enabled us to identify the air leak point in 29 patients (85%); the locations of the fistula were at apex (24 cases, 83%), the top of segment 6 (3 cases, 10%), and the lateral side of segment 4 (2 cases, 7%). In 28 of 29 cases (97%), the TG findings were identical to those of thoracoscopy whereas one patient disclosed no fistula during operation. TG demonstrated no leakage point in 5 cases (15%); only the movement of air bubbles was visualized in 3 cases whereas other two cases showed no informative TG findings although a large amount of air leakage through the chest drain tube was noted during TG procedure. No patients had any complications related to TG.

Conclusion: TG is effective examination to detect air leak point in real time. Its high detection rate of air leakage point and accuracy will facilitate endoscopic bronchial occlusion or make chemical pleurodesis perform more effectively.

P-B-005

PROSPECTIVE STUDY OF MODERATE SEDATION REQUIREMENTS AND COMPLICATIONS OF FLEXIBLE BRONCHOSCOPY

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Flexible bronchoscopy is a routine procedure that is carried out under moderate sedation. However, there is limited prospective data on the sedation used and complications incurred.

Aim: To prospectively audit sedation requirements and complications during flexible bronchoscopy.

Method: 703 patients were enrolled from Jan to Dec 2013. All had moderate sedation with fentanyl/midazolam. Patients on mechanical ventilation were excluded.

Results: 61.3% were male (mean age: 60 ± 2.5). The median duration of procedures was 22.6 min; range 5–105 with procedure times for EBUS(35 min; range 5–105); bronchoscopy(15 min; range 5–60); BAL(15 min; range 5–45); and lung biopsy (25 min; range 10–70). Median sedation was (3.2 mg midazolam, range 0–7.5; 35.1 Mcg fentanyl, range 0–200) with EBUS(3.5 mg midazolam, range 1–11; 50 Mcg fentanyl, range 0–200), bronchoscopy(2.5 mg midazolam, range 0–7.5; 0 Mcg fentanyl, range 0–100), BAL(2.5 mg midazolam, range 0–10; 0 Mcg fentanyl, range 0–100), and lung biopsy(2.5 mg midazolam, range 1–12.5; 50 Mcg fentanyl, range 0–100). Higher sedation requirements were noted for longer procedures (>30 minutes), but this was not associated with increased complications. Total complication rate was 16.35%. Bleeding was the most common complication (9.7%) but hypoxia was the most common sedation related complication (6.7%).

Conclusion: This study has demonstrated the risks of flexible bronchoscopy. There was a marked increase in complications compared to previous data because of the prospective nature of the study and all self-limiting events were reported.

P-B-006

P-B-007

DIAGNOSING OBSTRUCTIVE SLEEP APNEOA BY PERFORMING FIBEROPTIC BRONCHOSCOPY AND PEEP TITRATION OF MASK CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Fiberoptic bronchoscopy (FOB) is a procedure that pulmonologists perform to investigate the airway passages for diagnostic or therapeutic purposes. The patients undergoing FOB are either under local anaesthesia or moderate sedation depending on the complexity or time needed by the physician to complete the assessment and or treatment. During moderate sedation, several patients were observed manifesting snoring and hypopneas or apnoeas.

Obstructive sleep apnoea (OSA) is described as the repeated instability of the upper airway during sleep which results in hypopnea or apnoea. It is a serious condition that can affect an individual's activities which in turn can also cause long term health problems. Polysomnography or sleep study has been the gold standard in diagnosing sleep apnoea. It typically records the brain wave changes, eye movements, muscle motion, breathing and heart rate and rhythm. Once diagnosed, management depends on the severity of the condition. Some may use mandibular advancement splint, Continuous positive airway pressure (CPAP) or surgery. Although sleep study has been effective, the cost and unavailability of a sleep laboratory and technician has been a major concern in screening patients suspected of sleep apnoea. To compensate, methods such as sleep endoscopy and portable polysomnographic devices supported by sleep questionnaires are used in assessment of sleep apnoea.

Method of the Study: In Bangkok Hospital Medical Center, from January 2014–14 July 2014, 10 patients suspected of OSA, needed to undergo FOB for other reasons aside from sleep apnoea were diagnosed of OSA by using FOB and CPAP. The FOB allowed direct visualization of the oropharyngeal airways when the patient was moderately sedated. This view provided the physician the direct picture of whether upper airway collapse or obstruction was present therefore confirming sleep apnoea. The FOB was inserted via the mask CPAP to help titrate and adjust the (positive end-expiratory pressure) PEEP pressure providing accurate measurement needed in using CPAP.

Results: Post FOB with mask CPAP, the pulmonologist was able to perform FOB, diagnose OSA then provide CPAP management with specific PEEP level. For the 10 patients, the average level of PEEP was found to be 7 cm H₂O (5–12 cm H₂O) and no complications following the procedure such as pneumothorax or infection were noted.

Conclusion: The evolution and widespread availability of Interventional bronchoscopy has played a great importance in the development of diagnosing certain conditions such as OSA. This new technique is not only practical, cost-efficient, time-saving and beneficial for both patient and physician but this may also be considered as the new gold standard in diagnosing OSA.

STUDY OF SAFETY AND CO-EFFICIENCY OF THE TRANBRONCHIAL ABLATIVE TECHNIQUES

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Objective: In this thesis, in vivo study of safety and co-efficiency of the transbronchial ablative techniques.

Materials and Methods: To study the tissue effects of the four ablative techniques [YGA laser, electrocautery, argon plasma coagulation (APC), and CO₂ cryotherapy] performed on trachea wall. Bronchoscopic appearance of the treated area was documented photographically, and pathologic changes of the bronchial wall were observed. The recovery of trachea wall after damage by ablative techniques was also observed.

Results: (1) After each ablative technique performed on the mucosa of trachea, the bronchoscopic appearance of the lesions included: whitening of the mucosa with a small, well-defined lesions; crater-shaped lesions with charring; and tissue defects. Examination of histologic changes showed local necrosis and amotio of the mucosa lining epithelium, local submucosa coagulative necrosis or tissue defects. There is a good correlation between the visibility of mucosal damage during treatment session and the ultimate histologic changes. Even under the same power, tissue damage was deeper if the action time increased. The damage by APC was the most superficial, laser and electrocautery caused the worst damage, cryotherapy was more safe. The study also found that effects of electrocautery at 40 W × 1 second, laser at 20 W × 1 seconds, APC at 40 W × 5 seconds and cryotherapy at 100 Ω × 120 seconds were the equivalent point conditions. The appearance included mucosa absence, partial submucosa absence, and collagen fibre coagulation in treatment areas. At the same power and action time, we observed the cartilage layer was structural integrity, not perforation phenomenon. The doses for each ablative technique were safe. (2) The recovery process of the damaged trachea wall could be roughly divided into four periods: the acute injury stage; inflammatory reaction period; reparative phase; and healing phase. The restoration approach of trachea wall mainly was fibrous tissue hyperplasia. The entire process needs about three weeks.

Conclusion: Each coagulation technique has its own characteristic. It is very important to choose the appropriate power and action time of the suitable method according to the therapy requirement.

P-B-008

THE STUDY OF RAPID ON-SITE EVALUATION (ROSE) DURING ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA)

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Background: The role of rapid on-site evaluation (ROSE) during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is widely accepted for hilar-mediastinal lymphadenopathy, but its efficacy remains controversial.

Objectives: The purpose of this study was to evaluate the efficacy of ROSE during EBUS-TBNA with suspected lung cancer and sarcoidosis.

Methods: We retrospectively evaluated 40 patients with a clinically and radiologically suspected for lung cancer or sarcoidosis who underwent EBUS-TBNA from July 2012 to October 2013. Informed consent was obtained from all patients and they were enrolled in this study. All procedures were performed with local anaesthesia (lidocaine 2%) and conscious sedation (intravenous injection of 2 to 2.5 mg midazolam and intramuscular injection of 35 mg pethidine hydrochloride). EBUS-TBNA was performed with convex probe (BF-UC260F-OL8; Olympus, Tokyo, Japan) and a 22-gauge needle (NA-201SX-4022; Olympus). Materials obtained by the needle aspiration were immediately smeared onto slide glasses, air dried, and stained with Quik May-Giemsa for ROSE. The rests of smears were fixed with 95% ethanol for Papanicolaou staining for cytologic evaluation. When ROSE was negative for malignancy or epithelioid-like cells at the initial examination, but lymph node was still suspected with malignancy or sarcoidosis, additional biopsy was performed more than one time. The tissue of lymph node that was obtained by the needle aspiration was immediately fixed with 10% formalin and stained with hematoxylin and eosin staining for histologic evaluation. ROSE was compared with the final histologic or cytological diagnoses.

Results: EBUS-TBNA was performed on 61 lymph nodes. The total number of puncture was 154, the mean number of puncture in one site was 2.52. The final diagnoses were malignant in 29 patients, sarcoidosis in 8 patients, and inflammatory lymphadenopathy in 3 patients. There were no false-positive results on ROSE, however 3 cases (5.8%) were false-negative on ROSE. The concordance rate between ROSE and final pathologic diagnosis was 94.2%. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy rate of EBUS-TBNA was 94.2%, 100%, 100%, 75%, and 95.1%, respectively.

Conclusions: ROSE during EBUS-TBNA can be a useful tool for hilar-mediastinal lymphadenopathy because of high sensitivity, specificity, positive predictive value and diagnostic accuracy. This procedure is expected the improvement of accurate diagnosis.

P-B-009

FLEXIBLE BRONCHOSCOPY IN THE DIAGNOSIS OF RESPIRATORY DISEASE: ASSESSMENT OF 4982 PATIENTS AT A TERTIARY CARE UNIVERSITY HOSPITAL

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Background and Objective: Flexible bronscopy (FB) is the most widely used invasive procedure in clinical pulmonology. We appraise the utility of FB for diagnosis, and illustrate the bronchoscopic presentation of various pulmonary conditions in 4982 patients.

Methods: Patients with recent onset respiratory problems and/or with persistent opacities on thoracic radiography in the form of hilar mass, collapse, consolidation, or cavity (despite proper antibiotic therapy) were included in this study. Those with diagnosed lung cancer, pulmonary TB, recent myocardial infarction, allergic diseases and blood dyscrasias were excluded. Finally, 4982 patients were included, their demographic details, histopathology diagnosis were obtained from the case history. SPSS13.0 statistical software was used for data processing and a $p < 0.05$ was considered significant.

Results: 1515 cases were diagnosed as lung cancer (30.41%), 195 as tuberculosis (3.91%), 2 as pulmonary fungal disease (0.04%), and 1212 as acute or chronic non-specific inflammation (24.33%). Mass lesion was the most common FB observation among patients with cancer, and accounted for 68.71% of pathologically confirmed lung cancer. Acute inflammation presented as congestion and/or oedema among while chronic inflammation had granulation tissue. Tuberculosis presented as inflammatory infiltration in 37.95%, and proliferative granulation in 29.23% of the patients. Cancerous lesions commonly involved the right lung field, and upper lobes; inflammation and tuberculosis typically involved the upper lobes.

Conclusion: FB has a role in the diagnosis of respiratory diseases. Knowledge about the common presentation of lesions aids with obtaining correct specimen for microscopic and pathological characterization.

P-B-010

NEW PLUGGING TECHNIQUE FOR ENDOBRONCHIAL WATANABE SPIGOT (EWS): SIDE GRASPING METHOD

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Background: Bronchial occlusion using Endobronchial Watanabe Spigot (EWS) is reported to be useful for the management of persistent pulmonary air leaks. Many patients with persistent pulmonary air leaks have respiratory disability and poor general condition. These patients need minimally invasive therapies, such as bronchial occlusion, however, difficulties in plugging EWS at target bronchus is still debated. Recently, grasping forceps (FG-14P-1 OLYMPUS) have been recommended for controlling EWS. However, we found that by grasping the edge of EWS then using rotational forceps (FB-19CR-1, OLYMPUS) to manoeuvre the spigot make it simple to plug the EWS into the target bronchus. Since this method increases the variable angle making it possible to fix and rotate using a large angle, we have named this method the 'Side Grasping'.

Objective: The aim of this study is to evaluate the effectiveness of this method for easy plugging EWS.

Methods: First, on the tabletop, we measured the variable angle of EWS by conventional method, then by side heel kick method. Next, we measured the time to plug the EWS for the conventional and side grasping method using a dog.

Results: The variable angle in the conventional method was 45 degrees and that in the side grasping method was 90 degrees. The time to plug the EWS using the side grasping method was significantly shorter than the conventional method.

Conclusion: Side grasping method significantly reduced the time in plugging EWS. The superior lobe bronchus is notoriously difficult to plug, however, the side grasping method was easily able to plug the target bronchus.

P-B-011

FACTORS INFLUENCING DIAGNOSTIC YIELD OF RADIAL PROBE ENDOBRONCHIAL ULTRASOUND (EBUS) FOR THE DIAGNOSIS OF PERIPHERAL PULMONARY LESIONS

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Objectives: To evaluate factors that predict the diagnostic yield of radial probe endobronchial ultrasonography (EBUS) for peripheral pulmonary lesions (PPLs).

Methods: Design – retrospective analysis. We analyzed the diagnostic yields of TBB or brushing using EBUS for patients with PPLs in a tertiary university hospital from December 2007 to December 2010.

Results: A total of 640 patients with PPLs were included. A definite diagnosis was made by EBUS-guided TBB or brushing for 541 patients (85%). A total of 249 patients (38.9%) were examined by a rapid on-site cytological evaluation (ROSE) technique. The PPLs diagnostic yields using EBUS-guided TBB or brushing with ROSE were significantly higher than without ROSE (89.9% vs. 81.9%; $p = 0.006$), particularly for PPLs < 3 cm with negative bronchus signs on CT scans. ROSE can also increase diagnostic yield of smaller PPLs with size between 2.0 to 2.9 cm and large PPLs with central necrosis. Multivariate analysis identified the following independent factors for predicting PPL diagnostic yields of EBUS-guided TBB: EBUS probe within the lesion, ROSE examinations, bronchus sign negative for PPLs < 3 cm, PPLs located in the left apical-posterior or right apical segment, and PPLs surrounding with pleural effusion.

Conclusion: Position of the probe (within the PPLs) and ROSE assisted examinations are significant factors for predicting higher PPL diagnostic yields of EBUS-guided TBB. However, right apical and left apical-posterior segment locations, small PPLs < 3 cm without bronchus signs on CT scan, and PPLs surrounding with pleural effusion are significant factors for predicting lower PPLs diagnostic yields of EBUS-guided TBB.

P-B-012

UTILITY OF EBUS-TBNA IN PATIENT WITH TUBERCULOUS INTRATHORACIC LYMPHADENOPATHY

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Rationale: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a useful technique for cytological assessment of enlarged mediastinal lymph nodes with a high diagnostic yield for lung cancer. But its role in the diagnosis of tuberculosis intrathoracic lymphadenopathy has not been established. The aim of this retrospective study was to assess the clinical characteristics of tuberculous intrathoracic lymphadenopathy diagnosed by EBUS-TBNA and its utility.

Methods: From July 2011 to July 2013, intrathoracic tuberculous lymphadenopathy diagnosed by EBUS-TBNA were enrolled. For each EBUS-TBNA sampling, we documented patient's characteristics, sonographic features of L/Ns, pathologic findings and microbiologic results were recorded. All patients underwent routine clinical assessment and a CT scan prior to EBUS-TBNA.

Results: 20 patients (M : F = 6:14) with a mean age 41.3 years were studied. The most common chief complaints were CT abnormality ($n = 7$) and cough ($n = 5$) and dyspnoea, fever. At EBUS, short axis diameter of L/N size was 18 ± 5.4 mm. The subcarinal L/N station was the most common location for EBUS-guided sampling (70%), followed by the 4R (65%). 14 patients (70%) had two or more nodal stations sampled. AFB culture and tbc PCR positive of bronchial washing samples were detected in 8/20 (40%) and 11/20 (55%), respectively. And AFB culture and tbc PCR positive of EBUS-guided aspirates were 8/15 (53.3%) and 13/15 (86.7%), respectively. In sonographic features, oval shapes in 18/20 (90%), heterogenous echotexture in 15/20 (75%) and coagulation necrosis positive in 18/20 (90%) were detected. Comorbidity included malignancy(30%), DM (30%), CRF (15%). Pathology compatible with typical tuberculosis was 11 (55%) and only necrosis were detected in 9 (45%) but tbc PCR positive of EBUS sampled tissue were detected in 19/20 (95%).

Conclusions: EBUS-TBNA is a safe and effective first-line investigation in patient with tuberculous intrathoracic lymphadenopathy.

P-B-013

DIAGNOSTIC ROLE OF ENDOBRONCHIAL ULTRASONOGRAPHY IN RECURRENCES OF OPERATED LUNG CANCER

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Aim: We aimed to determine the role of endobronchial ultrasound guided transbronchial needle aspiration in the diagnosis of recurrences at operated non-small cell lung cancer(NSCLC) cases in the presence of new advanced hilar/mediastinal lymph nodes (LN).

Methods: The files of patients operated with the diagnosis of NSCLC previously whose current PET-CT study revealed increased metabolic activity at hilar/mediastinal LN and convex probe EBUS-TBNA was performed between January 2011–June 2013 were retrospectively analyzed. The age and gender of patient, diagnosis of primary tumour, operation performed previously, the LN present at current PET-CT and FDG uptake value were recorded. The station and size of LNs sampled by EBUS-TBNA and cytopathological results were obtained from the files. Malignant results were regarded as true positive whereas to confirm the diagnosis of benign results patients followed up radiologically for at least 6 months or invasive procedures were performed. The sensitivity, specificity, NPV, PPV and diagnostic accuracy of EBUS-TBNA in determining the recurrences of operated lung cancer were calculated from the obtained results.

Results: Twenty-four patients; 10 male, 4 female with a mean age of 59.3 ± 7.8 were included. The mean duration for the occurrence of post-operative enlarged LN was 24.5 ± 18.7 months. Operation was sublobar resection in one of the cases, lobectomy or pneumonectomy in the others. 42 LN stations were sampled with EBUS-TBNA in 24 cases. The cytopathological results of them were cancer recurrence in 9 cases, second primary small cell lung cancer in one case, reactive or anthracotic lymphadenitis in 13 cases, sarcoid reaction in 1 case. Low-grade lymphoma and atypical carcinoid tumour recurrence were diagnosed with invasive procedures in 2 cases which malignancy was not the result of EBUS-TBNA. The sensitivity, specificity, NPV and PPV of EBUS-TBNA in determining the relapses of operated lung cancer were 90%, 100%, 93.4% and 100%, respectively. The sensitivity of EBUS-TBNA in determining the malignancy was 83.4% and the accuracy for all diagnosis was 91.7%.

Conclusion: EBUS-TBNA is a safe and sensitive method to detect recurrence in lung cancer patients underwent surgery.

P-B-014

THE CHANGING FACE OF TBNA – TRANSITION FROM CONVENTIONAL TBNA (C-TBNA) TO EBUS-TBNA WITH ROSE: RETROSPECTIVE ANALYSIS OF 150 CASES FROM A TERTIARY CARE HOSPITAL IN NEW DELHI, INDIA

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Aim of the Study: To retrospectively analyze the diagnostic efficacy of EBUS-TBNA with ROSE compared to that of conventional TBNA done by the same operators in our department over a 18 month period.

Material and Methods: A retrospective analysis of case records of 150 consecutive patients with mediastinal or hilar lymphadenopathy who underwent TBNA, and the size of the lymph nodes were between 1 to 3 cm in shortest axis on CT scan were included of which the first 75 cases were done by conventional TBNA method and second 75 cases were done by EBUS-TBNA with ROSE. Results were compared in terms of diagnostic efficacy, number of lymph node stations punctured, number of total punctures per patient, representative and non representative samples and final diagnosis.

Results: 150 cases records were analyzed – first 75 (c-TBNA) and second 75 (EBUS-TBNA with ROSE).

Total number of punctures were 292 in c-TBNA and 269 in EBUS-TBNA.

Total number of punctures per patient was 3.89 in c-TBNA and 3.58 in EBUS-TBNA.

Commonest LN station in both groups was 4R (52% in c-TBNA and 50% in EBUS-TBNA).

Percentage of Representative samples was 47% (137/292) c-TBNA vs. 68% (183/269) EBUS-TBNA.

No of Diagnostic Punctures was 36% (106/292) c-TBNA vs. 53% (144/269) EBUS-TBNA.

Diagnostic yield was 72% (54/75) c-TBNA vs. 95% (71/75) EBUS-TBNA.

Conclusion: 1. Starting an EBUS programme at our hospital improved the diagnostic efficacy of FNA of Mediastinal and Hilar LN from 7% (c-TBNA) to 95% (EBUS TBNA with ROSE). 2. Total no of punctures in both groups was comparable (292 vs. 269). 3. Percentage of Representative samples was higher in the EBUS Group (68% vs. 47%). 4. The most common diagnosis was granulomatous inflammation in both the groups.

P-B-015

DIAGNOSTIC YIELDS FOR PERIPHERAL LUNG NODULES WITH SUSPICIOUS MALIGNANCY THROUGH THE ENDOBROCHIAL ULTRASONOGRAPHY WITH A GUIDE SHEATH (EBUS-GS)

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Background: EBUS-GS has been established to diagnose the peripheral pulmonary lesion endoscopically. Several tips can facilitate introducing a GS probe to the intended branch and obtaining sufficient samples from the site of interest. We made several efforts and developed tips of something like saline injection, increase of sampling frequency and navigation. To assess the effect of the introduction of EBUS-GS method, annual data were analyzed retrospectively before and after the introduction into our hospital.

Design: Retrospective analysis of single centre.

Material and Methods: The lesion included in this retrospective analysis is one without any endoscopic abnormal findings, one with final diagnosis of malignancy. Our hospital introduced EBUS-GS method in April 2009 in earnest. EBUS-GS method was not performed until April of 2008. We analyzed data annually and compared the data between April 2007 and March 2008 as a control with the other annual data. Between April 2009 and March 2014, 201 lesions that were suspected malignancy by CT scan and underwent EBUS-GS proved to be malignancy by either endoscopy, surgery or further pathological examinations. Three kinds of samples for cytology of one tapped the brush on slide glass (B), bronchial lavage fluid (L) and fluid flashed in guide sheath (S) were evaluated separately.

Results: Mean long / short diameter of the lesion: 25/19 mm, Location pattern of probe and lesion: within/adjacent to/outside = 136/55/10, Final pathological diagnosis: Ad/SqCC/Small/LCNEC/AdSq/NSCLC/Meta/BALT/Mucoepi = 133/43/8/8/3/2/2/1/1, Number of brushing and biopsy: 3.8 / 3.8, Positive rate of cytology: 163/200 (81.5%), Diagnostic yield of pathology: 132/188 (70.2%), Final diagnostic yield of cytology and pathology: 173/201 (86.1%). Results of three cytology methods: B : L : S = 77.4%(154/199): 41.8%(81/194): 61.0%(114/187). To gather more cells, we flush the GS with saline and collect cells adhering to the internal wall of the GS. This attempt revealed to be effective. Separate results of each annual of 2007, 2009, 2010, 2011, 2012 and 2013 were 31.6, 82.8, 83.7, 87.5, 84.4 and 90.0 %, respectively. Annual results of diagnostic yields from April 2009 to March 2014 after introduction of EBUS-GS method were superior to that of control significantly.

Conclusion: EBUS-GS improved diagnostic yields clearly. If a higher diagnostic yield than this is warranted (e.g. 90% in 2013), a fully planned strategy on a case-by-case basis is needed.

P-B-016

BRONCHOSCOPIC LUNG VOLUME REDUCTION IN PATIENTS WITH EMPHYSEMA WHO REFERRED A PULMONARY REHABILITATION CENTRE

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Endobronchial lung volume reduction (EBLVR) is a current treatment option for chosen symptomatic cases that are refractory to medical treatment and pulmonary rehabilitation (PR). The purpose of this study is to evaluate patients that have undergone EBLVR referred to the chronic respiratory insufficiency clinic-pulmonary rehabilitation and home care department. Between April 2013 – June 2014, data of 10 emphysema patients who were candidates for EBLVR at the Chronic Respiratory Insufficiency-Pulmonary Rehabilitation and home care department of Atatürk Chest Disease and Chest Surgery Teaching and Research Hospital were evaluated. Patients were evaluated before EBLVR and at the 3rd and 6th months following EBLVR. Eight patients underwent EBLVR after being symptomatic following 12 weeks of multidisciplinary PR. Two patients directly underwent EBLVR where one of them received 12 weeks of PR following EBLVR. Indications for EBLVR were determined following HRCT, basic spirometric evaluation and body box for lung volumes and quantitative perfusion scan for necessary cases. All patients were evaluated with the following: SGRQ, ISWT, ESWT, FFMI, HADS. Data following the procedure was unattainable for three patients that died and three that have not yet completed their control time period. Following evaluation of their HRCT by a radiologist and pulmonologist, seven out of ten patients decided to treat with coil and three patients received the valve procedure. Data that was obtained from three patients following the EBLVR procedure demonstrated 33.7% increase in FEV1, 9.3% decrease in TLC, 28.8% decrease in RV and a 23.6% decrease in RV/TLC. The patients that had ISWT evaluation following EBLVR showed 90 m, 40 m, 40 m and 10 m increase and an average of 45 m increase was noted. All patients stated that they felt a decrease in dyspnea following EBLVR. Quality of life evaluation with the SGRQ demonstrated improvement with a total score of 64.28 before EBLVR and a decrease to 34.71 following EBLVR. Improvement was seen in the data for body composition. Mortality rate was three out of ten; 2 patients died due to pneumonia within the first three months while one patient died following myocardial infarction at the ninth month. Endobronchial volume reduction should be considered in emphysema patients as a complementary treatment with pharmacological and non-pharmacological treatments including pulmonary rehabilitation. Although our study included a small group of patients, the results demonstrated an overall improvement in respiratory functions, exercise capacity, body composition, psychological questionnaires and quality of life. We believe that these treatments should be undertaken at tertiary hospitals settings that have experience in interventionist bronchoscopy and have complete lung function laboratories and pulmonary rehabilitation units.

P-B-017

PREVALENCE OF AIRWAY FOREIGN BODIES IN CHILDREN IN PERSAHABATAN HOSPITAL

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Background: Aspiration of airway foreign bodies (FB) can cause significant morbidity and mortality in children if the diagnosis and management were not done immediately and properly. Diagnosis and extraction of airway FB can be managed with non-invasive procedure using bronchoscopy (rigid and flexible). Previous study showed that the most frequent cases of FB aspirations were found in male children between 1 to 3 years of age. The most frequent symptoms are cough and dyspnea. The most frequent site of FB were in right bronchus. We have done a retrospective study to see the prevalence of airway FB in paediatric patients at Persahabatan Hospital during period of 2009–2014.

Method: We reviewed data of FB aspiration cases at Persahabatan Hospital from 2009–2014 who underwent rigid and flexible bronchoscopy for diagnostic and therapeutic purposes.

Results: We found 27 cases whom underwent bronchoscopy for airway FB. There were only 11 cases that have complete data and we analyzed the 11 cases for this study. Most of the subjects were female (7 patients, 63.6%) and the most frequent cases was found in subjects age 13 years old 3 children (27.3%). The most frequent FB found was pins (4 pts, 36.4%), peanuts, nails, ballpoint cap, whistler. The age ranged between 1 until 14 years of age. The most frequent site of FB lodging was in right main bronchus, 4 children (36.4%).

Conclusion: FB aspiration cases in this study were mostly found in female patients, with the most frequent age being 13 years old. Most children did not complain of any specific respiratory symptom. The most frequent site of FB found on bronchoscopy were in right main bronchus.

P-B-018

CLINICAL OUTCOMES OF ELECTROCAUTERY AS THE PRIMARY ENDOBRONCIAL ABLATIVE THERAPY FOR CENTRAL AIRWAY OBSTRUCTION AT THE UNIVERSITY OF SANTO TOMAS HOSPITAL, PHILIPPINES FROM JANUARY 1, 2003 TO DECEMBER 31, 2013

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Objective: This study aimed to evaluate the clinical outcomes of electrocautery as the primary heat therapy for malignant and benign airway obstruction in the University of Santo Tomas Hospital, Philippines.

Methods: A 10-year retrospective descriptive study was done reviewing all patients who underwent flexible bronchoscopy with endobronchial electrocautery, alone or in combination with other airway tools, at the University of Santo Tomas Hospital from January 1, 2003 to December 31, 2013. In patient charts, bronchoscopy reports and bronchoscopy videos were evaluated. Data on efficacy (luminal patency, symptomatic, radiographic, or physiologic improvement) and safety (complications) were collected. The patients were categorized into two groups according to the aetiology of central airway obstruction. Group I: Malignant Group and Group II: Non-malignant Group. The evaluation of performance and quality of life status done pre-operatively were likewise recorded. The complications of the procedure such as bleeding, hypoxemia, perforation, air fire and even death were also noted. In this study, success was defined as $\geq 70\%$ restoration of the airway patency and less than that was considered failure.

Results: One hundred nineteen patients with symptomatic central airway obstruction were included in the study. There were 76 males (64%) and 43 (36%) of females with a mean age of 59.64. The oldest was 90 years old and the youngest was 16 years old. Eighty four (71%) of the subjects were smokers with an average of 11.5 pack-year smoking history. Majority (71%) of the central airway obstruction was due to malignant aetiology (Group I) while 29% is secondary to benign lesions (Group II). In Group I: Malignant Group, airway patency restoration success with immediate palliative relief was noted in 83% of the patients. With hypoxemia and moderate bleeding as the common complications. In the Group II: Non-malignant Group, the success rate was 91%. Still the most common complications were hypoxemia and bleeding. No mortality was documented during the procedure on both Groups I and II.

Conclusion: This study further affirms that endobronchial electrocautery as the primary endobronchial ablative therapy for central airway obstruction is a safe and reliable procedure.

P-B-019

TWO CASES OF ENDOBRONCHIAL SCHWANNOMA TREATED WITH INTERVENTIONAL BRONCHOSCOPY

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Background: Schwannoma is a benign tumour, originating from the schwann cells of the peripheral nerve system. Tracheal schwannoma is particularly rare, and there have only been a few reports describing bronchoscopic intervention or surgical resection as treatment. In this case series, we report successful bronchoscopic intervention in 2 patients with endobronchial schwannoma.

Case 1: A 36 year-old woman was admitted to our hospital complaining of numbness in her lower limbs due to spinal cord meningioma. Although she was scheduled for an operation, a tracheal tumour was found that needed initial treatment.

Bronchoscopy resection was performed using a high-frequency snare and argon plasma coagulation. The bronchoscopic sample was then diagnosed pathologically as schwannoma. Three months after intervention, bronchoscopic findings showed tracheal patency was maintained.

Case 2: A 69 year-old man was admitted to our institution with narrowed both main bronchus. Rigid bronchoscope was inserted into the trachea and endobronchial ultrasonography with guided transbronchial needle aspiration (EBUS-TBNA) was performed. Subsequently, a Dumon Y stent was placed.

The specimen taken by EBUS-TBNA was not able to diagnose histologically; therefore, gastrointestinal fiberoptic with transesophageal endoscopic ultrasound-guided fine needle aspiration (TEUS-FNA) was performed. However TEUS-FNA was also unable to diagnose the sample histologically, and subsequently, thoracotomy was performed. The mediastinal tumour was partially resected and this sample was pathologically diagnosed as schwannoma. Since the mediastinal tumour decreased in size, six months after stent placement the stent was removed and dyspnea improved.

P-B-020

ATROPINE PREMEDICATION FOR FIBROPTIC BRONCHOSCOPY IN ADAM MALIK GENERAL HOSPITAL MEDAN INDONESIA

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Background: Atropine is widely used as premedication for fiberoptic bronchoscopy. The anticholinergic action of atropine may reduce tracheobronchial secretions to improve visualization of the tracheobronchial tree, prevent bronchoconstriction and vasovagal reflex. Anticholinergic agents have several adverse effects, some of which could be potentially harmful, particularly in elderly patients. In 2001, British Thoracic Society guidelines on diagnostic flexible bronchoscopy had given recommendation that atropine was not required routinely before bronchoscopy.

Objective: The aims of this study were to compare premedication with and without atropine in reducing tracheobronchial secretion during bronchoscopy procedure in Adam Malik general hospital, to describe characteristic of patients, and to find vasovagal reflex as complication event during bronchoscopy procedure.

Methods: In this quasi-experimental study, we took 60 inpatients eligible in study according with inclusion and exclusion criteria between April and June 2014. All of patients were given 20 mg codein tablet and 5 mg intramuscular diazepam 3 hours prior to bronchoscopy. Then patients were randomly allocated to receive subcutaneous atropine (0.25 mg) or saline placebo (1 mL) as premedication 30 to 60 minutes prior to bronchoscopy. During the procedure an estimate was made of tracheobronchial secretions with grading secretions as grade (1) almost none, grade (2) needing saline to wash out, and grade (3) excessive, making bronchoscopy procedure difficult to do. Patients also monitored for oxygen saturation, pulse rate, procedure time, and bronchoscopy complications.

Results: Most of patients were >40 years old (n = 55; 91,7%), male (n = 49; 81,7%), ex-smoker (n = 48; 80,0%), farmer (n = 23; 38,3%), and had intermediate education level (n = 39; 65%). Grading of tracheobronchial secretions detected as grade (1): no patient with atropine, 2 patients without atropine (6,7%); grade (2): 27 patients with atropine (90,0%), 23 patients without atropine (76,7%); and grade (3): 3 patients with atropine (10,0%), 5 patients without atropine (16,7%). Statistically, there was no significant difference in reducing tracheobronchial secretion between premedication with and without atropine (p = 0,297). Complications occurred in 15 patients with atropine (44,1%): minor bleeding (7 patients; 23,3%), bronchospasme (12 patients; 40%), and 19 patients without atropine (55,9%): minor bleeding (11 patients; 36,6%), bronchospasme (10 patients; 33,3%), pulmonary oedema (1 patient; 3,3%). There was no difference found for complication rates between these groups, and no event of vasovagal reflex in this study.

Conclusions: Atropine premedication prior to bronchoscopy did not affect better visualization during bronchoscopy and complication rates.

P-B-021

CORRELATION BETWEEN PLEUROSCOPIC FINDINGS AND HISTOPATHOLOGICAL DIAGNOSIS OF UNDIAGNOSED EXUDATIVE PLEURAL EFFUSION: A MALAYSIAN COHORT

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Introduction: Pleuroscopy is a minimally invasive procedure to inspect the pleura, perform a biopsy and proceed with therapeutic interventions. However, not many studies have been done to look at the correlation between pleuroscopic findings and their histopathological diagnosis. By knowing the correlation, the aetiology of exudative pleural effusion can be better predicted, even before getting the histopathological diagnosis which will usually take at least 3–5 days, and this will further expedite the patient management plan.

Objective: The aim of this study was to look at the correlation between pleuroscopic findings and their histopathological diagnoses and to determine the diagnostic yield of pleuroscopic findings, in undiagnosed exudative pleural effusion in a Malaysian Tertiary Hospital setting.

Methodology: Clinical data from Hundred and Forty Three patients who had undiagnosed exudative pleural effusion recruited for pleuroscopy in Hospital Selayang from January 2011 to December 2013 were reviewed. Statistical analysis was done by using contingency table to assess sensitivity, specificity and association of each pleuroscopic findings with their histopathological diagnosis.

Results: A total of 143 patients (98 males and 45 females, mean age 75 years) underwent pleuroscopy, and being diagnosed as malignancy (n = 55), tuberculosis (n = 70), empyema (n = 10), normal pleura (n = 3), and abandoned procedure (n = 5). The pleuroscopic diagnostic yield was 96.5%. The pleuroscopic diagnostic yield was 96.5%. The pleuroscopic findings were mainly described by the chest physicians as multiloculated effusion (n = 26), 'sago'-seed appearance (n = 22), pleural mass (n = 5), pleural nodules (n = 59), and diseased pleura (n = 11). In patients with pleuroscopic findings of 'sago'-seed appearance, 77.2% were found to have TB. With multiloculated effusion, 84.6% were diagnosed with TB. With 'nodules' findings, 70% were diagnosed with malignancy, and with 'mass' findings, 80% were diagnosed with malignancy. Statistical analysis was done to assess sensitivity, specificity and association of each pleuroscopic findings: Sago-seed appearance and multiloculated effusion are specific but not sensitive for tuberculosis. Nodules and mass pleuroscopic appearances are both sensitive and specific for malignancy.

Conclusion: Pleuroscopy is a valuable diagnostic tool in the diagnosis of undiagnosed exudative pleural effusion, and is very useful in predicting aetiology of exudative effusion in our centre, especially in diagnosing tuberculosis and malignancy.

P-B-022

COMPARISON OF DIAGNOSTIC PERFORMANCES AMONG BRONCHOSCOPIC SAMPLING TECHNIQUES IN THE DIAGNOSIS OF PERIPHERAL PULMONARY LESIONS

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Background: Radial endobronchial ultrasound (R-EBUS) has been developed to enhance the diagnostic yield of peripheral pulmonary lesions (PPLs) and is widely accepted by interventional pulmonologists nowadays. However, data regarding the diagnostic performances among bronchoscopic sampling techniques is limited.

Objective: To compare the diagnostic yields among bronchoscopic sampling techniques in the diagnosis of PPLs.

Methods: A prospective study was conducted on 96 patients who were diagnosed with PPLs and underwent EBUS-guided bronchoscopy between October 2012 and June 2014. Sampling techniques, included transbronchial lung biopsy (TBLB), brushing cell block, brushing smear, rinsed fluid of brushing, and bronchoalveolar lavage (BAL), were evaluated for the diagnosis.

Results: The mean diameter of the PPLs was 23.3 +/- 9.2 mm. The final diagnoses included 64 malignancies and 32 benign lesions. The overall diagnostic yield of EBUS-guided bronchoscopy was 82.3%. The performance of TBLB rendered the highest yield among these specimens (74.0%, 35.4%, 63.5%, 51.0%, and 42.7% for TBLB, brushing cell block, brushing smear, rinsed brushing fluid, and BALF, respectively; p < 0.001). TBLB provided high diagnostic yield irrespective of size and aetiology of the PPLs. Combination of TBLB and brushing smear achieved the maximum diagnostic yield. Of 27 infectious PPLs, BALF culture gave additionally microbiological information in 14 cases.

Conclusion: The performance of TBLB rendered the highest diagnostic yield; however, to achieve the highest diagnostic performance, TBLB, brushing smear and BAL should be performed together.

P-B-023

A RARE TUMOUR OF TRACHEA: INFLAMMATORY MYOFIBROBLASTIC TUMOUR DIAGNOSIS AND ENDOSCOPIC TREATMENT

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Inflammatory myofibroblastic tumours (IMTs) are rare childhood neoplasms, with benign clinical course. Although aetiology of IMTs are not clear, recent studies have reported that IMT is a true neoplasm rather than a reactive or inflammatory lesion. IMTs are rarely seen in adults and tracheal involvement is also rare both in adults and also in children. We describe a 16-year old female patient who was misdiagnosed and treated as asthma in another centre for a few months, and presented with acute respiratory distress due to upper airway obstruction. Computerized tomography (CT) of the chest and rigid bronchoscopy revealed a mass lesion that was nearly totally obliterating tracheal lumen. Bronchoscopic resection was performed under general anaesthesia and the final pathological diagnosis was tracheal IMT.

P-B-024

A RARE CASE OF TRACHEAL LYMPHOMA PRESENTING WITH SEVERE TRACHEAL STENOSIS

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No organizations provided

Primary malignant lymphoma of the trachea is rare and its underlying mechanism remains unknown. Primary tracheal tumours are also among the very rare causes of airway obstructions. In this case report, a 60 year-old woman who presented with the complaint of dyspnoea was reported. A mass narrowing the tracheal lumen posteriorly in the subglottic area and mediastinal lymphadenopathy was detected on computed tomography scan and rigid bronchoscopy was performed. This showed polypoid, variable-sized and irregular nodules causing narrowing of the tracheal lumen through 3 cm segment in the middle part of the trachea and a mass protruding into the tracheal lumen from the posterior part of proximal trachea. Multiple biopsy was carried out from the nodules and threatened airway obstruction with APC (Argon Plasma Coagulation). After the removal of the debris, tracheal lumen patency were obtained. The histopathological examination revealed small lymphocytic lymphoma of primary non-Hodgkin lymphoma of the trachea. In our knowledge, this is the first primary tracheal small lymphocytic lymphoma case in the literature.

P-B-025

DIAGNOSTIC YIELD OF CT GUIDED THORACIC BIOPSIES AND COMPLICATIONS AT CHIANGRAI PRACHANUKOH HOSPITAL

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Background: Nowadays with the development of computed tomography (CT), an increasing number of pulmonary lesions are detected. The diagnostic of pulmonary lesion needed for definite diagnosis for proper management. One of the techniques for obtained tissue from pulmonary lesion is CT guided thoracic biopsy. The objective of this study was to determine diagnostic yield of CT guided thoracic biopsies of pulmonary lesion. Correlation factors to malignancy and complication of procedures.

Materials and Methods: Retrospective cohort study of diagnostic yield of thoracic CT guided thoracic biopsies and complications at Chiangrai Prachanukoh Hospital during July 2013 and March 2014. 88 patients were performed CT guided thoracic biopsies by pulmonary physicians for evaluated diagnostic yield and complications. Correlation between factors of demographics data, imaging studies information, pathologic diagnosis and complications were summarized for evaluated.

Result: A total of 88 patients had 61 male (69.32%) with mean age 62.89 ± 10.67 years. The lesion mean diameter was 6.98 ± 3.29 cm. The mean distance puncture from pleura to lesion was 0.21 ± 0.51 cm. 75 patients (85.23%) had positive yield with 64 patients (72.73%) had malignancy disease. The overall complication rates were 2.28%. From 2 out of 88 patients were complicated with pneumothorax (2.28%). There was 1 patient (1.14%) complicated with large pneumothorax which required intercostals drainage. Minor complication was found in 1 patient (1.14%) with small pneumothorax. Aged was factor related to malignancy significantly ($P < 0.05$) and sized of pulmonary lesion related to complication significantly ($P = 0.05$).

Conclusion: CT guided thoracic biopsy of the pulmonary lesions had great diagnostic yield with rare severe complications. Aged was risk factor related to malignancy. Sized of pulmonary lesion was risk factor related to pneumothorax. CT guided thoracic biopsy is effective, simple and safe technique for diagnosis of pulmonary lesion.

P-B-026

DIFFERENT APPROACHES ON VARIOUS CASES OF TRACHEAL STENOSIS

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Introduction: Narrowing of the airway caused by several factors is a serious condition manifesting different signs and symptoms. Immediate attention and treatment must be performed as this is a life-threatening condition. In the past decade, there has been massive advancement on management of airway stenosis. Some of these are stent placement, tracheal reconstruction and tumour debulking. This article focuses on 5 different cases with distinct strategies in conducting treatment.

Objective: We performed this study to analyze the different techniques used in handling 5 patients with different causes of airway stenosis.

Method: Between September 2012 and November 2013, we identified 5 patients diagnosed of central airway narrowing. We analyzed each case study, considered the pathology of the disease, treatment, prognosis, and improvement in quality of life.

Case Reports:

1. A case of lung cancer stage III, post right upper lobe lobectomy, following irradiation and chemotherapy. Neck CT scan presented a demonstrable consolidative mass that caused pressure to the upper trachea and esophagus. Polyflex airway stent placement was successfully performed via rigid bronchoscopy.
 2. A case of 46-year-old male, who presented progressive dyspnoea, hoarseness of voice, stridor, fever and cough underwent fiberoptic bronchoscopy which revealed tracheal stenosis. Polyflex airway stent was inserted under complications. Cytology report was positive for adenoid cystic carcinoma.
 3. A case of esophageal cancer with metastatic brain tumour status post-craniotomy. The neck CT scan revealed a mass that invaded the posterolateral aspect of upper intrathoracic trachea. Rigid bronchoscopy for stent placement was done without difficulty.
 4. A 27-year-old woman who is a foreign health care worker exposed to tuberculosis (TB) patients, was diagnosed of TB and underwent treatment for 6 months. 10 months later, she presented with stridor, wheezing, shortness of breath and dyspnoea. Bronchoscopy revealed narrowing near the mid-trachea. Tracheal resection and reconstruction under general anaesthesia were done. No untoward complications were noted post-surgery.
 5. An asthmatic patient on bronchodilators has been complaining of dyspnoea. Chest CT scan revealed a lobulated well-defined soft tissue density at trachea. The mass was extracted via the combination of rigid and fiberoptic bronchoscopes with snare and electrocautery.
- Conclusion:** Airway stenosis is a life-threatening condition with severe complications caused by several factors. Treatment is individualized and management requires technical expertise. If caught early and treatment has been determined following diagnosis, improvement on quality of life and potential survival may be achieved.

P-B-027

P-B-029

ENDOBROCHIAL ULTRASOUND IN THE PHILIPPINES: A CASE SERIES

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Background: Endobronchial ultrasound is an ultrasound combined with bronchoscopy to obtain images in and around the bronchial tree or the lungs. It can be used in the diagnosis of lung cancer, infections and other diseases that cause enlarged lymph nodes in the chest. It is useful in the diagnosis and staging of lung cancer through the performance of either needle aspiration of mediastinal masses and lymph nodes or brushing and forceps biopsy of peripheral mass lesions. This intervention was first performed in the Philippines last May 2013 with four cases and subsequent procedures were done recently in June 2014 at University of Santo Tomas Hospital.

Methods: Subjects with mediastinal and peripheral masses inaccessible by ordinary flexible bronchoscopy or computer tomography scan-guided transthoracic needle aspiration were identified. The patients with mediastinal masses underwent endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and patients with peripheral masses underwent brushing and forceps biopsy through endobronchial ultrasound guide sheath (EBUS-GS).

Results: Eight patients underwent endobronchial ultrasound were done in the Philippines from the years 2013 to 2014. Three patients underwent EBUS-TBNA, while four patients underwent EBUS-GS. One patient was subjected to both EBUS-TBNA and EBUS-GS. Three of the patients were diagnosed to have adenocarcinoma, two were found to have squamous cell carcinoma, and two cases were identified to have tuberculosis, while one had no definitive diagnosis. There were no peri-procedural complications that were encountered.

Conclusions: Endobronchial ultrasound procedures are safe and have high diagnostic yield in patients with mediastinal masses and peripheral lung lesions that are otherwise inaccessible by conventional methods.

ENDOBROCHIAL VALVE IN PROLONGED AIR LEAKAGE (CASE REPORT)

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Endobronchial valve is a bronchoscopically applied procedure, generally performed for volume reduction in emphysema. We used endobronchial valve for prolonged air leakage in a patient that has von-willebrand disease. In this case report we want to indicate that the endobronchial valve procedure can also be performed successfully for prolonged air leakage. A 21-year-old man was admitted to our department with effort dyspnoea. Cavity in the right hemithorax and thrombocytopenia was detected in the examination tests. The patient was operated for the cavitary lesion with a haematology consultation that was expressed as operable. The patient was taken to the operation room in the postoperative early period for the increased hemorrhagic drainage. No major focus for the bleeding was found intraoperatively. Drainage was controlled with administration of erythrocyte suspension and fresh frozen plasma. The patient was consulted to the haematology department again and von-willebrand disease was diagnosed after further evaluation. Prolonged air leakage was found in the patient postoperatively. Because of haematologic disorder of the patient, endobronchial valve was applied to the patient. After application of three valves to the right upper lobe the patient was discharged. The valves were taken out after three months and no air leakage was found. Endobronchial valve is a safely applied bronchoscopic procedure that requires no surgical intervention. The advantages of the procedure are safety and easy applicability, disadvantage is expensive. Much more clinical trials are needed, for the exact effect of the endobronchial valve procedure in the prolonged air leakage.

P-B-028

ENDOBROCHOSCOPIC ELECTROCAUTERY IN A RARE CASE OF PULMONARY EPITHELIOID HEMANGIOENDOTHELIOMA LIMITED TO THE AIRWAY

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Background: Epithelioid hemangioendothelioma (EHE) is a rare vascular tumour of intermediate behaviour with only fifty documented cases of pulmonary epithelioid hemangioendothelioma (PEHE) in the literature. Cases reported involved the lung parenchyma and liver with no reports of PEHE limited to the airway. As of this writing, there is no clear standard for treatment of PEHE.

Case Presentation: A 61-year-old female presented with chronic cough and hemoptysis. Chest radiograph and three sputum AFB smears were negative. Chest CT scan showed a polypoid lesion at the distal trachea with normal lung parenchyma. Bronchoscopy confirmed two vascular polyps at the distal trachea measuring 0.5 cm × 0.5 cm and at the junction of the superior segment and basal segments of the right lower lobe measuring 0.2 cm. Histopathological examination revealed multiple slit-like blood vessels lined by endothelial cells that appear plump and epithelioid-looking with rare mitotic figures suggestive of an EHE. Immunohistochemical stains for CD34 and Factor VIII antigen were positive, confirming the diagnosis. Treatment options for EHE range from observation in asymptomatic patients, surgery in resectable lesions and chemotherapy in disseminated disease. Patient underwent a repeat bronchoscopy with electrocautery. Forty watts with blend three setting was used. Patient remained symptom-free on follow-up after 1 year.

Conclusion: We present a rare case of PEHE limited to the airway. We found that endobronchial electrocautery is a safe and cost-effective option for curative intent of localized lesions.

POSTER PRESENTATION – CELL AND MOLECULAR BIOLOGY

P-C-001

NEXT GENERATION SEQUENCING: GENOMIC CHARACTERISTICS AND ANTIMICROBIAL PROFILES OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS COLLECTED FROM INPATIENTS IN INTENSIVE CARE UNIT OF HIROSHIMA UNIVERSITY HOSPITAL, HIROSHIMA, JAPAN

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Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) are responsible for 20–40% of hospital-acquired pneumonia (HAP) cases and 1–5% of community-acquired pneumonia (CAP) cases, while MRSA mortality rates of HAP and CAP are 55.5% and 29% respectively. The bacteria show resistance to β -lactam antimicrobials and some strains may also exhibit resistance to other antimicrobial classes, by means of horizontal gene transfer, which would further creates challenge in MRSA antimicrobial therapy of choice. Whole genome sequencing of MRSA could rapidly identify the sequence type (ST) and thus predict the genomic antimicrobial resistance pattern from large number of samples within relatively short time. Ultimately, rapid determination of antimicrobial resistance would deduct the rationalization of targeted antibiotic therapy in intensive care setting.

Material and Methods: Forty one MRSA isolates were obtained from clinical specimens (i.e. nasal swab, sputum, throat swab, endotracheal suction sputum) of the patients treated in intensive care unit in Hiroshima University Hospital of two different time frames: 16 isolates from year 2009 and 25 isolates from year 2013. Isolates were then determined for its antimicrobial susceptibility by disc diffusion method, extracted for its genome using Qiagen QIAamp DNA Mini Kit and sequenced using Illumina MiSeq sequencer. Paired-end sequence reads were then aligned to multilocus sequence typing (MLST) tool, ResFinder tool, Ridom SpaServer, CLC Genomics Workbench, Unipro UGENE and BLAST tools.

Results and Discussion: The on-going study shows that all strains are resistant to β -lactam antimicrobials as expected, with additional resistant to fluoroquinolone (15/16 and 23/25), lincosamide (13/16 and 15/25), aminoglycoside (7/16 and 22/25), tetracycline (5/15 and 10/25) and teicoplanin (0 and 1/25) in both 2009 and 2013 cluster respectively. Clonal complex (CC) ST5 MRSA strains are predominant in both 2009 and 2013 cluster (68.75% and 56% respectively), which consist of ST5, ST512, ST764 and ST2389, followed by CC8 strains (12.20% and 24.39% in 2009 and 2013 cluster, respectively) and a singleton of ST89 (CC91) strain in 2013 cluster. The spa typing of CC5 cluster shows predominant t002 pattern while the CC8 cluster shows t211 pattern. Several resistance genes may correlate with the antimicrobial profile, for instance β -lactam resistant strains possess *mecA* gene and/or *blaZ* gene with or without mutations; aminoglycoside resistant strains possess all *spc*, *aadD* and *aac(6')-aph(2'')* genes, lincosamide resistant strains have *erm(A)* gene, and tetracycline resistant strains possess both *tet(38)* and *tet(M)* genes. We will discuss the inheritance of these resistant genes and the outbreak of MRSA infection in both eras.

P-C-002

THE ROLE OF SECRETORY IMMUNOGLOBULIN A AND NEUTROPHILS EVENTS ON EARLY ONSET-VENTILATOR ACQUIRED PNEUMONIA BASED ON ANALYSIS OF SPECIMENS BRONCHOALVEOLAR LAVAGE

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Background: The VAP is linked to the local immune system in the respiratory system. Secretory immunoglobulin A (s-IgA), a component of humoral immunity, along with innate immunity neutrophils protects from infection. Neutrophils is two distinct functions, is as the defense component and on the contrary, excessive inflammation, damage of lung tissue and this may lead to ARDS. The aims of study to prove the role of s-IgA and neutrophils in patients on mechanical ventilators, towards the incidence of early-onset VAP, ARDS and s-IgA capability to suppress overreaction from elevated neutrophils counts. **Method:** The study was a prospective analytic observation cohort on s-IgA and neutrophils from BAL, the VAP(-/+) with a scores of CPIS > 6 is VAP(+). Bronchoscopy techniques and BAL: FOB was inserted through the endotracheal tubes via sterile connector to maintain ventilation during procedure. BAL commonly performed on left subsegment lingula or right middle lobe, selected based on chest radiograph or according to the presence of direct inflammatory signs, with protected BAL Balloon Catheter. Finally fluid from BAL was immediately delivered to microbiology laboratory, cytological, and serological analysis.

Results: Subjects observed were 61 people, with initial diagnosis no pneumonia. On the third day group VAP(-) with CPIS scores ≤ 6 (± 2.86), 28 subjects, and group VAP(+) with CPIS scores > 6 (± 7.94), 33 subjects. The first day and on the third day of s-IgA is different significantly ($p < 0.05$), but Mann-Whitney test s-IgA for two groups did not differ significantly ($p > 0.05$). Neutrophils on first day and on third day is significantly ($p < 0.05$). T-test results of neutrophils from both groups also differ significantly ($p < 0.05$), with the correlation(r) is -0.444 , which mean any increase in s-IgA will be accompanied by decreased in neutrophils overreaction. Analysis of the correlation between neutrophils and CPIS scores shows strongly related correlation (0.595). By Spearman correlation, a strong correlation between neutrophils and the incidence of ARDS was found. S-IgA in the VAP(+) and VAP(+) with ARDS is different significantly ($p < 0.05$).

Conclusion: S-IgA is able to suppress neutrophils overreaction. Neutrophils was contribute to the incidence of VAP and strong correlation the incidence of ARDS. In ARDS, the increased neutrophils causing damage to the alveoli environment, then the s-IgA declined, not able to maintain a good environment back in the alveoli.

POSTER PRESENTATION – CLINICAL ALLERGY & IMMUNOLOGY

P-D-002

THE PREVALENCE AND DIAGNOSTIC VALUE OF TOXOCARIASIS IN PATIENTS WITH PULMONARY INFILTRATES WITH BLOOD EOSINOPHILIA

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Objective: To evaluate the prevalence of toxocariasis and its clinical features in patients with pulmonary infiltrates on chest radiograph combined with peripheral blood eosinophilia at a tertiary hospital in South Korea.

Design: From January 2008 to August 2013, total 102 patients were identified as pulmonary infiltrates with simultaneously elevated blood eosinophil. We retrospectively reviewed history of raw meat intake, clinical symptoms, blood eosinophil count, toxocara seropositivity by ELISA, total Ig E and radiological features.

Results: Among the 102 patients, 79 patients were diagnosed as simple pulmonary infiltrates with eosinophilia (SPIE) and the others are 12 acute eosinophilic pneumonia, 5 pulmonary paragonimiasis, 4 Churg-strauss syndrome, 1 chronic eosinophilic pneumonia and 1 drug induced eosinophilic infiltration. Among 79 SPIE patients, 50 patients (63.0%) were diagnosed as SPIE by toxocariasis and 29 (37%) as SPIE without toxocariasis. History of raw meat intake was found in 80% (40/50) patients of toxocariasis and 86% (25/29) in SPIE without toxocara. Common respiratory symptoms of pulmonary toxocariasis were cough (14%), chest discomfort (10%) and 78% (39/50) patients are asymptomatic. Most common radiological features of toxocariasis were ground glass opacity (66%) and nodules (24%). Mean serum eosinophil counts was 1160/uL (730–1,590) and elevated total Ig E was found in 97% of toxocariasis. Between toxocariasis and SPIE without toxocara, there was no significant difference in age, sex, intake of raw meat and respiratory symptoms. 86% of toxocariasis patients were treated by oral albendazole.

Conclusions: In patients with simple PIE, the prevalence of toxocariasis was relatively high. Whether SPIE patients have toxocara (+) or toxocara (–) by ELISA, they are closely related with dietary habits of raw meat intake. Toxocara infection should be considered in a differential diagnosis of patients who exhibits simple PIE in South Korea.

P-D-003

COMPARISON OF CLINICAL CHARACTERISTICS, QUALITY OF LIFE AND SLEEP IN PATIENTS WITH ALLERGIC RHINITIS WHEN CATEGORIZED AS “SNEEZERS AND RUNNERS” AND “BLOCKERS”

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Introduction: Patients with allergic rhinitis (AR), as per their predominant symptoms, can be classified into “sneezers and runners (SR)” and “blockers”. Since these two groups have distinct profiles, they were assessed and compared in terms of quality of life (QoL) and sleep disturbances.

Methods: The study comprising 106 consecutive patients (males:60/females:46), 18 to 60 years with AR, diagnosed as per ARIA guidelines, were enrolled from outpatients department of VP Chest Institute, University of Delhi. Patients were categorized into “SR” (group1) and “blockers” (group2) with the help of a visual analog scale (VAS) of 10 centimetres with 0 being “no symptoms” and 10 being “symptoms extremely bothersome”. Scores for global VAS, sneezing, runny nose, nasal congestion, post nasal drip and loss of smell were recorded and patients classified as “SR” and “blockers”. Impact on QoL was assessed with Sinonasal Outcome Test 22 (SNOT-22) and sleep was assessed by Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ), the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI) instruments.

Results: Just over two thirds (n = 73:68.9%) of the patients, were categorized as “SR” (group1) while remaining third (n = 33:31.1%) were categorized as “blockers” (group2). The significant features in group1 were: age at onset lower than 20 years (n = 60:82.2% P = 0.002); birth dates were between June and September (n = 42:57.5% P = 0.003); family history of atopy (n = 59:80.8% P = 0.001); itching of skin (n = 25:34.2% P = 0.002), eye (n = 30:41.1% P = 0.001), ears (n = 28:38.4% P = 0.002), and throat and palate (n = 42:57.5% P = 0.001); and aggravation with dust (n = 65:89.1% P = 0.001). History of breathlessness (n = 28:84.8% P = 0.002), mouth breathing (n = 28:84.8% P = 0.003), loss of smell (n = 13:39.4% P = 0.004), and prior nasal surgery (n = 8:24.2% P = 0.001) were significantly higher in group2. Patients in group1 were significantly more sensitized to seasonal allergens like pollens [Kigelia (P = 0.045); Salvador (P = 0.005)] while patients in group2 had more sensitization to perennial allergens like house dust (P = 0.001), house dust mite (P = 0.044) and fungus including Aspergillus species (P = 0.001). Mean SNOT-22 scores (group1:60.89; group2:61.66 P = 0.763) and mean NRQLQ scores (group1:47.66; group2:50.91 P = 0.238) were not significantly different between the groups, while mean ESS (group1:10.52; group2:12.30 P < 0.001) and mean global PSQI scores (group 1:9.71; group 2:11.27 P = 0.009) were significantly higher in group2.

Conclusions: The two groups differ significantly in terms of their respective profiles, whether be demographic or clinical. Further, the sensitivity patterns to allergens differ significantly between the groups. “Blockers” experienced significantly higher sleep disturbances as compared to “sneezers and runners”.

P-D-004

LOWER AIRWAY EOSINOPHILIC INFLAMMATION CAN ALSO EXIST IN NONASTHMATIC PATIENTS WITH NONALLERGIC RHINITIS PATIENTS

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Background: Whether patients with nonallergic rhinitis (NAR) has the airway inflammation resembling allergic rhinitis is uncertain. Objective: Our aim is to investigate the characteristics of airway inflammation in nonasthmatic patients with nonallergic rhinitis and compared with patients with allergic rhinitis.

Methods: Peripheral blood routine, fractional exhaled nitric oxide (FeNO), nasal lavage, lung function test, methacholine challenge test and induced sputum test were performed in 146 patients with nonallergic rhinitis, 252 patients with allergic rhinitis (AR) and 123 non-atopic healthy controls (HC).

Results: Eosinophilia in induced sputum was observed in 10.64% of patients in NAR group, 31.25% of patients in AR group, and 0.83% of patients in HC group, however, (all $P < 0.01$). The increased FeNO value was detected in 15.56% of patients in NAR group 36.27% in AR group, and 5.81% in HC group (all $P < 0.05$). The percentage of eosinophilia in nasal lavage is the highest in AR group, followed by NAR group and HC group (47.37% vs 17.36% vs 5.69%, all $P < 0.01$). Eosinophilia in peripheral blood existed in 2.78% of patients with NAR, 6.12% of patients with AR and 0.81% of HC (AR vs HC, $P < 0.05$). In NAR group, 3.42% of subjects showed BHR, which is significantly lower than that of AR group(10.32%), higher than that of HC group(0%). Eosinophilia in nasal lavage and induced sputum sample tended to coexist in the same patient with rhinitis.

Conclusion: In addition to inflammation in the upper airway, eosinophilic inflammation can also exist in lower airway in nonasthmatic patients with nonallergic rhinitis. Airway inflammation in nonallergic rhinitis is similar to, but not as severe as that in allergic rhinitis. A long-term observational study is required to determine whether those patients will develop asthma in the future. This study provides evidence for "United airway, United disease".

P-D-005

PROFILE OF ALLERGY IN CENTRAL SRI LANKA: A SINGLE UNIT EXPERIENCE

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Introduction: Skin prick test (SPT) is standard for diagnosis of atopy and identifying the sensitization to specific allergens.

Objective: To identify the sensitivity to various allergens in patients with nasobronchial and skin allergy by a skin prick test.

Setting: Respiratory Unit 2, Teaching Hospital Kandy, Sri Lanka

Method: A descriptive study involving 202 patients attending Respiratory Diseases Clinic with symptoms related to allergy and asthma. Interviewer administered questionnaire was used to collect information on demographic data, indication for testing, symptoms, triggers, allergen exposures, and blood Investigations (Full Blood Count, ESR, Serum IGE). A total of 5252 skin prick tests were performed using 26 allergen extracts. Procedure was carried out according to the standard technique. Standard exclusion criteria regards to medications were adhered.

Results: Out of a total of 202 subjects, 77 were males. The age distribution was from 5 to 89 years. (mean 49.5 years). The indications for testing were Allergic Bronchopulmonary Aspergillosis 40 (19.8%), Allergic Rhinitis and Bronchial Asthma 81 (40%), Urticaria 10 (4.95%), other fungal infections 05 (2.47%) and eczema 17 (8.41%). Of the 202 subjects, 126 (62.3%) showed SPT positivity to one or more allergens. the identified allergens were, House Fly (53) 42%, Cockroach 41% House Dust Mite (46) 36.5%, Mosquito (40) 31.7%. and others which included aeroallergens, animal danders and domestic animals. Of clinically suspected ABPA patients only 10 (25%) were positive for *A. Fumigatus* and/or *A. Niger*. Among patients with Bronchial Asthma and Allergic Rhinitis, highest sensitization was seen for House Fly (35) Cockroach 41% and House dust mite (30).

Conclusion: We were able to identify common allergens in a cross section of patients with nasobronchial and skin allergy in central Sri Lanka. These findings offer a new insight to clinical practice in Sri Lanka where allergy testing is a relatively new concept with majority of the clinicians not having access to the test. Most of the patients were sensitized to common insects that are found ubiquitously in our country. It is of interest to note that highest prevalence of allergy in this region was to that of cockroach, which has been described as an important domestic trigger for asthma. This information can be used as a measure of prevention in atopic symptoms and also to introducing immunotherapy which is currently not available in our country.

P-D-006

P-D-007

DYSPNOEA AS A CHIEF COMPLAINT OF EOSINOPHILIC GASTROENTERITISSEUNG JOO BYUN¹, MIN HO JO¹, YU RAN NAM¹, EO JIN KIM²,
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Eosinophilic gastroenteritis (EGE) is a rare disease characterized by peripheral eosinophilia, eosinophilic infiltration of the gastrointestinal tract and functional gastrointestinal abnormalities. Common symptoms are abdominal pain, nausea, vomiting, diarrhea (bloody or non-bloody), weight loss, and ascites. Other symptoms have few been reported. A 59-year-old man was admitted to this hospital with a chief complaint of dyspnoea that developed five years ago. His symptom was not particularly exacerbated in any season, and he showed no signs of orthopnea, generalized oedema, chest pain nor palpitation. The initial laboratory data showed that WBC 5520/ μl (with 50.1% neutrophil, 38.2% lymphocyte, 6.8% monocyte, 4.5% eosinophil and 0.4% basophil); haemoglobin, 15.8 g/dL; BUN, 25.6 mg/dL; creatinine, 0.84 mg/dL; sodium, 139 mmol/L; potassium, 4.4 mmol/L; chloride, 105 mmol/L. The ECG showed normal sinus rhythm. The chest radiograph was within normal limits. Pulmonary function test showed FEV₁, 101% of predicted while FVC 127% of predicted. The methacholine provocation test and skin prick test was negative. Through these tests we concluded that the patient's dyspnoea was from neither pulmonary nor cardiac origin. Besides he had suffered an uncontrolled five-time-a-day watery diarrhea and tenesmus for the last fifteen years. we could guess that his dyspnoea might have developed secondary to chronic diarrhea. Under a suspicion of EGE based on the eosinophil level of 250/ μl and uncontrollable diarrhea, He underwent colonoscopy. Colonoscopy showed no visual abnormalities, but biopsies of colon and rectum were performed for the diagnosis of eosinophil infiltration. The histopathologic test showed eosinophil infiltrations. The final diagnosis was EGE presenting as dyspnoea in an adult. The patient was treated with methylprednisolone and he had neither recurrent diarrhea nor tenesmus. The patient has been asymptomatic for about 3 month after discharge. For eosinophilic gastroenteritis presenting dyspnoea in adult patient has not been previously reported in the literature, we thought this could guide diagnosis in future cases.

GOODPASTURE SYNDROME: FIRST CASE FROM SAUDI ARABIA

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Introduction: The kidney can be involved in many pulmonary disorders include sepsis, vasculitides and connective tissues diseases. Goodpasture Syndrome (GPS) related to anti-Glomerular membrane antibodies is a rare disease which can have devastating effects on the patient if not diagnosed. We describe the first case of GPS from Saudi Arabia and discuss the presentation and management.

The Case: 35 years old Saudi Female presented with cough productive of green sputum for 3 months duration. She had sought medical advice in different institutions and was treated with antibiotics with no improvement. She attended our Emergency department with the same symptoms associated with dyspnoea and wheeze. She had crackle in the bases of the lung with expiratory rhonchi. She was not clubbed and had no features of heart failure. Her blood count showed leukocytosis with high ESR. The CXR showed bilateral peri hilar infiltrate. She was treated as lower respiratory infection with bronchiectasis and admitted for further work. She had CT chest and bronchoscopy. Her urine showed hematuria with normal renal profile. She had autoimmune screen done. She was discharged on antibiotics to review the serology and autoimmune screen as out patient. As she improved she missed her appointments and presented one day to the clinic with fatigue. She was found to have Creatinine of 2.7 and so was admitted urgently to further evaluate. Her Renal biopsy showed rapidly progressive glomerulonephritis (RPGN) and her AGBM was positive. She was treated with IV pulse steroids, Plasmapheresis and later immunosuppressant therapy. Her current Creatinine is 1.2 and she is asymptomatic.

Discussion and Conclusion: Goodpasture syndrome, a rare human autoimmune disorder, is characterized by the presence of pathogenic auto antibodies that react with the components of the Glomerular basement membrane. The clinical condition of the Goodpasture syndrome is characterized by an RPGN and pulmonary haemorrhage. It is a rare disease and younger patients usually present with the full syndrome while older patients present with isolated glomerulonephritis. Options of therapy include immunosuppression and Plasmapheresis. We present the clinical presentation and radiology with the review of the literature.

P-D-008

UNRESOLVED PNEUMONIA WITH RENAL IMPAIRMENT

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Introduction: The kidney can be involved in many pulmonary disorders include sepsis, vasculitides and connective tissues diseases. Goodpasture Syndrome (GPS) related to anti-Glomerular membrane antibodies is a rare disease which can have devastating effects on the patient if not diagnosed. We describe the first case of GPS from Saudi Arabia and discuss the presentation and management.

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POSTER PRESENTATION – CLINICAL RESPIRATORY MEDICINE

P-E-001

PULMONARY MALAKOPLAKIA PRESENTING AS A SOLITARY PULMONARY NODULE IN A RENAL TRANSPLANT RECIPIENT

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Malakoplakia is a rare inflammatory condition characterized by the accumulation of aggregates of histiocytes that contain concentrically layered basophilic inclusions called Michaelis-Gutmann bodies. It is usually an infectious process associated with immunocompromised states. Involvement of the pulmonary system is quite uncommon. A 47-year-old male patient who had received a cadaveric renal transplant 18 months ago referred to our clinic for the evaluation of a solitary pulmonary nodule detected during routine follow-up. The patient was asymptomatic and there was no evidence of infection. He was using immunosuppressive medications. Physical examination was normal. Routine laboratory analysis including complete blood count, biochemical analysis, urine analysis were normal apart from a mild elevation of creatinine 1.5 mg/dl. Anti-HCV was positive. On chest radiography, there was an irregular margined solitary pulmonary nodule, 1.5 cm in diameter, located on the third anterior intercostal region. That nodule was not present on a previous chest radiography obtained 6 months before. We performed a PET/CT with the suspicion of malignancy. There was only a high FDG uptake (SUVmax: 9.78) on the pulmonary nodule of 1.5 cm located on the superior segment of lower lobe. The nodule was not suitable for a transthoracic fine needle biopsy that we referred the patient to chest surgery clinic for diagnostic thoracotomy. The nodule is resected by wedge resection. The frozen section was benign. The histologic examination of the surgical specimens was compatible with malakoplakia. In conclusion, despite being a rare clinical entity, pulmonary malakoplakia should be kept in mind in the aetiology of pulmonary nodules in transplant recipients. Its rarity might be due to underdiagnosis. Malakoplakia should be added to the list of unusual infectious disease occurring at unusual sites in immunocompromised hosts. Strong suspicion is required both clinically and histologically to diagnose this condition.

P-E-002

P-E-003

PREVALENCE OF RESPIRATORY SYMPTOMS AND THEIR PATHOLOGICAL SIGNIFICANCE IN PATIENTS WITH END STAGE RENAL FAILURE; A DESCRIPTIVE STUDY

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Objectives: To describe the prevalence of respiratory symptoms in patients with stage five renal failure, and to identify their clinical significance in terms of respiratory pathology. Study setting: Respiratory Disease Treatment Unit 2 and renal disease treatment unit, Teaching Hospital Kandy, Sri Lanka.

Methodology: A descriptive study involving 125 consecutive patients with end stage renal failure treated at nephrology unit and respiratory unit 2 during November 2013 to January 2014. All patients with known chronic lung disease were excluded. Demographic data, presence of respiratory symptoms and examination findings were recorded using an interviewer administered questionnaire. Investigation findings including chest radiographs and microbiological tests were recorded.

Results: In the sample of 125 patients, 69% were male. Mean age of the sample was 43.2 years ranging from 15 to 69 years (43.2 ± 12.03). 33.3% had at least one respiratory symptom. Commonest symptom was cough 35 (87.5%) with mean duration of 32.71 ± 43.21 days. The other symptoms and their frequency were breathlessness (77.5%), sputum production (52.5%), hemoptysis (32.5%), wheezing (10%) and chest pain (7.5%). Considering symptomatic patients, 2 (5%) were in stage 5 non dialysis group. 29 (72.5%) were on regular hemodialysis. Rest, 9 patients (22.5%) were in post transplanted category. The final diagnoses of symptomatic patients were tracheobronchial infection 14 (37.8%), pulmonary oedema 8 (21.6%), tuberculosis 7 (18.9%), pneumonia 4 (10.8%), uraemic pleural effusion 2 (5.4%), lung abscess 2 (5.4%), non infectious bronchitis 3 (8.1%). Patients with two or more respiratory symptoms were significantly ($p=0.032$) more likely to have a diagnosis of infection than those with less than two symptoms. CRP had positive predictive value of 66% in diagnosing an infective aetiology. Thirty one patients out of 40 (77.5%) were having ESR more than 40 mm/1st hour. However there was no significant relationship of having an ESR of more than 40 mm with respiratory tract infection. CXR abnormalities were found in 92.5% patients with respiratory symptoms.

Conclusion: Prevalence of respiratory symptoms in the study group was 33.3%. Respiratory symptoms are common in stage 5 renal failure patients out of which majority were on dialysis. Presence of more than 2 symptoms was predictive of infective respiratory pathology. Cough was the most frequent symptom and most common disease was tracheo bronchial infection. CRP was a better inflammatory marker in diagnosing infective aetiology. Presence of a high ESR did not help in distinguishing between non infective and infective aetiologies of respiratory symptoms in this group of patients.

ADJUSTED NECK CIRCUMFERENCE SCORE IN SEVERITY OF OBSTRUCTIVE SLEEP APNEOA

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Background: Obstructive sleep apnea is the most common form of sleep disordered breathing which can affect the quality of life when left untreated. It may also lead to the development of disorders, such as hypertension and cardiovascular disorders. Overnight polysomnography remains the gold standard for diagnosis of OSA; however, it is resource intensive and may not always be available in some parts of the country. Therefore a screening tool is necessary to detect those who would benefit from further work-up for OSA.

Objective: To determine if the ANC score is associated with severity of obstructive sleep apnea.

Methodology: The records of all adult patients who underwent overnight polysomnography from January 2011 up to May 2013 at Respicare Enterprises were reviewed. Subjects' clinical profile, including age, sex, BMI, neck circumference, and history of hypertension, snoring and nocturnal choking/gasping was obtained and ANC score for each subject was computed. Likewise, the result of the polysomnography was also obtained.

Results: A total of 223 subjects were included in the study. Of them, 21, 56, 25, and 121, have no, mild, moderate, and severe OSA, respectively. An r coefficient of 0.2727 with a p value of <0.0001 was computed showing a positive relationship between ANC score and OSA severity. Using simple ordinal logistic regression with only ANC score as the independent variable, an estimated odds that a person's response is in the more severe direction rather than the less severe direction increases multiplicatively by almost 11% for every 1-point increase in ANC score (odds ratio of 1.1050 with a p value of <0.0001). While the estimated odds that a person's response is in the more severe direction rather than the less severe direction when BMI and age are held constant increases multiplicatively by almost 7% for every 1-point increase in ANC score (odds ratio of 1.071 with a p value of 0.012).

Conclusion: Adjusted neck circumference score is positively associated with OSA severity.

P-E-004

PROFILE OF ACUTE RESPIRATORY DISTRESS SYNDROME PATIENTS WHO WERE HOSPITALIZED IN RS CIPTO MANGUNKUSUMO

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Background: Acute respiratory distress syndrome (ARDS) is a criticalness in the pulmonology with a very high mortality rate. Knowing the characteristic profile of ARDS patients is important, because it is a factor which affecting the patient's outcome. Until recently, there is no research found which explain the ARDS patients characteristics in Indonesia, especially RSCM.

Purpose: Finding the profile of ARDS patients hospitalized in RSCM.

Methods: This research is a descriptive study to ARDS patients in RSCM between 2008–2012. Clinical data, laboratory, thorax photo expertise and outcome status are drawn from medical records. Results of this research are presented by categorical data with total sum and percentage. Numeric data with normal distribution are presented in average and standard deviation. Numerical data with abnormal distribution are presented in median and span.

Result: 368 patients are included in this research. Founded mortality rate during hospitalization is 75.3%. Subject's median age is 51 (between 18 to 95) years and most of the subject's age are under 60 (67.2%) years. Patients with komorbid are 243 (66%) with Charlson 2 comorbidity index between 0 to 6. Immunocompromise is the komorbid most found at 148 patients (60.9%) of total, diabetes mellitus 71 (29.2%) patients, chronic kidney disease 58 (23.9%) patients, stroke 51 (13.9%), and sirosis hepatitis at 14 (5.8%) patients. Median score of APACHE II from research subjects is 18 (spanned 3 to 122). Most cause of ARDS patients is sepsis at 287 (77.7%) patients. As many as 160 (60.5%) patients have ratio of $PaO_2/FiO_2 > 100$. As many as 256 (69.6%) patients have ARDS with less than 48 hours after hospitalization. As many as 64 (17.4%) patient do not utilize mechanical ventilator during hospitalization, and 74 (20.1%) patient use ventilator more than 48 hour after diagnosed with ARDS.

Conclusion: Most of ARDS patients hospitalized in RSCM have age under 60 years, with komorbid, experience ARDS < 48 hours after treatment, had ratio of $PaO_2/FiO_2 > 100$ and caused by sepsis. Currently there are ARDS patients hospitalized with treatment without ventilators and some patients are late to use ventilators. Mortality of ARDS patients in RSCM is still high.

P-E-005

A RARE ANOMALY: IDIOPATHIC PULMONARY ARTERY ANEURISM

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A pulmonary artery diameter exceeding 30 mm is defined as pulmonary artery aneurism (PAA). Aneurisms of the main pulmonary artery or both branches are known as proximal PAA. Although many factors are considered to be responsible for pulmonary artery aneurism, isolated or idiopathic PAA is uncommon. A 70-year-old male patient was admitted with complaints of dyspnoea, cough and high fever. Teleroentgenogram showed an enlargement in the region corresponding to pulmonary artery. Left and right cardiac dimensions and functions were within normal limits in transthoracic echocardiography, EF measurement was 60%. Congenital anomalies such as patent ductus arteriosus and atrial septal defect that may directly affect pulmonary artery were absent. There was no thrombus or intracardiac mass. Doppler echocardiography showed 20 mmHg peak gradient at pulmonary valve and gradual increase in pulmonary velocity. A computerized tomography (CT) revealed an aneurism and the main pulmonary artery, left pulmonary artery and right pulmonary artery were 34 mm, 39 mm and 23 mm, respectively. A pathology test was made with a negative result. Surgical intervention was not a treatment choice as the aneurism was confined to only proximal pulmonary artery and there was no symptom directly related to the aneurism.

P-E-006

A CASE OF ANAEMIA WITH PERSISTENT PULMONARY INFILTRATES: A DIAGNOSTIC DILEMMA

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This is a case of a 13 year old female, who came in for pallor and hemoptysis. Since 4 years old, patient had several hospital admissions due to iron deficiency anaemia with multiple blood transfusion. Patient had onset of cough and hemoptysis at 7 years old, chest X-ray revealed presence of fine diffusely scattered nodular densities on both lungs. She was diagnosed to have pulmonary tuberculosis and was treated with triple anti-tuberculosis drug combination. Repeat chest X-ray after treatment however showed persistence of previously noted nodular densities on both lungs. CT scan and bronchoscopy were advised, however, the family refused. Several chest X-rays were taken which showed persistence of diffusely scattered nodules on both lungs interpreted as military tuberculosis. A week prior to admission, patient complained of dyspnoea on exertion, relieved by rest. Patient's condition was tolerated. On the day of admission, onset of hemoptysis and pallor was noted associated with body malaise. Patient was then brought to a local physician. CBC taken showed anaemia thus was advised admission. On admission, patient was pale, tachycardic, afebrile and not in respiratory distress. Patient had clear breath sounds, no organomegaly, no palpable lymph nodes noted. CBC revealed anaemia and reticulocytosis. Peripheral smear showed diminished red cells, moderately hypochromic and microcytic, with macrocytes, ovalocytes, schistocytes and tear drop cells. Iron studies taken showed low serum iron, elevated serum ferritin with normal TIBC. Chest X-ray showed tiny innumerable nodular densities in both lungs suggestive of military tuberculosis. Arterial blood gas taken showed respiratory alkalosis with mild hypoxemia, oxygen inhalation was then started. Sputum AFB smear and Mantoux test done were negative. Urinalysis, Complement C3, creatinine, APTT and protime were within normal limits. 2D echocardiogram showed mild tricuspid regurgitation and moderate mitral regurgitation. Chest CT scan revealed findings suggestive of interstitial lung disease with associated perihilar and mediastinal lymphadenopathy, but cannot totally rule out chronic inflammatory process. Antibiotic and Quadruple anti-tuberculosis combination were started. Blood component therapy was initiated early however several blood units were incompatible to patient's blood with +3 to +4 reaction. Coombs test done revealed positive for direct and indirect tests. Methylprednisolone IV was started. Two units of packed RBC were transfused. Bronchoscopy was done and samples were taken for laboratory tests and histopathologic staining. Bronchoalveolar lavage showed no microorganism and negative for AFB. Lung tissue biopsy revealed mild chronic inflammation with several hemosiderin-laden macrophages noted. This findings clinched the diagnosis of Idiopathic Pulmonary Hemosiderosis. Methylprednisolone IV was shifted to prednisone PO. Patient was eventually discharged improved.

P-E-007

STRATEGIES TO IMPROVE DIAGNOSIS IN RESPIRATORY MEDICINE

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Diagnostic performance is a pivotal clinical expertise. The aim of this study is to develop practical strategies to improve diagnostic accuracy in respiratory medicine from the reporting of adverse events. We analyzed 738 adverse events voluntarily reported by clinicians from 2005–2013. Diagnostic errors were noted in 485 cases (66%). They consisted of patients with breathlessness (15%), tuberculosis (15%), cancer (15%), pleural problems (13%) and pulmonary embolism (8%). With the exception of cancer, the errors usually occur in the early phase of the diagnostic process. We developed a model of diagnostic expertise in respiratory medicine from recent studies on perceptions of renowned physicians and structured reflective practice. For the presentations in which errors occurred in the early phase of the diagnostic process we have implemented evidence based, enhanced diagnostic pathways. These include, bedside ultrasound in high risk breathlessness and pleural disease, Xpert MTB testing of pooled induced sputum in suspected pulmonary tuberculosis and age adjusted D dimer assays in suspected pulmonary embolism. In conclusion, diagnostic errors occur frequently in patients with breathlessness, tuberculosis, cancer, pleural problems and embolism. Reporting of adverse events by clinicians can initiate a process in which innovative strategies may be formulated and tested to improve diagnosis in respiratory medicine.

P-E-008

LUNG AGENESIS PRESENTING IN AN ADULT

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Introduction: Pulmonary agenesis is a very rare congenital malformation which has been classified morphologically by the extent to which bronchopulmonary tissue is absent. It is divided into: bilateral complete agenesis, unilateral lung agenesis and lobar agenesis. The presentation in adults is extremely rare. We describe a 43 years old male who presented with dyspnoea and cough and was found to have agenesis of the left lung.

The Case: 43 year-old Saudi gentleman, who smokes Hubble Bubble (Shisha) presented with progressive dyspnoea and cough for 3 month duration. He denied hemoptysis but had intermittent wheeze and yellow sputum at times. He had no chest pain or palpitation or lower limb oedema. On Examination he had no clubbing or lower limb oedema. His saturation was 89% in room air. He had limited chest movement with displaced cardiac apex. Percussion showed dullness on left lower region and hyper-resonance on the right side with decreased cardiac dullness. He had no clinical evidence of heart failure. The CXR showed Hyperinflated right lung with displaced heart to the left and aeration of the left upper lobe. On CT scan the right lung was hyperinflated and extending to the left side with extreme cardiac displacement to the left confirmation left pulmonary agenesis. His Pulmonary Function test showed severe obstructive airway disease with no bronchodilator reversibility. He was treated with standard therapy for COPD and referred for vaccinations.

Discussion and Conclusion: Variable degrees of Lung agenesis are diagnosed during childhood or infancy. The adult diagnosis of this condition is very rare. Since 2000 there have been less than 20 cases reported in the English literature. The patients commonly present with dyspnoea and variable degree of air way obstruction. Some had been associated with other syndromes like Klippel-Feil syndrome. The treatment is usually medical. We present the case with the review of the literature with emphasis on the radiology and classification of the condition.

P-E-009

SUSPICION OF METASTASIS OR GRANULOMATOUS DISEASE IN AN ADULT WOMAN: CASE REPORT

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Introduction: The surveillance of cancer patients is an important issue to discover any metastatic disease at an early stage and to treat the patients properly. However, this can be challenging especially in a country where the tuberculosis or other granulomatous diseases are epidemic.

Case Report: A 42-year-old woman admitted with right-sided multiple small nodular lesions on her Chest CT. These nodular lesions were discovered on her ovarian cancer follow-up after two years of surgical treatment. The patient focused on her disease excessively and she decided by herself to perform PET-CT imaging for these nodular lesions which were under one centimeter. And there was no pathologic FDG uptake. The patient underwent Chest CT surveillance for three months interval. Interestingly, these parenchymal lesions were absent at her first follow-up. We recommended her a one more Chest CT four months later which revealed multiple small nodular lesions with different locations from previous lesions and mediastinal lymph node enlargement. We performed PET-CT again, before planning any invasive procedures to help us. The FDG uptake of right parenchymal lesions, left lingular lesion and superior and inferior right paratracheal lymph nodes were pathologic. These findings of PET-CT was helpful as a guide when deciding invasive diagnostic approach. The patient refused to have a bronchoscopic biopsy. Then we discussed mediastinoscopy with the patient for her mediastinal paratracheal lymph nodes and if it was not diagnostic to perform a wedge resection of one of right parenchymal nodular lesion at the same time. She received this surgical diagnostic approach. She underwent mediastinoscopy and superior and inferior paratracheal lymph nodes and subcarinal lymph node were biopsied. The frozen section revealed a granulomatous lymphadenitis which was enough for her diagnosis avoid the wedge resection of paranchymal nodule. Her final histopathologic result was the same with frozen section result.

Conclusion: PET-CT can be helpful in a patient who has cancer history and with mediastinal or parenchymal disease when planning invasive diagnostic methods despite its false positivity.

P-E-010

EFFECTIVE TREATMENT OF DIFFUSE PULMONARY LYMPHANGIOMATOSIS WITH PROPRANOLOL

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Introduction: Diffuse pulmonary lymphangiomas (DPL) is a rare congenital disease, which shows the overgrowth of lymphatic vessels in the lungs, pleura, and mediastinum. Although DPL has a progressive course and poor prognosis, treatment options are limited and often ineffective. We report on a patient with DPL, who was managed with propranolol.

Case: A previously healthy 53-year-old man visited our hospital with cough and shortness of breath. He underwent chest computed tomography (CT) examination and it showed a large amount of pleural fluid on left side with crazy paving pattern on both lung fields. Pleurocentesis was conducted and the pleural fluid showed chylous effusion with the triglyceride level of 1288 mg/dL. Milky colour fluid was retrievable through bronchoalveolar lavage examination, then transbronchial lung biopsy was proceeded. Because the tissue consisted of only bronchial mucosa with chronic inflammation and pleural effusion increased insidiously, we performed a video associated thoracoscopic surgery (VATS) for a wedge resection of the lung and a pleurodesis with talc. Microscopically, the obtained tissue through VATS showed the dilated lymphatic channels growing in connective tissue and these lymphatic channels revealed positive D2-40 staining immunohistochemically. Under the diagnosis of DPL, the patient was treated with a low-fat medium-chain triglyceride diet and discharged with improved symptoms of cough and dyspnea. We followed up the patient one month later after his discharge, he complained of mild degree of cough and dyspnea again. Compared with initial chest CT, follow-up chest CT revealed more extended crazy paving appearance on both lungs with recurrent pleural effusion. Oral propranolol, which had been proposed as an alternative treatment for lymphatic malformation, was attempted to administrate at 0.5 mg/kg/day, divided into 3 doses initially, then it was increased to 1.5 mg/kg/day which was tolerable dose. At 5th month after initial administration of propranolol, the patient presented relieved respiratory symptoms with slightly improved ground glass appearance and interlobular septal thickening on follow-up chest CT.

Conclusions: Recently propranolol, which is thought to cause down-regulation of the RAF mitogen-activated protein kinase signaling pathway, with reduced expression of vascular endothelial growth factor (VEGF) has been reported as an alternative treatment for a DPL patient with high plasma VEGF level. Because VEGF is suggested as not only an angiogenic factor but also a lymphangiogenic factor in the studies, propranolol might have an effect on patients with DPL. In our case, the patient was improved clinically after administration of propranolol without additional treatment although we could not demonstrate the decline of plasma VEGF level. As a conclusion, we expect that our report contributes to the treatment strategy of DPL.

P-E-011

CATAMENIAL PNEUMOTHORAX

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A 41-year-old female was diagnosed with right Catamenial pneumothorax. She suffered from recurrent chest pain related to menstruation since 2003. From 2003–2014, she had 5 times of pneumothorax related to menstruation (May 2007, August 2007, October 2007, September 2013, and May 2014), and undergone water sealed drainage insertion for 3 times (May 2007, August 2007, and October 2007). She also had undergone pleurodesis as therapy on October 2007, had hormonal therapy on March and April 2013, and undergone thoracotomy on February 2014. During thoracotomy, we found endometrium tissue on right diaphragm, and confirmed by histopathological finding. Thoracic Endometriosis (TE) is a rare case, defined as a growth of functional endometrial glands and stroma on the lung parenchyma, pleura or airway. Catamenial pneumothorax is the most common clinical manifestation of TE. The diagnosis based on clinical history and histopathological examination. Management TE are hormonal therapy, surgery or combination of both.

P-E-012

UNIQUE RADIOLOGICAL FINDINGS IN PULMONARY LYMPHANGIOLEIOMYOMATOSIS: A PATTERN OF GROUND GLASS OPACITY CORRESPONDING TO LYMPHOSCINTOGRAPHIC EVIDENCE OF PULMONARY LYMPHATIC CONGESTION

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Lymphangioleiomyomatosis (LAM) is a rare, multisystem disease with a predominance in females of childbearing age. Pulmonary LAM is characterized by thin walled cysts which are evenly distributed throughout the lung fields. Extra-pulmonary manifestations include angiomyolipomas (a form of abdominal tumour), and involvement of the axial lymphatics in the form of lymphangioleiomyomas. We present a case of a 36 year old lady with an established diagnosis of LAM on lung biopsy and imaging. Four months after diagnosis she was noted to have mildly worsening shortness of breath, a productive cough and a slow but progressive decline in gas transfer on lung function tests. High resolution CT imaging demonstrated evidence of bilateral thin walled cysts throughout both lung fields, consistent with her previous imaging, as well as evidence of a new superimposed pattern of ground glass opacities involving the left lingular and lower lobes and the right middle lobe. Subsequent lymphoscintigraphy revealed partial obstruction of the lymphatic duct at the superior aspect at the level of T6 as well as in the right paraoesophageal chain, with evidence of lymphatic dilatation and pooling. The areas of lymphatic pooling correlated with the new ground glass opacities on high resolution CT imaging. Pulmonary complications of LAM are well recognized. Pneumothoraces occur as a result of rupture of cysts that are pathognomonic of pulmonary LAM. Chylothoraces occur when there is disruption to the lymphatics and leakage of chyle into the pleural space. In this case, we demonstrate a pattern of ground glass opacity corresponding to lymphoscintigraphic evidence of pulmonary lymphatic congestion. To our knowledge this represents a pulmonary complication of LAM that has not previously been described.

P-E-013

CLINICAL PROFILE OF ADULT PATIENTS UNDERGOING SPIROMETRY AT THE OUT-PATIENT DEPARTMENT OF THE UNIVERSITY OF SANTO TOMAS HOSPITAL: A DESCRIPTIVE STUDY

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Background: Spirometry is said to be the most useful and readily available pulmonary function test, however, the cost of undergoing such procedure remains prohibitive for indigent Filipinos. Spirometry would aid in the early detection and prompt treatment of obstructive lung disease. This would prevent the onset of complications, progressive decline of lung function, as well as a decline in the productivity of these individuals. The Section of Pulmonary and Critical Care Medicine of the University of Santo Tomas Hospital offers free spirometry at the Out-Patient Department for patients with low socioeconomic status. The goal of the study is to investigate the profile of these patients.

Methods: A retrospective study of patients who went to the Out-Patient Department of the University of Santo Tomas Hospital for screening of obstructive lung disease for spirometry were identified. Medical records of all spirometry done from March 2012 to June 2014 were reviewed. Data on the patient's demographics, height, weight, body mass index, smoking history and their pulmonary function test were extracted.

Results: One hundred ninety eight patients were included in the study. Ninety seven were male (49%) and one hundred one were female (51%). Pulmonary function test were interpreted as follows: Normal for 82 subjects (41%), probably restrictive for 69 subjects (35%), obstructive for 22 subjects (11%), mixed obstructive and probably restrictive for 9 subjects (5%) and 16 subjects were not able to tolerate the test (8%).

Conclusions: A significant number of subjects were identified to have obstructive and restrictive lung disease. Access to spirometry would provide prompt diagnosis of these diseases especially among those in the low socioeconomic status. This would have a great impact in the management and outcome of these patients and consequently improve their productivity.

P-E-014

IMPORTANCE OF RECOGNITION OF SINOBRONCHIAL SYNDROME (SBS) BECAUSE OF EXCELLENT EFFECT OF LOW DOSE ERYTHROMYCIN (LDEM) THERAPY IN THAILAND

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Background: SBS, a well characterized chronic neutrophilic inflammation involving both upper and lower airways, is not widely known and usually not included in the differential diagnostic approach in chronic cough. The diagnosis is established according to the Japanese Respiratory Society Guidelines and could be simply made when all of the following criteria are met: (1) Chronic productive cough lasting longer than 8 weeks, (2) Any one of followings: (2.1) clearing throat (2.2) post nasal drip (2.3) cobble stone appearance and/ or secretion deposition on the posterior pharynx (2.4) imaging evidence of sinusitis, and (3) These are responsive to 14 or 15 member macrolide or mucolytics.

Aim of Study: To clarify the existence of SBS and efficacy of LDEM therapy in Thailand.

Methods: Retrospective study was conducted in Central Chest Institute of Thailand between 2010–2014. Patients with chronic productive cough without considerable remission despite according treatment received were carefully re-evaluated. Those who met the above 2 criteria were included for therapeutic LDEM (500 mg/day). Cough response was assessed by using cough visual analogue scale (VAS). SBS was diagnosed when all the above criteria were met. Response grading: (a) good when cough decreased by more than half (b) excellent when cough remained free or almost free.

Results: SBS was uncovered in 213 patients (81 males and 132 females), ages 17–94 years [mean = 64.5]. The concurrent diseases with according therapy were as the following: bronchiectasis with or without old pulmonary TB (112), asthma (47), bronchitis (29), emphysema (10) and allergic rhinitis (13). These patients had been prior treated for years but still had considerable discomfort from chronic cough before ultimate SBS diagnosis making. Notably, it could be found in association with chronic airway inflammation. Following LDEM therapy, 100 and 113 patients had well and excellent response respectively.

Conclusion: From our study, SBS actually exists in Thailand it could be associated with several chronic airway disorders so an index of suspicion is needed, especially in those who still experience unremitting productive cough despite appropriate treatment for the concurrent respiratory conditions. This underscores the importance of recognition of SBS because of excellent effect of LDEM therapy.

P-E-015

RELIABILITY AND VALIDITY OF A KOREAN VERSION OF THE COUGH SYMPTOM SCORE

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Cough symptom score is a simple and useful tool to measure severity of chronic cough. We developed a Korean version of the cough symptom score and tested its scaling and clinical properties. Cough symptom score was adapted for Korean conditions following a forward-backward translation procedure. All patients referred to chronic cough clinics of 5 university hospitals between May 2011 and October 2013 completed two questionnaires, the LCQ and the Short-Form 36 (SF-36) upon presentation and completed Leicester Cough Questionnaire (LCQ) and the Global Rating of Change upon follow-up visits with two or four weeks intervals. Concurrent validation, internal consistency, repeatability and responsiveness were determined. For the concurrent validation, the correlation coefficients ($n = 202$ patients) between the cough symptom score and LCQ varied between -0.66 and -0.60 and between cough symptom score and VAS varied between -0.51 and -0.58 . The internal consistency of the cough symptom score ($n = 207$) evaluated as correlation between scores of night and day symptoms was 0.24 ($p = 0.0006$). The repeatability of the cough symptom score in patients with no change in cough ($n = 23$) was high with intra-class correlation coefficients varying between 0.66 and 0.81 . Patients who reported an improvement in cough ($n = 30$) on follow-up visits demonstrated significant improvement on each of the domains of the cough symptom score. The Korean version of cough symptom score is a valid and reliable method to measure severity of chronic cough.

POSTER PRESENTATION – CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

P-F-001

RELATIONSHIP BETWEEN METEOROLOGICAL CONDITIONS AND COPD EXACERBATIONS

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COPD (chronic obstructive pulmonary disease) is a major cause of morbidity and mortality in exacerbations. Moreover, a negative impact on quality of life and increases health care costs. COPD guidelines emphasize the importance of patient assessment and treatment planning exacerbation frequency. Therefore, pharmacological and non-pharmacological approaches for the prevention of exacerbations agenda. In this study, a randomized trial in patients with COPD exacerbation days for the group by determining the relationship between meteorological conditions were investigated. For this purpose, the Social Security Institution (SGK), the records of patients diagnosed with COPD were randomized to a two-year period an a group of patients on hospital admissions application has been examined and evaluated as an exacerbation. In this study antibiotic and/or steroids used, which were treated in hospital or symptom exacerbation increases were considered. Between the same dates, city centre, meteorological data (daily/hourly temperature, humidity and pressure of radiation, the solar and wind characteristics) has been the General Directorate of State Meteorology jobs. With daily and monthly frequency of exacerbations in the two calendar years at that time, temperature, pressure, humidity, wind speed and direction, as compared with the parameters. Spearman's correlation test was used to evaluate correlations and statistical software. A total of 411 people in 2,710 who were randomized to once admitted to hospital during the study period, 59% of them (1,590 applications) is understood to be due to an exacerbation. Flare-ups in 2010 and 2011, respectively, 558 and 562, respectively, 1.35 per patient/year and 1.36/year were flare-ups. Research during the period of the patients with exacerbation frequency, temperature, humidity and pressure were correlated. Temperature and pressure decreases, the humidity increases, more patients were seen flare-ups. Southern wind speed did not affect the frequency of attacks (LODOS) and Northern (POYRAZ) winds were different from the frequency of exacerbations. Weather events and climate conditions that cause these conditions examined the development of personal and mass measures, COPD can contribute to the reduction of morbidity and mortality.

P-F-003

EFFICACY OF MONO-THERAPY WITH TIOTROPIUM OR INDACATEROL OR THE COMBINATION OF THE TWO DRUGS ON DYNAMIC LUNG HYPERINFLATION AND EXERCISE TOLERANCE IN COPD

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Objective: The purpose is to make clear the superiority of efficacy among the long-acting muscarinic antagonist (LAMA), super partial beta-2-agonist (super LABA) and the combination therapy on dynamic lung hyperinflation (DLH).

Patients and Methods: 24 stable patients with mild to severe COPD were enrolled from our out-patient clinic and divided into the two groups at random following basement measurements after 48-hour washout current long-acting bronchodilator therapy. One group was treated with 5 µg of tiotropium (Respimat inhaler) for 4 weeks following the 4 week-treatment with 150 mg of indacaterol, while the other group was treated with indacaterol for 4 weeks following 4 week-treatment with tiotropium, and finally treated with the combination of the two drugs for 4 weeks. Pulmonary function tests, including DLH evaluated by the method of metronome-paced incremental hyperventilation (MPIH) and exercise tolerance evaluated by shuttle walking test, were examined at the end of the each treatment period.

Results: Both the treatment with tiotropium and indacaterol alone significantly increased FEV1 and the shuttle walking distance, and improved COPD assessment test (CAT) score. However, tiotropium significantly improved the DLH following MPIH, but the treatment with indacaterol did not. The combination therapy resulted in further improvement of lung function and exercise tolerance.

Conclusions: The mono-therapy of tiotropium or indacaterol improves airflow obstruction and exercise tolerance as well, and the combination therapy results in further improvement. However, the efficacy of tiotropium for DLH may be superior to indacaterol.

P-F-004

BURDEN IN FAMILY CAREGIVERS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Caregiving is a demanding and overwhelming process that impacts all aspects of a caregiver's life. Previous studies have demonstrated that family caregivers of patients with COPD experience increased physical and psychological health problems, restricted daily activities and social roles, strain in marital relationships, financial difficulties, and decreased quality of life (QOL). The adverse effects of caring for a patient with COPD may affect caregivers' ability to care for the patient as a result. Thus, measuring caregivers' burden is important to identify factors related to caregiving burden and develop interventions in order to enhance QOL of caregivers.

Aim: The aim of study was to investigate burden and effecting factors on burden among primary family caregivers for patients with COPD.

Methodology: The study included 100 family members with a mean age of 47 who provided primary care for patients with COPD. Data were collected by the Zarit's Burden Interview, the Medical Outcomes Study MOS 36-Item Short Form Health Survey (SF-36) and The Medical Research Council (MRC) Dyspnoea Scale. We performed statistical analyses with Statistical Package for the Social Sciences. Pearson's correlation coefficients were calculated to examine associations between two continuous variables. The ANOVA and t-test were carried out to analyze the associations between the numerical variables and caregiver burden. The study was approved by the Local Research Ethics Committee.

Results: Most of the caregivers were females and were the patients' children (46%) or spouse (28%); they had been providing care for 4.6 years and 15.7 hours per day; 79 of them were living together with the patients. More than half of the caregivers (52%) had a health problem. Family caregivers' burden mean score was 40.2, indicating moderate to severe level of burden. High caregivers' burden score was related to having children ($p < 0.05$), having poor economic status ($p < 0.01$), having bedridden patient ($p < 0.001$), the duration of time which spent for caregiving in a day ($r = 0.28$), perceived poor health ($p < 0.05$) and patients' dyspnoea level ($p < 0.01$). Mean scores for physical health or QOL, and mental health or QOL in SF-36 were 52.3 and 45.3, respectively. The correlation between caregiver burden and PCS ($r = 0.53$) and MCS ($p = 0.59$) were strong.

Conclusions: These findings increase our understanding about how family members perceive burden and effects of socio-demographic and patient-related variables on burden influencing the health and well-being of family caregivers. Helping family members to maintain and enhance a supportive environments may represent a useful means to reduce caregiver burden.

P-F-005

ASSOCIATION BETWEEN SARCOPENIA AND METABOLIC SYNDROME IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim: It is not clear whether the restrictive or obstructive pattern of spirometry is associated with metabolic syndrome. We investigated the associations between restrictive and obstructive spirometric patterns and metabolic risk factors using data from the Korea National Health and Nutrition Examination Survey (KNHANES). Additionally, we investigated whether sarcopenia is associated with metabolic syndrome in patients with chronic obstructive pulmonary disease (COPD).

Methods: Using data from KNHANES between 2008 and 2011, we enrolled 8,145 subjects (normal lung function: 6,077, obstructive spirometric pattern: 1,039, restrictive pattern: 1,029) aged ≥ 40 years who underwent anthropometric measurement, laboratory tests, spirometry and estimation of appendicular muscle mass. Sarcopenia was defined as an appendicular skeletal muscle mass divided by body weight squared < 2 SD below the sex-specific mean for the young reference group.

Results: Sarcopenia was found in 32.8% of male and 12.2% of female patients with COPD. The odds ratio (OR) of metabolic syndrome for the restrictive spirometric pattern in male was 1.29 (95% confidence interval [CI], 1.02–1.65), and that for obstructive pattern in males was 0.99 (95% CI, 0.79–1.26) after adjustments for covariables (female restrictive pattern (ORs, 1.45; 95% CI, 1.09–1.91) and female obstructive pattern (ORs 0.73; 95% CI, 0.49–1.09). After adjustment for other confounding factors, the risk of metabolic syndrome was higher in sarcopenic male (OR, 1.88; 95% CI, 1.27–2.77) with COPD than in those without sarcopenia.

Conclusions: The restrictive spirometric pattern is associated with metabolic syndrome, and sarcopenia may contribute to the risk of metabolic syndrome in male patients with COPD.

P-F-006

STAGING IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ACCORDING TO THE 2011 GOLD IN RESPIRATORY CENTER – BACH MAI HOSPITAL IN VIET NAM

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Background: Chronic obstructive pulmonary disease (COPD) is a major public health problem and its prevalence and mortality are increasing throughout the world. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of COPD does not always match with other clinical disease descriptors such as exacerbation frequency and quality of life, indicating that forced expiratory volume in 1 s (FEV₁) is not a perfect descriptor of the disease. In the 2011 GOLD, COPD assessment must consider the following aspects of disease separately: current level of patient's symptoms, severity of the spirometric abnormality, exacerbation risk, presence of comorbidities. This study aimed to compare the classification of COPD between the 2006 GOLD and the 2011 GOLD.

Methods: Descriptive prospective study. 112 patients with COPD treated in Respiratory Center – Bach Mai Hospital in Viet Nam from 01-02-2013 to 31-08-2013.

Results: The 2006 GOLD: GOLD 1 (2.7%), GOLD 2 (25.9%), GOLD 3 (37.5%), GOLD 4 (33.9%). The 2011 GOLD: GOLD A (1.8%), GOLD B (13.4%), GOLD C (4.5%), GOLD D (80.3%). The correlations between FEV₁ with: number pack years of smoking ($r = -0.009$, $p > 0.05$), exacerbations in the previous 12 months ($r = -0.221$, $p = 0.019$), CAT-score ($r = -0.253$, $p = 0.007$), mMRC ($r = -0.284$, $p = 0.002$). GOLD C, D had longer disease duration, more exacerbations in the previous 12 months, higher prevalence of comorbidities, higher CAT-score and higher mMRC than GOLD A, B ($p < 0.05$).

Conclusion: Classification of COPD according to the 2011 GOLD is a more comprehensive assessment of health status and future risk of patients COPD.

P-F-007

CONFLICTING ROLE OF SARCOPENIA AND OBESITY IN MALE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Background and Objectives: This study aimed to determine the impact of sarcopenia and obesity on pulmonary function and quality of life (QOL) in chronic obstructive pulmonary disease (COPD) patients.

Methods: Data were obtained from the Korea National Health and Nutrition Examination Survey, including data from health interviews, health examinations, nutritional questionnaires, and laboratory findings. Laboratory data included pulmonary function assessment and dual energy X-ray absorptiometry results. Sarcopenia in male COPD patients was measured by dual energy X-ray absorptiometry between 2009 and 2011. Patients were then classified into 4 groups according to the status of sarcopenia and obesity.

Results: In male patients with COPD, the prevalence of sarcopenia was found to be 29.3%, and that of sarcopenic obesity was 14.2%. Furthermore, 22.5% of the patients observed in this study had impaired QOL. Following multivariable statistical analysis, both sarcopenia and obesity were independent risk factors associated with worsening lung function. Adjusted values of forced vital capacity and forced expiratory volume in 1 second were the lowest in the sarcopenic obesity group. Sarcopenia was also associated with more subjective activity limitation and poorer QOL, however obesity was related to less subjective limitation and better QOL after multivariable analysis. Adjusted value of QOL was lowest in sarcopenic subjects without obesity.

Conclusions: Both sarcopenia and obesity were found to be associated with worsening lung function in male COPD patients. However, obesity was positively correlated with improved QOL while sarcopenia was negatively correlated with QOL.

P-F-009

INHIBITION OF CIGARETTE SMOKE-INDUCED AIRWAY EPITHELIAL MESENCHYMAL TRANSITION: LONG-ACTING MUSCARINIC RECEPTOR ANTAGONIST OR DEXAMETHASONE?

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Rationale: The interactions between cigarette smoke, muscarinic receptors, and epithelial mesenchymal transition (EMT) in the development of chronic obstructive pulmonary disease (COPD) remains unclear.

Objectives: To determine whether NVA237 (a new long-acting muscarinic receptor antagonist) and dexamethasone can inhibit cigarette smoke-induced airway EMT *in vitro* and in a mouse model of COPD.

Methods: *In vitro*, primary human bronchial epithelial cells (PBEC) were applied for cigarette smoke extract (CSE) and acetylcholine stimulation tests. In mice, airway EMT was induced by cigarette smoke exposure (3 cigarettes/day for 28 days). Daily intra-peritoneal injection of NVA237 and dexamethasone were given for 28 days. Alpha-smooth muscle actin (α-SMA) and fibroblast secretory protein-1 (FSP-1) were used as biomarkers of EMT.

Measurements and Main Result: NVA237 could inhibit acetylcholine and CSE-induced α-SMA and FSP-1 expressions in PBEC. However, dexamethasone could inhibit neither α-SMA nor FSP-1 expressions in PBEC. NVA237 inhibited α-SMA and FSP-1 expressions of bronchial epithelial cells in cigarette smoke-exposed mice on day 28. In addition, dexamethasone did not inhibit α-SMA and FSP-1 expressions.

Conclusion: NVA237 exerts a potent inhibitory effect on acetylcholine and cigarette smoke-induced airway EMT *in vitro* and in a mouse model of COPD.

P-F-010

P-F-008

THE RELATIONSHIP BETWEEN INTERLEUKIN-1β SERUM AND OSTEOPOROSIS INCIDENCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN MOHAMMAD HOESIN GENERAL HOSPITAL PALEMBANG INDONESIA

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Background: Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease characterized by systemic inflammation associated with many extrapulmonary manifestations such as osteoporosis. The pro-inflammatory cytokine interleukin-1β (IL-1β) level increase in the circulation of COPD patients.

Aims: To identify the serum interleukin-1β level in patients with COPD and its relationship with osteoporosis incidence in this group of patients.

Methods: The study design is a cross-sectional survey. The subjects are 74 patients with COPD, consisting of 37 patients with osteoporosis and 37 patients with normal BMD. The routine blood test, chest X-ray, spirometry, BMD, and serum IL-1β level examinations were performed in both groups.

Results: The mean levels of IL-1β serum in osteoporosis COPD group was 0.56 ± 0.96 pg/ml and COPD group without osteoporosis was 0.49 ± 0.56 pg/mL, obtained from statistical test was not significant correlation in both groups ($p = 0.792$). There is a significant relationship between the degree of COPD and the value of femur and lumbar T-scores, that is $p = 0.036$ and $p = 0.009$. There was no significant relationship between mean level of serum IL-1β and COPD severity ($p = 0.896$). There was no significant relationship between IL-1β level and osteoporosis in both groups ($p = 0.684$).

Conclusions: The mean level of serum IL-1β in COPD patients with osteoporosis was not significantly different compared with COPD patients with normal BMD.

CLINICAL FEATURES AND PROGNOSTIC FACTORS OF PATIENTS HOSPITALIZED DUE TO ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are important causes of hospital admission and mortality. We investigated the clinical features of hospitalized patients with severe AECOPD and evaluated prognostic factors associated with readmission or mortality due to re-exacerbation of COPD within 6 months.

Methods: The prospective study enrolled 314 patients hospitalized with severe AECOPD. We collected demographic, clinical and laboratory findings at admission. Lung function was evaluated using the COPD assessment test (CAT) questionnaire, the modified Medical Research Council (mMRC) dyspnoea scale and spirometry in stable state.

Results: The mean age was 72.2 ± 9.4 years (76.4% male). The rate of re-admission within 6 months was 45.2% and mortality rate was 16.6%. When multivariate analysis was performed using the significant variables, age ($P < 0.001$), CAT score ($P < 0.001$), old pulmonary tuberculosis ($P = 0.003$), initial PaO₂ ($P = 0.026$), haemoglobin ($P = 0.009$), albumin ($P = 0.005$) and CRP at discharge ($P < 0.001$) were significantly associated with mortality. CAT score ($P < 0.001$), diabetes mellitus ($P = 0.030$) and CRP at discharge ($P = 0.004$) were also significantly associated with readmission. In receiver operating characteristic curves, CRP at discharge than CAT score showed a good accuracy to predict the mortality. But CAT score showed good accuracy to predict readmission due to severe AECOPD.

Conclusion: CRP at discharge as well as CAT score was significantly associated with both mortality and readmission due to AECOPD.

P-F-011

BURDEN OF RESPIRATORY DISEASE IN TURKEYBOZDOĞAN S¹, AKGÜN S²¹Hatem Hospital/Chest Diseases, Clinic/Gaziantep, Turkey, ²Public Health and Medicine in Başkent University School of Medicine, Ankara, Turkey

Objective: The aim of this study was to assess the burden of disease for respiratory disease in a developing country, Turkey, and to identify the effects of risk factors for the burden of respiratory disease in the country.

Methods: COPD is among the leading causes of chronic morbidity and mortality in the European Union and Turkey. Approximately 200,000 to 300,000 people die each year in Europe because of COPD, and among respiratory diseases, it is the leading cause of lost work days. For this purpose, a comprehensive search was conducted including international and national MEDLINE searches, publications from universities and other scientific institutions, relevant surveys and thesis results in Turkey, and Turkish and international congress documents about respiratory disease. After checking the inter-consistency by the help of DISMOD software programme developed by WHO, the most appropriate incidences for COPD and other respiratory diseases were used in DALY calculations after the evaluations.

Results: In the Turkish Burden of Disease Study, which was conducted between the years 2000–2004, 430,460 deaths were determined while the number of DALYs was found to be 10,802,494. The reported prevalence of COPD among adults aged 15 years was 6.2% in Turkey by World Health Organization (WHO). There was no country representative study for chronic obstructive lung disease (COPD) that reflected all of Turkey. When the first 10 causes of death and DALYs are investigated for national, urban and rural areas, it was determined that COPD was in the third rank at national level (5.8 %) and as for DALY, at national, urban and rural levels COPD was found to be the seventh leading cause of DALY in the country.

Conclusion: Respiratory system diseases and are a significant cause of death and a factor of burden of disease in Turkey. It is seen that COPD causes much of the burden of disease in rural areas and the main reason for that is smoking habit at high levels. For this reason, providing non-smoking common environments; reinforcing, supervising and monitoring current legal sanctions; providing a widespread assistance network for those who want to quit smoking, and especially raising awareness of the society on the harms of smoking, may take place effects among the basic suggestions.

P-F-013

COPD-6: A SCREENING DEVICE TO DETECT OBSTRUCTIVE AIRWAYS DISEASE IN PATIENTS WITH RESPIRATORY SYMPTOMS FROM A PRIMARY CARE CENTRE IN INDIABANSAL S¹, NAIR V¹, TALWAR D¹, VAIDYA A²¹Metro Centre For Respiratory Disease, Metro Hospitals & Heart Institute; L-94, Sector-11, Noida, Delhi NCR, 201301 India, ²Medical Service (Clinical Research Division), CIPLA Ltd., Mumbai Central, Mumbai, Maharashtra, 400008 India

Introduction and Background: Despite rising mortality and health care costs, COPD and asthma remain the most undiagnosed diseases due to lack of required infrastructure in primary care hospitals.

Aims and Objectives: To evaluate clinical equivalence in terms of sensitivity, specificity and reliability of COPD-6 device in comparison with pneumotach spirometer in detecting patients with obstructive airways disease with respiratory symptoms.

Methods: This was a descriptive, crossover, prospective study which included 60 participants. Screening was done sequentially with COPD-6 device and pneumotach spirometer. The validity and specificity of the COPD-6 device in detecting obstruction was determined using standard formula, and the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. We also estimated the area under the ROC (Receiver-Operating Characteristic) curve of the FEV1/FEV6 ratio (measured with the COPD-6) in the discrimination of the obstruction, using the FEV1/FVC < 0.7 quotient obtained with spirometry as the gold standard.

Results: There were 29 participants detected to have obstructive airways disease. The kappa index was 0.66 when an FEV1/FEV6 cut-off point of <0.7 was used as gold standard. The ROC AUC was 0.88. To detect obstruction, if the cut-off point of FEV1/FEV6 for COPD-6 was <0.70, the sensitivity, specificity, PPV and NPV were 65.5%, 93.5%, 90.5% and 74.4%, respectively. For a cut-off point of <0.76, they were 76.9%, 95.2%, 96.8% and 69%, respectively.

Conclusion: COPD-6 is a moderately accurate device to detect airway obstruction in patient with respiratory symptoms. Greater accuracy is observed when cut-off point is 0.76.

P-F-014

RESEARCH OF SMOKING AND COPD (CHRONIC OBSTRUCTIVE PULMONALY DISEASE) AWARENESS IN UNIVERSITY STUDENTS

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Purpose: Previously, we reported that awareness of COPD is low in who visited to a certain hospital over the age of 18. Recognition rate is slowly increasing, however, still been not satisfactory. Furthermore easy native language (Japanese) is even a similar tendency. In addition, some study showed that young-youth-adult student's in university started smoking. So, in this study, aimed at anagenesis about understanding, education and improvement of above situation.

Methods: The questionnaire for all university students was performed using our University Original Internet system in 2012–13. Participants status were conducted who enrolled over 18 age and examined in 641 cases (Group A) that consent were obtained. As the control subject, 335 cases (mean ± SD, 56.5 ± 15.8 yrs) who visited to a certain hospital was (Group B). We used the disease name "COPD" and "TOBACCO BYOU" that is abbreviation word [Guidelines for the Diagnosis and Treatment of COPD (The Japanese Respiratory Society)].

Results: Base of analyzed student's subjects status were male/female (%) = 53.4/46.6, 20.4 ± 1.6 (mean ± SD, yrs), smoking prevalence (%) was: Current 8.4 (M/F,%: 6.6/1.6), Former 5.6, Never 86.0, respectively. COPD is association with smoking is strong; however, "Know" was only 9.8% (Heard of: 24.8%; Unknown: 61.8%) in Group A (Similar data of Group B: Know: 9.3%; Heard of: 17.6%; Unknown: 73.1%). In contrast, the knowledge of package warning was high in Group B rather than A. However, "risk of lung cancer" knowledge was similar higher than other risk disease (e.g. stroke, myocardial infarction) warning message in both groups.

Conclusions: This results was considered that source of the text size of tobacco package warning documents is small and mild. In addition, smoking is a harm to health, nevertheless the knowledge of package warning recognition ratio was not unified. Furthermore it was speculated that the elderly from the young adolescents in Japan who were not exposed to anti-tobacco messages and/or were not taught about the harmful effects. Therefore we should more educate and message the awareness of smoking and COPD.

P-F-015

P-F-016

CLINICAL STUDY OF COPD, BRONCHIAL ASTHMA OR OSAS PATIENTS WHO UNDERWENT A HOME SLEEP TEST

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Purpose: In recent years, both COPD (Chronic Obstructive Pulmonary Disease) and OSAS (Obstructive Sleep Apnea Syndrome) have been recognized as systemic inflammatory diseases. Sleep disorders are considered as indicators of systemic inflammatory brain natriuretic peptide, vascular endothelial dysfunction, albuminuria, lung epithelial cell failure, pulmonary surfactant protein -A (SP-A) and also myocardial expansion failure (BNP).

Method: Between April and December 2013, we conducted tests on OSAS using portable equipment to measure sleeping time and other key factors on 88 patients with bronchial asthma, 89 patients with COPD (34 of them having bronchial asthma) and finally 34 OSAHS patients without bronchial asthma merger nor COPD. Study parameters measured by the equipment were the apnea hypopnea index (AHI), urinary albumin/creatinine ratio, serum SP-A and blood BNP.

Results: (1) OSAHS merger rate was higher in the COPD group showing ratio of AHI5 for 77.5% of the patients and AHI15 for 48.3% of them compared to the bronchial asthma group in which this ratio is 69.3% to 35.2%. In the COPD group the number of patients with OSAHS was quite high. (2) As our Society already reported, significant differences were observed between the COPD group, the COPD/bronchial asthma group and the OSAS group on the urinary albumin/creatinine ratio and the blood BNP.

Conclusion: Urinary albumin content is an indicator of vascular endothelial injury correlated with the AHI severity level of OSAHS. OSAHS and COPD are systemic inflammatory disease in which an upward trend was observed on urinary albumin excretion. Impact of OSAHS that were merged at a high rate in the COPD group is suggested to be associated with hypoxic stimulation suggesting that OSAHS, a potentially systemic disease, was also affecting the alveolar epithelial cells or the cardiomyocytes.

FREQUENCY OF EXACERBATION – THE RESULTS FROM REAL LIFE: RECORDS OF SOCIAL SECURITY SYSTEM IN TURKEY

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Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease exacerbation periods. Increase in hospital admissions due to exacerbation of symptoms is also increasing. During this period, the rise of direct and indirect health care costs, quality of life and mortality adversely affected. Exacerbation frequency in recent years, is one of the primary goals of COPD treatment. However, the frequency of exacerbations varies from person to person and are known not to have the same importance for each patient. Moreover, the definition and treatment of attacks varies for the time being, and is known to be differences of opinion among physicians. In this study, a two-year period, all diagnosed with COPD exacerbation frequency studied a group of patients who were randomized. For this purpose between 01/01/2010 and 01/31/2011, two second and third stage health care organizations in our city, according to their pharmaceutical report, the total 3185 people diagnosed with COPD records identification numbers, applied clinics, dates, costs of treatment, was evaluated in terms of ICD codes. Due to the removal of duplicate records from 3185 have a total of 620 people were examined records of 2,565 people. Four hundred eleven people were randomized to 1235 people living in the city. COPD causes examining applications for 411 people for two years, the total number of hospital admissions, flame application, the number of applications was non-flammability. Chronic Obstructive Pulmonary Disease patients' clinical notes, treatment, and on the basis of the ICD-code, hospital admission, systemic steroid/antibiotic use was evaluated as an exacerbation. A total of 2710 patients in the hospital this application 1120'si (41%) of exacerbations, 1590'i (59%) were applying for a non-exacerbation of COPD. 1.35, respectively, per patient/year and 1.36/year was determined attack. Examined in patients with chronic obstructive pulmonary disease patients in 2010, 18.5% in ve2011 13.5% hospitalized because of COPD. In 2010, 33.8% in 2011, 33.1% had not spent any flare-ups. The percentage of patients who had an exacerbation per year for two years, respectively, 33.1% and 32.4%, respectively. The remaining patients have undergone two or more exacerbations. 3.9–5% of the patients 'i in the 10 or more day hospital admissions were induced COPD. Induced effects on hospital admissions and exacerbation of the disease is important because of the cost as well. The results of this study should be discussed in these respects.

P-F-017

THE ACTIVATION OF NLRP3-INFLAMMASOME BY CHALLENGE OF DIESEL EXHAUST PARTICLES (DEPS) IN ELASTIN-INDUCED EMPHYSEMA ANIMAL MODEL

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Introduction: Diesel exhaust particles (DEPs) lead to elevation of reactive oxygen species which have ability to activate NLRP3-inflammasome. By these findings we speculated that DEPs-induced activation of NLRP3-inflammasome may be related with the pathogenesis of AECOPD. In this study, we elucidated whether NLRP3-inflammasome is activated by DEPs and anti-oxidants (N-acetylcysteine, NAC) can inhibit DEP-induced activation of NLRP3-inflammasome.

Methods: RAW 264.7 cells and lung tissues from elastase-induced emphysema animal models were stimulated with cigarette smoke extract (CSE), DEP, and LPS to measure the level of IL-1 β , protein expression of NLRP3 and caspase-1 by Western blot and immunohistochemical stain.

Results: NAC and caspase-1 inhibitor inhibit CSE- and DEP-induced increased secretion of IL-1 β in RAW 264.7 cells. The expression of NLRP3 and caspase-1 are upregulated by stimulation with CSE and DEP by Western blot in RAW 264.7 cells. These expressions were inhibited by caspase-1 inhibitor. Mean linear intercept was significantly higher in emphysema-induced emphysema group compared to that in control group (23.6 \pm 2.2 μ m vs 90.4 \pm 6.7 μ m, $p < 0.01$). CSE and DEP increased the secretion of IL-1 β in lung tissues from both normal and elastin-induced emphysema group. The secretion of IL-1 β by CSE and DEP are more increased in elastin-induced emphysema group compared to those in normal group (CSE 309 \pm 19 vs 151 \pm 13, $p < 0.05$, respectively; DEP 350 \pm 24 vs 281 \pm 15, $p < 0.05$, respectively). NAC and caspase-1 inhibitor inhibited the CSE- and DEP-induced IL-1 β secretion in both normal and elastin-induced emphysema group. The expressions of NLRP3, by immunohistochemistry, were increased by CSE and DEP in both normal and elastin-induced emphysema group. These expressions were suppressed by NAC and caspase-1 inhibitor.

Conclusion: NLRP3-inflammasome is activated by DEP in elastin-induced emphysema animal model and this activation is inhibited by anti-oxidants.

P-F-018

MEASUREMENT OF THE WHEELCHAIR-OPERATING TIME IN DAILY LIVING USING A NEW TRIAXIAL ACCELEROMETER SYSTEM

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Background: The physical activity of patients with chronic obstructive pulmonary disease (COPD) or other diseases is less than that of healthy people. The decrease in physical activity causes patients to experience disuse syndrome, and patients sometimes use wheelchairs to move about in daily life. However, no research has been reported with regard to instruments that could evaluate the time spent operating a wheelchair in daily living.

Objective: The primary purpose of this study was to verify the validity of a triaxial accelerometer system for measuring the time spent operating a wheelchair. The secondary purpose was to measure the time that stroke patients in a convalescence ward spent operating a wheelchair as well as the time spent lying down, sitting, standing, and walking over the course of one day.

Participants: Twelve healthy subjects (21.3 years \pm 1.2 years) participated in Experiment 1. Thirty stroke patients (69.1 years \pm 10.9 years) in a rehabilitation centre participated in experiment 2.

Interventions: Physical activity was measured using a new triaxial accelerometer system (A-MES; Activity Monitoring and Evaluation System) that consists of two sensors, a station, and analytical software used with a personal computer.

Measure: The times that the healthy subjects spent operating a wheelchair, lying down, sitting, standing, and walking were measured both by the A-MES and by videotaping. The Bland-Altman analysis method was used to compare the time spent in each posture or movement type as measured by both the A-MES and the videotape in Experiment 1. Then, A-MES was used to measure the amounts of time the stroke patients spent lying down, sitting, standing, walking, and operating a wheelchair in a single day.

Results: The time spent operating a wheelchair as measured with the A-MES was significantly correlated with the video time in the healthy subjects. No systematic error was found between the time measured by A-MES and that observed on the videotape. The stroke patients' times (minutes) of operating a wheelchair, lying down, sitting, standing, and walking were 57.1 \pm 28.8, 265.0 \pm 86.3, 263.3 \pm 60.6, 7.8 \pm 7.0, and 7.7 \pm 6.0, respectively, for a total of 601.0 \pm 18.1 minutes.

Conclusion: A-MES was able to accurately evaluate the time spent operating a wheelchair in healthy subjects and stroke patients. A-MES will be a useful tool to examine whether pulmonary rehabilitation improves the wheelchair-operating time of daily living in COPD patients.

P-F-019

P-F-020

MATRIX METALLOPROTEINASE-9 DEGRADATION CYCLASE-ASSOCIATED PROTEIN 1 IN THE PATHOGENESIS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background: As is known. The increased expression of matrix metalloproteinases-9 (MMP-9) is considered to be a key factor in the development of COPD. In addition. Cyclase-associated protein 1 (CAP1) is associated with MMP-9. Which was identified as a novel and most efficient substrate of gelatinase B/MMP-9. but the details of structural changes and underlying mechanism are poorly described or understood. We aimed to answer the following questions: (1) Is the expression of MMP-9 and CAP1 different in patients who develop COPD and in patients who do not develop COPD? (2) What the relationship between MMP-9 and CAP1? (3) The role of MMP-9, CAP1 in the human alveolar epithelial cell.

Methods: A total of 90 patients (52 COPD group, 38 non-COPD group) were recruited into the study. Firstly. Pulmonary function tests were measured of 90 cases. Secondly, the concentration of MMP-9 in serum was performed by ELSIA. Then, we analysis the relationship between MMP-9 in serum and Pulmonary function tests. Thirdly. To observe CAP1 and MMP-9 Level in Immunohistochemistry (IHC) and Pulmonary Function tests. Lastly, to examine the MMP9 and CAP1 level in COPD patients by Immunofluorescence and Bronchoalveolarlavage fluid samples Analysis. Lastly. To confirm the relationship between MMP-9 and CAP1. The human alveolar epithelial cell line HP-APEIC was cultured by Inflammatory stimulation. Then, we analysis the level of CAP1 at different time or concentration of rMMP-9 (The inhibitor of MMP9).

Results: Firstly, there were significant differences in FEV1, FEV1%, FEV1/FVC%, RV, TLC, RV/TLC% values among COPD and non-COPD patients ($Z = -3.159, -7.976, -5.209, -8.098, -8.078, -7.689$, respectively, $p < 0.01$). Secondly, the concentrations of MMP-9 were significantly greater in serum of COPD patients (mean \pm SEM; 3.02 ± 0.77) than in serum of non-COPD subjects (mean \pm SEM; 0.96 ± 0.48) ($Z = -8.030$, $p < 0.01$). Negative correlations were also noted between MMP-9 and FEV1, FEV1%, and FEV1/FVC % values ($r = -0.316, -0.691, -0.411$, respectively, all $p < 0.01$). But, the expression of MMP-9 was positively correlated among RV, TLC, and RV/TLC % values ($r = 0.720, 0.776, 0.593$, respectively, $p < 0.01$). Thirdly, by IHC analysis, there were significant difference between MMP-9 and FEV1, FEV1%, FEV1/FVC % values ($Z = -4.360, -4.183, -3.720$, respectively, $p < 0.01$). In addition, there was a significant positive correlation between the MMP-9 levels and FEV1, FEV1%, and FEV1/FVC % values ($r = -0.583, -0.559, -0.497$, respectively, all $P < 0.01$). In addition, there were significant difference between CAP1 and FEV1, FEV1%, FEV1/FVC %, $Z = -2.838, -2.886, -4.012$, respectively, $p < 0.01$). It was negative correlated among FEV1, FEV1%, and FEV1/FVC % values ($r = -0.379, 0.386, 0.53$, respectively, all $p < 0.01$). To sum up, the expression of CAP1 in contrast to MMP9 ($r = -0.51$, $p < 0.01$). Lastly, from Western blot analysis of Bronchoalveolarlavage fluid and the human alveolar epithelial cell line HP-APEIC in vitro.

Conclusions: Our results showed that there exists over-expression of MMP9 and low-expression of CAP1 in COPD patients. In addition, MMP-9 can degradation CAP1 to destruct the bronchial or/and alveolar wall, which is likely to play a major role in airway obstruction of COPD.

Key Words: matrix metalloproteinase-9, cyclase-associated protein 1, chronic obstructive pulmonary disease.

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A CORRELATION BETWEEN INSPIRATORY CAPACITY-TO-TOTAL LUNG CAPACITY RATIO (IC/TLC RATIO) AND FORCED EXPIRATORY VOLUME IN ONE SECOND (FEV1) IN PATIENTS WITH COPD IN PHILIPPINE HEART CENTER

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Methodology: This is a Cross-sectional Study among Adult patients aged 40 years old and above with COPD diagnosed by pulmonary function test with post Broncho dilator study FEV1/FVC ratio of < 0.70 , with significant smoking history of more than 10 pack years, chronic sputum production or cough for at least 3 months for the past 2 years and shortness of breath or easy fatigability, not on acute exacerbation for the past 4 weeks or 30 days and No active lung infection for the past 4 weeks or 30 days, a lung volume study was conducted on all patients deemed qualified for lung volume study. To determine the Correlation between IC/TLC a Pearson correlation analysis was used. An Analysis of Variance were used to compare IC/TLC on the different stages of COPD. Cut-off points of IC/TLC that will predict stages of COPD was determined. Kappa test was used to determine significance of agreement between IC/TLC cut-off and COPD stages by FEV1. A p-value ≤ 0.050 will be considered significant.

Results: One hundred twenty eight patients were included in the study, with mean age from GOLD I (57.48276 (+9.44)), GOLD II (60.02 (+7.810)), GOLD III (59.88 (+11.28)), GOLD IV (58.25 (+9.72)) with p-value 0.9813 which was not statistically significant smoking history of subjects includes the following in GOLD I (38.724 + 14.362), GOLD II (41.318 + 13.09), GOLD III (38.0232 + 10.289), GOLD IV (37.666 + 11.499) with a p-value of 0.653 which was not statistically significant. The mean IC/TLC ratio was correlated with all GOLD STAGES, in GOLD I (.5237 + 0.3447), GOLD II (.4375 + .0266), GOLD III (.3269 + .0510), GOLD IV (.155 + .0202) with lower values on the IC/TLC ratio was noted as the stages of GOLD becomes higher, with a p-value of < 0.001 which was statistically significant. cut off values for IC/TLC were obtained in correlation with the different stages of GOLD with values of IC/TLC ratio decreasing as the stages of GOLD becomes higher. GOLD 1 > 0.496945 , GOLD II $0.338464 \rightarrow < 0.496945$, GOLD III $0.23281 \rightarrow < 0.338464$, GOLD IV < 0.23281 with a p-value of < 0.001 which was statistically significant.

Conclusion: This study has shown a good correlation of IC/TLC ratio to FEV1 and has established cut off values for IC/TLC in relation to the GOLD staging.

P-F-021

EFFECT OF ANTI-INFLAMMATORY SUPPLEMENTATION WITH WHEY PEPTIDE AND EXERCISE THERAPY IN PATIENTS WITH COPD

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Study Objectives: The aim of this study was to investigate the effects of anti-inflammatory nutritional supplementation combined with low-intensity exercise on body components, exercise tolerance, and HRQOL and the degree of systemic inflammation in patients with COPD.

Design: A prospective randomized trial.

Patients: Thirty-six moderate to severe elderly COPD patients.

Methods: Patients were randomly divided into anti-inflammatory nutritional supplementation with low-intensity exercise group and a control group. Lung function, the Chronic Respiratory Disease Questionnaire (CRQ), and the 6-minute walking distance (6MWD) were measured at baseline and were re-assessed at 3 month after intervention. The degree of systemic inflammation and the changes in levels of systemic CRP, TNF- α , IL-6 and IL-8 were assessed before and after intervention.

Results: Body weight and FFM increased significantly after 12 weeks of anti-inflammatory nutritional supplementation therapy in patients with COPD. The dietary intake energy increased and the REE: REEpred ratio decreased significantly in the nutrition with low-intensity exercise group. Quadriceps muscle force and 6MWD increased significantly from baseline through week 12. Health status, as assessed by CRQ, improved in the domains of dyspnea, emotional function, mastery, and total scores significantly in the nutrition with low-intensity exercise group after intervention.

Conclusions: The combination of anti-inflammatory nutritional supplementation with low-intensity exercise training was successful in increasing weight and energy intake as well as exercise capacity and health-related QOL in COPD patients. The present study suggests a potential role for the combination of anti-inflammatory nutritional supplementation and low-intensity exercise in the management of elderly patients with COPD.

P-F-022

AIRWAY INFLAMMATION AND ITS RELATIONSHIP TO LUNG FUNCTION AND EMPHYSEMA IN PATIENT WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Chronic Obstructive Pulmonary Disease is a heterogeneous disease with enhanced chronic inflammatory response in airways and lung. Cellular inflammatory markers like neutrophils, macrophages, lymphocytes, epithelial cells and their mediators are known to cause progressive deterioration in lung function. This leads to low FEV1 as well as emphysema. Induced sputum neutrophils are marker of inflammation in COPD. Neutrophils are thought to be mechanically involved in the disease pathophysiology. Neutrophil count in healthy non smoker is 40 to 60%, while in a stable COPD, absolute neutrophil numbers as well as percentages are exceptionally high. Therefore the aim of our study was to assess the relationship between airway inflammation and lung function and CT quantified emphysema.

Methods: After informed consent we enrolled 53 COPD patients reporting to a respiratory diseases hospital outpatient clinic. Inclusion criteria were males and females ≥ 40 yrs of age and COPD was diagnosed by GOLD Guidelines 2009, with post bronchodilator FEV1/FVC $< 70\%$ in stable state. We excluded patients with asthma, pulmonary tuberculosis, lung resection, diagnosis of silicosis, asbestosis, pulmonary fibrosis and COPD exacerbation within 4 weeks of enrollment. Spirometry was performed as per ATS/ERS 2005 guidelines using certified spirometers. Sputum induction and processing was done as per Medical Evaluation Unit (UK) guidelines. The slides were read by pathologist blinded to clinical details. Volumetric CT was performed in full inspiration using Siemens Somatom Definition AS multidetector CT with low dose radiation protocol. Images were read with PULMO CT software. % low attenuation area was defined as % of total lung volume that contains voxels of less than -950 Hounsfield Units.

Results: Mean age of study subjects 63.9 (8.4) years, Males 35 (66%), smokers 35 (66%), mean % FEV1 Post 59.2 (19), % sputum neutrophils 87.9 (11.6), % sputum eosinophils 5.8 (7.4), % sputum macrophages 5.0 (7.8), % sputum lymphocytes 1.3 (2.2), Mean total cells per gram of sputum 3.2×10^6 (1.9) and % emphysema (LAA) 23.6 (12.5). There was no correlation between % sputum neutrophils and FEV1 predicted $r = 0.079$ $p = 0.58$ as well as no association between %neutrophils and %emphysema $r = 0.081$, $p = 0.56$.

Conclusion: Sputum neutrophils are raised in stable COPD. There is a disassociation between induced sputum neutrophils and lung function. Similarly there is no association between sputum neutrophils and low attenuation areas of emphysema. Therefore sputum neutrophils are independent biomarkers in COPD, reflecting the burden of inflammation in the airways and are not major surrogate marker of pathophysiological abnormalities in COPD.

P-F-023

COMPARATIVE STUDY ON SMOKING AND CHRONIC OBSTRUCTIVE PULMONALY DISEASE (COPD) AWARENESS

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Purpose: Previously, we reported that awareness of COPD is low in who visited to a certain hospital over the age of 18. Recognition rate is slowly increasing, however, still been not satisfactory. Furthermore easy native language (Japanese) is even a similar tendency. In addition, some study showed that young-youth-adult student's in university started smoking. So, in this study, aimed at anagenesis about understanding, education and improvement of above situation.

Methods: The questionnaire for all university students was performed using our University Original Internet system in 2012–13. Participants status were conducted who enrolled over 18 age and examined in 641 cases(Group A) that consent were obtained. As the control subject, 335 cases (mean \pm SD, 56.5 ± 15.8 yrs) who visited to a certain hospital was(Group B). We used the disease name "COPD" and "TOBACCO BYOU" that is abbreviation word <Guidelines for the Diagnosis and Treatment of COPD (The Japanese Respiratory Society).

Results: Base of analyzed student's subjects status were male/female(%) = 53.4/46.6, 20.4 ± 1.6 (mean \pm SD, yrs), smoking prevalence(%) was Current 8.4 (M/F,%:6.6/1.6), Former 5.6, Never 86.0, respectively. COPD is association with smoking is strong, however, "Know" was only 9.8%(Heard of: 24.8%/Unknown:61.8%) in Group A (Similar data of GroupB: "Know: 9.3%/Heard of: 17.6%/ Unknown:73.1%"). In contrast, the knowledge of package warning was high in Group B rather than A. However, "Risk of Lung cancer" knowledge was similar higher than other risk disease (e.g. Stroke, Myocardial infarction) warning message in both groups.

Conclusions: This results was considered that source of the text size of tobacco package warning documents is small and mild. In addition, smoking is a harm to health, nevertheless the knowledge of package warning recognition ratio was not unified. Furthermore it was speculated that the elderly from the young adolescents in Japan who were not exposed to anti-tobacco messages and/or were not taught about the harmful effects. Therefore we should more educate and message the awareness of Smoking and COPD.

P-F-024

P-F-026

YEARLY PROGRESSION OF LOW LUNG ATTENUATION AREA IN LOW DOSE CT SCAN FOR ASYMPTOMATIC CURRENT SMOKERS WITH NORMAL LUNG FUNCTION OR GOLD STAGE 1 COPD

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Purpose: There is still no biomarkers identifying subjects at risk for COPD though the early detection and prevention of COPD is important. The purpose of this study was to investigate if we can identify yearly progression of low lung attenuation area (LAA-950) in smokers with normal lung function or GOLD stage 1 COPD.

Material and Methods: From March 2007 to Oct 2012, initial and annual follow-up low dose CT scans with the measurement of low lung attenuation area (LAA-950) were performed in a total of 86 current smokers (mean age; 48.1 years, mean initial pack years; 27.3 ± 17.98) and 17 non-smokers (mean age; 46.7 years) among lung cancer screening male subjects at our institution. Visceral fat, body fat, BMI, and pulmonary function test (FEV1, FEV1/FVC) were also obtained at each low dose CT scan which was performed with designated single machine (Siemens, Sensation 16) with the same protocol (120 kVP, 30 mAs) for the follow-up scans. For statistical analysis, Mann-Whitney U test, Spearman correlation coefficient and Wilcoxon signed rank test were used.

Results: Mean smoking pack year increased from 27.38 ± 17.98 to 31.40 ± 18.13 for one year. Only baseline FEV1/FVC was significantly decreased in smokers compared to non-smokers (mean 77.57 ± 6.59 vs 82.44 ± 4.17 , $P = 0.006$) and negatively correlated with smoking pack year ($r = -0.355$, $P = 0.001$). However, only LAA-950 was significantly increased (mean 7.88 ± 3.93 , vs 9.85 ± 5.50 , $p = 0.001$) in smokers on the annual follow-up study. BMI (23.88 ± 2.54 vs 23.88 ± 2.56), visceral fat (100.41 ± 16.81 vs 100.73 ± 19.74), body fat (21.29 ± 3.96 vs 21.64 ± 3.88), FEV1% (99.80 ± 12.63 vs 99.33 ± 12.67) and FEV1/FVC% (77.57 ± 6.59 vs 77.39 ± 6.47) were not significantly changed ($P > 0.05$) in smokers on the annual follow-up study. There were no significant differences in the paired LAA-950, BMI, visceral fat, body fat, FEV1 and FEV1/FVC% in non-smokers on the annual follow-up study.

Conclusion: Measurement of LAA-950 in low-dose CT scan may show individual yearly progression of microscopic emphysema in current smokers with normal lung function or GOLD stage 1 subjects who do not show significant annual changes in lung function.

P-F-025

USEFULNESS OF NEUTROPHIL TO LYMPHOCYTE RATIO IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY

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Background: Neutrophil to lymphocyte ratio (NLR) in peripheral blood is a useful systemic inflammatory response biomarker. However, NLR has not been studied in patients with chronic obstructive pulmonary disease (COPD). We aimed to evaluate the usefulness of NLR in patients with COPD.

Methods: NLR was prospectively measured and compared in patients with COPD exacerbation ($n = 59$), patients with stable COPD ($n = 61$), and healthy controls ($n = 28$). NLR in patients with COPD exacerbation was repeatedly measured in the convalescent period. The correlation between NLR and clinical parameters was evaluated, and the predictors for respiratory hospitalization were analyzed by multivariate logistic regression.

Results: NLR values were significantly higher in patients with COPD exacerbation compared with stable COPD patients and controls (12.4 ± 10.6 , 2.4 ± 0.7 , 1.4 ± 0.5 , respectively; $p < 0.001$). NLR was significantly decreased during the convalescent period in patients with COPD exacerbation (4.5 ± 4.6 versus 11.5 ± 8.8 ; $p < 0.001$). NLR exhibited a significant correlation with the BODE index, the six-minute walk test, and the modified Medical Research Council scale. Body mass index and forced expiratory volume in 1 second were independent predictors for respiratory hospitalization. $NLR \geq 2.8$ was an independent predictor with a borderline significance for respiratory hospitalization (odds ratio, 2.083; $p = 0.079$).

Conclusion: NLR is a straightforward and effective biomarker of COPD exacerbation that may serve as a predictor for respiratory hospitalization in patients with COPD.

SEVERE VITAMIN D DEFICIENCY IS ASSOCIATED WITH EXERCISE CAPACITY AND ITS DECLINE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Vitamin D is suggested to play a role in airway and systemic inflammation in chronic obstructive pulmonary disease (COPD). Low serum 25-hydroxyvitamin D (25-OHD) levels have been suggested to be associated with lower lung function and poorer exercise capacity in COPD.

Objectives: The main purpose of this study was to explore whether the rate of decline in exercise capacity differs between COPD patients with and without vitamin D deficiency.

Methods: A total of 166 subjects were selected from the Korean Obstructive Lung Disease cohort. Serum levels of 25-OHD below 20 or 10 ng/ml were defined as vitamin D deficiency or severe vitamin D deficiency, respectively. Exercise capacity was assessed by 6-minute walk distance (6MWD).

Results: Significant differences between 25-OHD ≥ 10 ng/ml group ($n = 121$) and < 10 ng/ml group ($n = 45$) were observed for age, smoking status, lung function, and 6MWD. The 6MWD was independently associated with severe vitamin D deficiency. The deterioration of exercise capacity was more rapid in the group with severe vitamin D deficiency over a 3-year period of follow-up ($P < 0.034$).

Conclusions: The serum level of 25-OHD < 10 ng/ml is clinically relevant to decreased exercise capacity in COPD. Severe vitamin D deficiency is associated with a greater decline in exercise capacity in patients with COPD.

P-F-027

ROLE OF L-TYPE Ca^{2+} CHANNEL/KCA CHANNEL LINKAGE IN THE SYNERGISTIC RESPONSE BETWEEN ANTICHOLINERGIC AGENTS AND BETA2-ADRENOCEPTOR AGONISTS IN AIRWAY SMOOTH MUSCLE

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Rationale: In the pharmacological therapy for chronic obstructive pulmonary disease (COPD), long-acting muscarinic antagonists (LAMAs) and long-acting beta2-adrenoceptor agonists (LABAs) are regularly inhaled; short-acting beta2-adrenoceptor agonists (SABA) are used on demand to improve symptoms and lung function. This study was designed to determine whether synergistic effects cause between LAMAs and beta2-adrenoceptor agonists (LABAs, SABAs) in airway smooth muscle. Moreover, mechanisms underlying this phenomenon were examined focused on ion channels and G proteins.

Methods: For record of isometric tension, the strips of tracheal smooth muscle of guinea pigs were placed in the organ bath and were perfused with the physiological solution at constant flow rate of 3 ml/min.

Results: 1 nM Glycopyrronium (LAMA), 10 nM Indacaterol (LABA), and 0.3 nM Procaterol (SABA), caused approximately 4.8 ($n = 10$), 28.2 ($n = 12$) and 34.1 ($n = 8$) %inhibition of 1 μ M methacholine-induced contraction, respectively. However, when 10 nM Indacaterol and 0.3 nM Procaterol were applied in the presence of 1 nM Glycopyrronium, the inhibitory effects of these beta2-adrenoceptor agonists combined with Glycopyrronium were markedly augmented to 46.2 and 53.9% inhibition, respectively (each $n = 10$, $P < 0.01$). Moreover, when the tissues were treated with 1 μ g/ml pertussis toxin, which inhibits Gi, or 2 μ g/ml cholera toxin, which activates Gs irreversibly, for 6 h, respectively, the effects of Indacaterol or Procaterol/Glycopyrronium combination were significantly enhanced. On the other hand, in the presence of 100 nM charybdotoxin, an inhibitor of large conductance Ca^{2+} -activated K^{+} (KCa) channels, this greater effect in Indacaterol or Procaterol/Glycopyrronium combination was markedly attenuated. However, in the presence of 0.3–3 μ M verapamil, an inhibitor of L-type Ca^{2+} channels, this reduced responsiveness induced by charybdotoxin was significantly attenuated in concentration-dependent fashion, and roughly reversed to the control response.

Conclusions: The combination of LABAs or SABAs with LAMAs causes synergistic relaxation against muscarinic contraction in airway smooth muscle. This phenomenon is mediated by inhibiting in L-type Ca^{2+} channels induced via dual regulation of KCa channels by G proteins (Gi, Gs). Therefore, combined inhalation of LAMAs and beta2-agonists may be a useful therapy for COPD as a potent bronchodilator.

P-F-028

THROMBOCYTOPENIA A MARKER OF POOR OUTCOME IN ACUTE EXACERBATION OF COPD

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Background and Objectives: Recent studies show thrombocytopenia (TP) is associated with poor outcome in patients with pneumonia, burn, H1N1 influenza, both paediatric and adult ICU patients. Since chronic obstructive pulmonary disease (COPD) is recently considered to be a systemic inflammatory disease. To best of our knowledge there is no study of impact of TP on outcome in COPD. The aim of this study is to determine impact of cheap and easy available platelets count on outcome in patients with acute exacerbation of COPD (AECOPD).

Methods: TP was defined as a platelet count of $<150,000$ /mm³. In this study, patients who admitted to our teaching hospital with AECOPD divided to cohort with and without TP based on admission day CBC. Outcome of patients were followed. Adverse outcome was defined as death in hospital, transfer to ICU, intubation and mechanical ventilation.

Results: Of 200 patients with AECOPD 55 (27.5%) had TP. Of them 14 (25.5%) died in hospital while of 145 non-TP patients 11 (7.5%) died (p value = 0.001). Transfer to ICU among TP and non-TP patients was consecutively 34.5% vs. 13.8 p value = 0.001). Similarly there was significantly higher rate of mechanical ventilation in TP patients (p value = 0.008). On the other hand Of 200 patients with AECOPD 25 (12.5%) died in hospital. Mean platelet count was 161,672 cell/ml in died patients vs 203,005 cell/ml in discharged patients (p value = 0.017) There was negative correlation between duration of hospitalization and platelet counts.

Conclusion: TP is associated with poor outcome in AECOPD. TP could be considered as a new inflammatory marker for assessment of inflammation and prognosis in AECOPD patients with its fast, cheap, easily available property with routine CBC.

P-F-031

VALIDITY OF FEV1/FEV6 COMPARED WITH FEV1/FVC IN DIAGNOSING CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Chronic Obstructive Pulmonary Disease (COPD) is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airway and the lung to noxious particles or gases. Spirometry is a lung function test which common used in detecting obstruction with ratio forced expiration volume in 1 second divided with forced vital capacity (FEV1/FVC) post bronchodilator less than 70% as a gold standard. Some factors such as fatigue, and fear of breathlessness made patients stop their exhale before FVC manoeuvre has been finished. This study recommend forced expiration volume in 6 seconds (FEV6) to replace FVC so patient do not required to exhale more than 6 seconds, patient can minimize fatigue and breathlessness.

Objective: To compare validity of FEV1/FEV6 with FEV1/FVC in diagnosing COPD.

Material and Method: A cross sectional study conducted on ≥ 40 years old participants with signs and symptoms of COPD in pulmonary clinic Dr. Moewardi Hospital Surakarta between February 1st 2014 and May 15th 2014. Participants must performed spirometry and fit the criteria of acceptable and reproducible based on American Thoracic Society (ATS) 2005. The gold standard in diagnosing COPD based on Global initiative for chronic Obstructive Lung Disease (GOLD) 2013 is FEV1/FVC ratio < 0.7 .

Result: From 78 patients who were diagnosed COPD based on FEV1/FVC, only 3 (3.8%) patients who were not diagnosed COPD based on FEV1/FEV6, and 15 (100%) patients who were not diagnosed COPD based on FEV1/FVC also were not diagnosed COPD based on FEV1/FEV6. This result show that there is no significant differentiation between FEV1/FEV6 and FEV1/FVC. The highest sensitivity and specificity is in the cut off point of FEV1/FEV6 = 71%.

Conclusion: FEV1/FEV6 can replace FEV1/FVC in diagnosing COPD.

P-F-029

RISK FACTORS FOR THE DEVELOPMENT OF PNEUMONIA IN PATIENTS TREATED WITH INHALED CORTICOSTEROIDS

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Background: Inhaled corticosteroid (ICS) is an important medicine in the treatment for bronchial asthma and chronic obstructive pulmonary disease (COPD) patients. However, several studies have shown that the use of ICS has been associated with an increased risk of pneumonia. The aim of this study was to evaluate the risk factors for the development of pneumonia in patients with asthma and COPD during a treatment with ICS.

Method: This was a retrospective cohort analysis of patients who were treated with ICS between January 2011 and August 2013. There were nine patients who had developed pneumonia out of the total 1,189 patients. We selected eighteen patients who had been treated with ICS but not developed pneumonia, and were matched with the pneumonia patients in the age, sex, underlying disease and the type of ICS. Then, we compared the patient characteristics and their clinical features to evaluate the risk factors for pneumonia.

Results: In the two groups [pneumonia (+) vs pneumonia (-)], a smoking history was seen in 88.9% vs 87.5% of the patients, respectively, oral corticosteroid therapy was given in 22.2% vs 5.6%, home oxygen therapy was performed in 22.2% vs 11.1%, a mean serum level of albumin was 3.76 g/dL vs 3.72 g/dL, and a mean body mass index was 18.9 vs 23.1. However, there were no significant differences in these parameters between the two groups.

Conclusion: Although the sample size of this study was small, there was a possibility that oral corticosteroid therapy, a use of home oxygen therapy and a low body mass index might be risk factors for the development of pneumonia. Further studies targeting a large cohort of patients are required.

P-F-032

UNDERSTANDING PERCEPTION OF COPD AMONG DOCTORS AT DIFFERENT SPECIALTY LEVELS IN INDIA: A FACE-TO-FACE SURVEY

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Background And Aim Of Study: India contributes a significant and growing percentage to the morbidity and mortality associated with COPD, and this is estimated to be amongst one of the highest in the world. However, despite such increased prevalence it remains highly under-recognized and under-treated and diagnosis of COPD usually does not occur until significant lung function has already been lost. This survey aimed to identify the existing barriers to an early and proper diagnosis and treatment of COPD in India by exploring the attitudes, beliefs, and knowledge of Indian doctors related to COPD.

Methods: A cross-sectional study in 91 randomly selected primary care physicians, internal medicine specialists (referred to collectively as physicians) and pulmonologists was conducted in 8 cities in India. It involved data collation through a questionnaire and face-to-face interviews.

Results: The overall response rate to the written questionnaire was 59.34% (54 out of 91). Majority of the doctors (57.4%) reported that COPD patients usually visit them at severe stages of the disease. Lung function testing is not routinely performed and diagnosis is largely symptom and history based- 44% physicians denied performing spirometry to make a diagnosis of COPD. About 35% of physicians believed that COPD occurs only in smokers. The most commonly reported challenges to diagnosis of COPD were a) spirometry related- access (22.22%), interpretation (27.77%), unwillingness of patients (44.44%), affordability issues (29.62%), b) doctor related- inadequate training on COPD diagnosis (11.11%) and c) patient related-lack of awareness about the disease. Doctors' perceived barriers to the treatment of COPD included difficulty in explaining COPD to patients (38.88%) and poor patient compliance to treatment (42.59%). 70% doctors agree that compliance with treatment is a major area of concern in case of COPD patients due to elderly age group, presence of multiple comorbidities, and the resistance associated with the use of inhaler devices. Resistance to inhaler usage by patients still remains high in the opinion of doctors (31.48%).

Conclusion: Lack of awareness about COPD, its symptoms and its implications contribute significantly in preventing people at risk from reaching out to their doctors. Inadequate use of or access to spirometry and the belief that COPD is a smoker's disease are important barriers to diagnosis. A large scale study will help to further understand the physician and patient perceptions. Educational and awareness programmes are needed both for doctors and patients to help address the awareness gap, under-diagnosis and under-treatment associated with COPD.

P-F-033

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN BEIJING

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Objective: To investigate the prevalence of Chronic Obstructive Pulmonary Disease (COPD) in Beijing.

Methods: Using multi-stage cluster random sampling, all residents 20 years of age or older in Beijing were randomly selected and interviewed with a standardized questionnaire, spirometry, physical examination, X-rays of chest and ECG tests. The categorical variables were described by the constituent ratio or prevalence and compared by X² test. The post-bronchodilators FEV₁/FVC < 70% was identified as having COPD.

Results: Among 1,472 sampling subjects, 1,156 participants completed the questionnaire and spirometry. The overall prevalence of COPD was 4.1% (47/1156), the prevalence was significantly higher in males [6.2%(31/502)] than in females [2.4%(16/654)]; among the smoking population, the prevalence rates of COPD is 7.8% (28/357), which is higher than that of non-smokers 2.4%(19/799); the prevalence of COPD aged over 40 years old [5.8%(41/705)] also higher than under 40 years old [1.3%(6/451)] (P = <0.05).

Conclusions: The prevalence of COPD in Beijing was high [4.1%(47/1156)] in people 20 years of age or older. Lung function test seemed to be of great importance to COPD diagnosis, especially in the earlier period of COPD.

P-F-034

LOW VITAMIN D LEVELS WERE NOT ASSOCIATED WITH OSTEOPOROSIS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Osteoporosis is an important comorbidity in patients with COPD. Although a low vitamin D nutritional status was closely linked to osteoporosis and asthma, its association with COPD has been controversial. We investigated whether low vitamin D levels were associated with osteoporosis in COPD patients.

Methods: We analyzed data from the 2008–2010 Korean National Health and Nutrition Examination Survey (KNHANES). Subjects aged 40 years or more and who had acceptable and qualified spirometry and dual-energy X-ray absorptiometry (DXA) results available were included. COPD was defined as having FEV₁/FVC < 0.7. Osteoporosis was defined as a value for bone mineral density (BMD) T-score ≤ -2.5 at femur or lumbar spine. Vitamin D deficiency was defined as serum 25-hydroxyvitamin D (25[OH]D) concentrations <20 ng/mL.

Results: A total of 6,192 subjects were enrolled. Among them, 782 had COPD. The prevalence of osteoporosis in subjects with COPD was higher than that in subjects without COPD (15.4% vs 11.5%, p < 0.0001). Compared to that in subjects without COPD, the prevalence of vitamin D deficiency was rather lower in COPD subjects (p = 0.01). Multiple logistic regression analysis revealed that age ≥65 years (OR 3.9, 95% CI 1.7–9.0), female (OR 8.0, 95% CI 2.7–21.5), low body mass index (BMI) (<18.5 kg/m² vs 18.5–25 kg/m² OR 9.7, 95% CI 3.1–29.3), lack of moderate exercise (OR 2.6, 95% CI 1.1–6.3), anaemia (OR 2.6, 95% CI 1.1–6.1) were independently associated with osteoporosis in COPD subjects. Vitamin D deficiency was not associated with osteoporosis in COPD.

Conclusions: Old age, female, low BMI, lack of exercise, and anaemia were risk factors of osteoporosis in COPD. Although this study did not demonstrate an association between vitamin D deficiency and osteoporosis in COPD, further study will be needed to clarify its relationship, considering relatively mild airway obstruction of our subjects.

P-F-035

THE CHARACTERISTICS OF CYTOSKELETON PROTEIN EXPRESSION AND PROLIFERATION OF HUMAN LUNG AND BRONCHIAL FIBROBLASTS

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Background: The lung and bronchial tissue remodeling is known to play an important role in airflow limitation of chronic obstructive pulmonary disease (COPD). It has been noticed that in COPD the proliferative response of different cells is prominent in bronchial tissue, while in lung tissue the destructive process is responsible for emphysema. Fibroblasts are key mediators in tissue remodeling. We hypothesized that there were some different repairing characteristics between lung and bronchial fibroblasts during the process COPD.

Methods: Human lung and bronchial fibroblasts were separately isolated as primary culture from patients with lung cancer experienced pneumonectomy. The expression of vimentin and α smooth muscle actin (α SMA) was detected by immunohistochemistry. MTT assay was utilized for measuring fibroblasts proliferation.

Results and Conclusion: Vimentin and α SMA were intensely expressed in cytoplasm, but the distribution was different between lung and bronchial fibroblasts. In cytoplasm of lung fibroblasts, vimentin was expressed mainly around the nuclear in a dot-like pattern, and α SMA was distributed along the cell membrane. In cytoplasm of bronchial fibroblasts, both vimentin and α SMA were uniformly distributed. Under the same culture condition, the proliferative degree was different. The bronchial fibroblasts proliferated significantly faster than the lung fibroblasts. These findings suggest that bronchial and lung fibroblasts behave differently in repair and regenerative process of lung and bronchial tissue remodeling, which might play a pivotal role in the airflow limitation of COPD and probably should be considered separately in COPD treatment.

P-F-036

MORTALITY RISK FACTORS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL

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Background: Chronic obstructive pulmonary disease will become the third leading cause of death worldwide by 2020. This increased mortality is mainly driven by the expanding epidemic of smoking. Identification risk factors of COPD mortality has widely studied abroad with varying results. Due to difference in patient characteristic, it is necessary to study on the factors associated with exacerbation of COPD in Indonesia.

Aim: To determine the incidence of mortality COPD in RSCM during 2010 until 2012. And to identify risk factors of COPD patients mortality who seek treatment at Cipto Mangunkusumo Hospital, both inpatient and outpatient.

Methods: This study was a retrospective cohort design in COPD patients who seek treatment at Cipto Mangunkusumo Hospital, both inpatient and outpatient, during 2010–2012. Clinical data and supportive data during treatment were obtained from medical records. Survival analysis performed on the variables gender, age, smoking history, comorbidities, severity of COPD, the history of treatment with systemic corticosteroids, and the frequency of exacerbations in one year. Variables that were proportional hazard assumption will be conducted cox regression analyzes. And variables that were eligible would be included in the multivariate analysis with cox regression analysis of time independent.

Results: A total of 184 patients enrolled in this study. Incidence of mortality in COPD patients was 9.2%. Age ≥ 60 years, frequency of exacerbations in a year ≥ 2 times, the degree of COPD stage III and IV, and treatment with systemic corticosteroids were significant variables in bivariate analysis. And from the results of multivariate analysis showed that the degree of stage III and IV COPD was a risk factor for mortality in COPD patients which was statistically significant (HR 3.24; 95% CI 1.16 to 9.04, $p = 0.025$).

Conclusion: The incidence of COPD mortality at RSCM in 2010 to 2012 was 9.2%. The risk factor for COPD patients mortality was stage III and IV of COPD degree.

P-F-037

PROFILE THE ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL

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Background: Exacerbation in chronic obstructive pulmonary disease (COPD) contributes greatly to the severity and progression of COPD. This condition increases the morbidity and mortality rate from COPD. Patients with exacerbation of COPD will experience a decline in lung function more quickly thus causing a decrease in performance and quality of life.

Aim: To determine the prevalence and profile of COPD exacerbations in RSCM during 2010 until 2012 from COPD patients who seek treatment at Cipto Mangunkusumo Hospital, both inpatient and outpatient.

Methods: This study was a cross sectional study design in COPD patients who seek treatment at CiptoMangunkusumo Hospital, both inpatient and outpatient, during 2010–2012. Clinical data, supportive data, and outcome (exacerbation or stable) data during treatment were obtained from medical records. Bivariate analyses were performed on age, history of smoking, comorbidity, severity of COPD, history corticosteroids treatment, and frequency of exacerbations in one year.

Results: A total of 184 patients enrolled in this study. There were 87.5% male patients and 12.5% female patients, the median age was 64 years old, with 66.3% of patients aged ≥ 60 years old and 33.7% of patients aged < 60 years old. Prevalence of COPD exacerbation was 70.7%. There were variables that role as risk factors of COPD exacerbation: grade III and IV of COPD (RR 1.58; 95% CI 1.34 to 1.87; $p < 0.001$), active smoker (RR 1.41; 95% CI 1.22 to 1.63; $p = 0.003$), frequency of exacerbations ≥ 2 per year (RR 1.59; 95% CI 1.39 to 1.84; $p < 0.001$), and Charlson Comorbid Index > 2 (RR 1.5; 95% CI 1.05 to 2.15; $p = 0.005$).

Conclusion: COPD patients in RSCM 87.5% were male patients, 66.3% were aged ≥ 60 years old, and the median age was 64 years old. The prevalence of COPD exacerbations in RSCM during 2010 to 2012 is 70.7%. The risk factors of COPD exacerbation were grade III and IV of COPD, active smoker, frequency of exacerbations ≥ 2 per year, and Charlson Comorbid Index > 2 .

P-F-038

FACTORS ASSOCIATED WITH EXACERBATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL

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Background: Exacerbation in chronic obstructive pulmonary disease (COPD) contributes greatly to the severity and progression of COPD. This condition increases the morbidity and mortality rate from COPD. Patients with exacerbation of COPD will experience a decline in lung function more quickly thus causing a decrease in performance and quality of life. Identification of factors associated with exacerbation of COPD has widely studied abroad with varying results. Due to difference in patient characteristic, it is necessary to study on the factors associated with exacerbation of COPD in Indonesia.

Aim: To determine the incidence of COPD exacerbations in RSCM during 2010 until 2012. And to identify factors associated with exacerbation of COPD patients who seek treatment at Cipto Mangunkusumo Hospital, both inpatient and outpatient.

Methods: This study was a retrospective cohort study design in COPD patients who seek treatment at CiptoMangunkusumo Hospital, both inpatient and outpatient, during 2010–2012. Clinical data, supportive data, and outcome (exacerbation or stable) data during treatment were obtained from medical records. Bivariate analyses were performed on age, history of smoking, comorbidity, severity of COPD, history corticosteroids treatment, and frequency of exacerbations in the previous year. Variables that were eligible would be included in the multivariate analysis in the form of logistic regression.

Results: A total of 184 patients enrolled in this study. Incidence of COPD exacerbation was 70.7%. Severity of COPD, history of smoking, frequency of previous exacerbations, history of systemic corticosteroid treatment, and comorbidity were variables found to be significantly different in bivariate analysis. Independent risk factors that were found to be significant in multivariate analysis were ≥ 2 times of COPD exacerbation in the previous year (OR 27.39; 95% CI 3.30 to 227.29; $p = 0.002$), current smoker (OR 5.11; 95% CI 1.07 to 24.35; $p = 0.041$), grade III and IV of COPD (OR 4.71; 95% CI 1.59 to 13.97; $p = 0.005$), and comorbid with charlson comorbid index value more of two (OR 4.09; 95% CI 1.37 to 12.18; $p = 0.011$). While treatment with systemic corticosteroid is protective factor against COPD exacerbations (OR 0.12; 95% CI 0.03 to 0.54; $p = 0.006$).

Conclusion: The incidence of COPD exacerbations in RSCM during 2010 to 2012 is 70.7%. Risk factors for COPD exacerbation are more than or equal to two times of COPD exacerbation in the previous year, current smokers, grade III and IV of COPD and comorbid with charlson comorbid index value more of two. While treatment with systemic corticosteroid is protective factor against COPD exacerbations.

P-F-039

A STUDY OF CORRELATIONS BETWEEN PATIENT PERCEPTIONS AND FINDINGS ON CLINICAL EXAMINATION IN COPD PATIENTS IN ROMANIA

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Purpose: Patient-perceived COPD symptoms vary over the day and the week with impact on daily activities, morning being the worst time of day. The study aimed to identify the correlation between patient perceptions of their ability to perform morning activities and the general health status visual scale, as assessed by the physician during physical examination. This was the first Romanian study to assess this correlation.

Methods: RELIEF (CorRELation Between Patient PERception and Findings on Clinical Examination, NCT01627743) was a non-interventional, multicentre, prospective, 12-weeks study of patients aged at least 40 years with COPD stage C or D treated for at least of month previous enrollment with ICS/LABA combined therapy. Patients were current or ex-smokers. In order to evaluate patients' perception on ability to perform morning activities, the CDLM (Capacity of Daily Living during the Morning Questionnaire) questionnaire was used. Investigators used a 5-items visual scale for assessing the health status (5 = very good, 1 = very bad).

Results: 505 patients were included in the final analysis. The majority of patients were male (85.1%), with a mean age of 65 years. 74.7% were reported as being ex-smokers with a mean of 20 cigarettes (1 pack) per day. The average duration of COPD was 5.31 years and more than half of the patients enrolled had COPD stage C (61%). The mean duration of inhaled combined therapy before study was 36 months. 67.9% patients reported comorbidities, majority being from the cardio-vascular area with hypertension the most frequent condition (38.2%). The mean score of CDLM increased during the prospective follow-up from 3.68 to 3.94, as well as the percentage of patients with a general health status of 4/5 from 41.2% to 57.4%. A weak-to-moderate positive correlation was found between the CDLM total score and the general health status (Kendall tau-b values from 0.2269 to 0.3181).

Conclusions: These results indicate a general improvement of subjective perceptions of both patients and health care providers and complete the COPD landscape in Romania, being the first study on quality of life. CLINICAL IMPLICATIONS: The regular contact with the health care provider might lead to a general health improvement and might represent an important motivational tool to be taken into account in treating severe COPD patients.

P-F-041

DIRECT COSTS OF ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASES IN A SECOND LEVEL HOSPITAL

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Introduction: The high prevalence and morbidity of chronic obstructive pulmonary disease (COPD) contributes to high costs. Hospitalization is a major cost driver in COPD management with hospital care projected to account for 45% of direct COPD costs. The aim of the present study was to investigate the direct costs of acute exacerbation of COPD (AECOPD) among hospitalized patients in a second level hospital.

Method: In this retrospective analysis, between september 2012 and March 2013 all AECOPD patients that were admitted to hospital were eligible for the study. Age, gender, duration of hospitalization, total cost including, radiology, laboratory, bed, and medicine cost were calculated.

Result: A total of 1117 hospitalization of 870 patients were investigated. Mean age was 71 ± 9,5 and male/female percent was 74/26. Mean duration of hospital length was 11,3 ± 5 days. Mean total cost was 1412 ± 916 Turkish liras (TL) per capita. Mean daily cost was 121 ± 32 TL. mean bed and medicine costs were 41% and 42 % of the total cost, respectively.

Discussion: COPD is an important health care problem. AE COPD is being the most important cause of COPD burn in our country and worldwide. Direct costs of COPD-related care for commercially insured patients are driven by hospital stays with or without ICU care. Prevention of exacerbations and shorter hospitalization may reduce need for inpatient care and could lower costs.

P-F-042

LONG TERM FOLLOW-UP OF MILD COPD PATIENTS

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Background: In Korea, Chronic obstructive pulmonary disease (COPD) is one of the main causes of morbidity and mortality and the prevalence of COPD is 13.4%. And 39.6% of Korean COPD patients have mild disease (GOLD 1). However, little is known about the course of mild COPD patients. The aim of this study was to explore the long term consequence of mild COPD patients.

Methods: We constructed COPD patient cohort retrospectively in 5 hospitals affiliated with Hallym University Medical School. The definition of mild COPD was adopted by the GOLD guideline. We obtained the clinical data from the medical record and compared the clinical, spirometric data according to the development of exacerbation during the follow-up period.

Results: A total of 613 patients were enrolled and there were 113 mild COPD patients in our cohort. The mean follow-up duration was 40.0 ± 33.3 months. Unfortunately, 26.5% of the patients were followed up less than 12 months. A total of 30.1% patients experienced acute exacerbation during the follow-up (exacerbators). Among the patients experience exacerbation, 38.2% of patients experienced exacerbation during the first year of follow-up (early-exacerbators). A total of 50% of the exacerbators had more than 3 exacerbations during follow-up (frequent exacerbators). A total 58.8 % of the frequent exacerbators experienced exacerbation during the first year of follow-up. Only 17.6% of infrequent exacerbators experienced exacerbation during the first year of follow-up (p = 0.032, chi-square test). When we compared clinical and laboratory data between early and late exacerbators or frequent and infrequent exacerbators, nothing was statistically significant. Only mean age showed the tendency for early and frequent exacerbations.

Conclusion: A total 30.1% of mild COPD patients experienced the exacerbation during long term follow-up. Frequent exacerbators experienced exacerbation earlier than infrequent exacerbators. Older patients were more likely to experience the exacerbation early and frequently. Clinical implication: Even in mild COPD, subsequent number of patients experienced exacerbations. A larger and prospective study will be warranted to clarify the parameters to predict the exacerbations.

P-F-040

"INSPIROM" – A NEW EXPLORATION OF THE PULMONOLOGIST – PATIENT RELATIONSHIP WITH COPD

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Aim: The aim of the study was to provide an insight of the investigation related to these multiple clinical and care problems entailed by COPD in this category of patients in their relations with the practitioner.

Method and Materials: In a prospective observational study set up in 2012 and completed in 2013, which was carried out over a 6-month period and which pursued, at out-patient settings we involved 39 doctors throughout the country and assessed the involvement of doctors and patients in their observance of the therapeutic indications, as well as patients' compliance with the medical instructions, 2 months after the therapeutic indication. All participating were trained before start of the study.

Results: In an observational study which followed the development of COPD patients at the time of recruitment to the monitoring visit in two months we have demonstrated for the first time an overview of outpatients in Romania through the new GOLD classification.. We have a first outlook of the COPD in Romania through the GOLD classification. We found out that, at detection time, 88% of the patients are obstructive, with 56% having mild and moderate obstruction (stage 1–2 GOLD), 44% patients are in old GOLD stage 3–4. If we use new GOLD classification, 46.4% patients are in GOLD C and D stages, with 35% having CAT over 20.25% and mMRC over 2.

Conclusions: There are some alarm signals related to the large number of smokers, the lack of involvement of doctors in fighting tobacco consumption, and over-assessment of mild stages of the disease. All these elements will guide future prevention programmes and actions of active screening for this disease.

P-F-044

COULD COPD PATIENTS WITH SEVERE AIR FLOW LIMITATION INHALE TURBUHALER® EFFECTIVELY?

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Background and Aim of Study: Main damage of COPD patients is expiratory air flow limitation but they must have inspiratory flow rate for inhalation therapy. Could COPD patients with severe air flow limitation inhale Turbuhaler® effectively? We reported at 17th APSR congress that CAT scores correlate with peak inspiratory flow determined by the InCheck device in COPD patients. We investigate that COPD patients with severe air flow limitation as low inspiratory flow rate could or couldn't inhale Turbuhaler® effectively.

Methods: Enrolled COPD patients pretreated with tiotropium-respimat 5 µ more than four weeks and were measured at entry maximum inspiratory flow rate using an inspiratory peak flow meter (In-Check Dial® Clement Clarke International Ltd. London UK) fitted with a Turbuhaler® adaptor. Patients whose inspiratory flow rate was low (30–60 L·min⁻¹) through Turbuhaler® adaptor were entered. Budesonide/formoterol (Symbicort® 640/18 µ/day) started in day 1 on LAMA therapy. During the 12 weeks follow-up period change in the pathological condition were analyzed based on pulmonary function value, IOS measured by mostography, RINT, CAT questionnaire, HADS questionnaire, CAS-Q questionnaire. This prospective study protocol was approved by the local ethics Committee and patients gave their written informed consents.

Results: Fifteen stable COPD patients were entered in this study. Entry COPD pts included all male, age: 71.5±5.3 (63–79), spirometric classification of airflow limitation:(II/III/IV:3/6/4/2), CAT score: 17.4±6.6 (5–32). In these parameter FEV1.0 and Fes value of IOS were significantly improved by ICS/LABA. But CAT and other questionnaire data were not improved significantly.

Conclusion: This meter can be used to identify the most suitable inhaler for each individual. We conclude that COPD patients with low inspiratory flow rate could inhale Turbuhaler® ICS/LABA effectively. We will publish details of the study results at the 19th congress of the Asian Pacific Society of Respiriology (APSR).

P-F-045

ASSOCIATION OF PULMONARY ARTERY ENLARGEMENT AND LONGITUDINAL CHANGE WITH COPD EXACERBATION IN A DUSTY AREA

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Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow obstruction. Exacerbation of COPD is an important phenotype and is associated with accelerated decline of lung function. It was recently reported that pulmonary artery enlargement, measured using computed tomography, is independently associated with severe COPD exacerbations. However, little is known about longitudinal change of pulmonary artery. We aimed to investigate the association of pulmonary artery enlargement and longitudinal change with COPD exacerbation in a cohort of subjects with COPD in Korea. We conducted a COPD cohort in a dusty area in Korea from 2012. Clinical characteristics and CT scans were evaluated at enrollment. The pulmonary artery diameter at the bifurcation and the aorta diameter from the same CT image were measured. We determined the association between ratio of the diameter of the pulmonary artery to the diameter of the aorta (PA : A ratio) and COPD exacerbation. Follow-up CT scans were performed after one year in a subset of the cohort. A total of 142 subjects with COPD were evaluated for clinical characteristics and pulmonary artery enlargement. PA : A ratio was significantly associated with BMI, mMRC, and lung function. PA : A ratio was significantly associated with exacerbation of COPD ($p = 0.04$). We measured the PA : A ratio on 75 subjects after one year. Mean change of the PA : A ratio was 0.01 ± 0.06 . The ratio of 34 subjects decreased, and the ratio of 41 subjects increased. The change in PA : A ratio was not associated with COPD exacerbation. In conclusion, there was a significant association between pulmonary artery enlargement and COPD exacerbation in the COPD cohort. However, there was no association between the longitudinal change of pulmonary artery over a year with COPD exacerbation.

P-F-046

NEW GOLD CLASSIFICATION IS AN INDEPENDENT PREDICTOR OF HOSPITALIZATION FOR ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: The new Global Obstructive Lung Disease (GOLD) classification of Chronic Obstructive Pulmonary Disease (COPD) categorized the patients based on degree of dyspnea, exacerbation history and severity of airflow limitation as well for treatment strategy. The utility of new ABCD classification system is unclear yet. We compared the clinical features between spirometric grades and new ABCD groups, and explored the association of clinical indexes of COPD and new ABCD classification with hospitalization for acute exacerbation of COPD (AECOPD).

Methods: We reviewed medical records of the patients with COPD (FEV1/FVC < 0.7 and FEV1 < 80% predicted) with more than 10 pack-years history of smoking, visiting pulmonary clinic at Gyeongsang National University Hospital from October 2011 to September 2013. The patients were classified to spirometric grades and ABCD groups, then compared of basal characteristics, forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), diffusing capacity for carbon monoxide (DLCO), COPD assessment test (CAT), modified medical research council (mMRC) dyspnea scale, six-minute walking distance (6MWD), BODE index and frequency of AECOPD including hospitalization for one year. And these indexes were analyzed as predictable factors of hospitalization for AECOPD.

Results: Of 155 patients, the distribution of patients was concentrated in GOLD 2 (45.8%) and 3 (36.8%), and group A (27.7%) and D (40.0%). mMRC was increasing from group A to D ($p < 0.001$), but CAT scores were higher in group B and D than group A and B ($p < 0.001$). 6MWD in group C is longer than that in group B (355.5 m vs. 332.2 m, $p < 0.001$). After multivariate analysis, GOLD was proved an independent predictor of hospitalization for AECOPD. The odds ratios of GOLD B, C, and D groups were 13.1 (95% CI, 1.4–120.1), 19.4 (95% CI, 1.5–252.3) and 25.4 (95% CI, 2.1–309.1) relative to group A for hospitalization for AECOPD.

Conclusion: By the new GOLD classification, distinct clinical features are shown in ABCD groups, and this group classification is determined an independent predictive factor of hospitalization for AECOPD in the present study.

P-F-047

A NEW INTEGRATED INDEX OF 6-MIN WALK TEST FOCUSED ON AN IMPACT OF OXYGEN DESATURATION – APPLICATION TO COPD

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Background: Desaturation distance ratio (DDR) has been proposed for evaluation of functional exercise capacity in interstitial lung diseases and it has been utilized chronic obstructive pulmonary disease (COPD). The present study was designed to apply the DDR to COPD and to examine whether DDR was more informative than 6-min walk distance (6MWD) for the assessment of pulmonary system and peripheral oxygenation on functional exercise capacity in patients with COPD.

Methods: Forty-one patients with COPD [age, 73 ± 8 years; body mass index (BMI), 22.0 ± 3.4 kg/m²] participated in the study. The 6-min walk test (6MWT) was performed with anthropometric measurements and pulmonary function test. Desaturation area was calculated as the total area above the curve created using peripheral oxygen saturation (SpO₂) values observed at each minute during 6MWT. The DDR was also calculated as the ratio of the desaturation area to 6MWD.

Results: The 6MWD was 375 ± 82 m and the decline in SpO₂ values (Δ SpO₂) was -5.8 ± 2.8 %. The DDR correlated with baseline pulmonary function in patients with COPD [FEV₁ (%predicted), $r = -0.602$, $p < 0.001$; DLCO, $r = -0.402$, $p = 0.009$, respectively], comparable to the findings of the 6MWD. The DDR also correlated well with Δ SpO₂ ($r = -0.600$, $p < 0.001$) and the increase in Borg scale scores ($r = 0.460$, $p = 0.002$) in contrast with the 6MWD which was not significantly correlated.

Conclusion: DDR was comparable to 6MWD for detection of pulmonary impairment with decreased functional exercise capacity in patients with COPD. Compared with 6MWD, however, the DDR is more informative for assessment of the impact of systemic oxygen desaturation and subsequent dyspnea during exercise in patients with COPD.

P-F-049

ROLE OF BODE INDEX AS PREDICTOR OF ACUTE EXACERBATION OF COPD IN HAJJ PILGRIMS

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Background: hajj activities increase risk of acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD) in hajj pilgrims. Diagnosis and grading of COPD before hajj is important to start treatment and reduce risk of acute exacerbation. BODE Index (Body mass, Obstruction, Dyspnoea, Exercise) is one of multidimensional grading system to predict risk of acute exacerbation COPD.

Methods: This was a retrospective cohort study among COPD hajj pilgrims year 2012 from Daerah Khusus Ibukota (DKI) Jakarta. BODE index was calculated from medical record. Medical record was obtained by screening process of COPD among hajj pilgrims 24 hours before flight. Exacerbation was determined immediately after arrival through anamnesis of subject, physician in charge from kloter, and record from personal hajj book. Difference between two means was calculated by Mann-Whitney U test, and difference between two proportions was calculated by Chi-Square test.

Results: 60 subject meet the inclusion criteria by random extraction from secondary data. There were 35 subject (58.3%) who had acute exacerbation of COPD. From all exacerbation, there were 5 subject (14.2%) hospitalized. BODE index range from 0–6, 48 subjects (80%) had BODE index 0–2, 6 subjects (10%) had BODE index 3–4, and 6 subjects (10%) had BODE index 5–6. Mean BODE index in acute exacerbation group was 2.1 ± 1.8 and 1.6 ± 0.8 in non acute exacerbation group (Mann-Whitney U $p = 0.29$). Fisher Exact Test result between low risk group (BODE index 0–3) and high risk (>3) is $p = 0.009$, RR 1.9 (CI 1.4–2.5) and Fisher exact test results of hospitalization risk between low risk group and high risk is $p = 0.03$, RR 5.06 (CI 1.02–25.2).

Conclusion: There was no difference of BODE index mean among hajj pilgrims between acute exacerbation COPD group and non acute exacerbation group. COPD hajj pilgrims with BODE index >3 had increased risk 1.9 times of acute exacerbation of COPD and increased risk 5 times of hospitalization compared with BODE index 0–3.

P-F-048

ANALYSIS OF COPD EXACERBATION MECHANISM USING CIGARETTE SMOKE COMBINED LPS MOUSE MODEL

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Background: Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) is caused by bacterial and viral infections and induced to progress decline in ventilator function and health status. Bacteria can cause directly epithelial damage and its endotoxin increases the expression of the pro-inflammatory cytokines TNF- α and IL-8, providing the mechanism to upregulate inflammation. Moreover, bacteria can activate macrophage phagocytosis, which induces TNF- α and LTB₄ release and then neutrophil chemotaxis. However, the relationship between the bacterial inflammation and progression of the COPD in exacerbation has not been investigated well. In this study, we examined the response of bacterial inflammation and the progression of emphysema in COPD, by using cigarette smoke combined LPS mouse model.

Methods: C57BL/6 mice were stimulated to smoke of four unfiltered cigarettes per day, 6 days a week for 6 months. Then, LPS was administered intratracheally to these mice. We analyzed the inflammatory response using BALF extraction at 3 days and 7 days, and the emphysematous change by micro CT at day28 after LPS administration.

Result: In cigarette smoke combined LPS mice, the numbers of neutrophils at 3 days and macrophages at 7 days increased more than in only LPS mice. Moreover, MMP12 protein was increased in alveolar macrophages in immunofluorescence and LAA% was extended in micro CT analysis at 28 days.

Conclusion: In cigarette smoke combined LPS mice, the inflammatory response by LPS was remarkably strong, getting longer. Further the strong inflammation was lead to the progression of emphysema. We assume that the pathology of COPD exacerbation has the complicated inflammatory mechanism in connection with the progression of COPD.

P-F-050

PROPORTION AND DISTRIBUTION OF RISK FACTORS ASSOCIATED WITH ACUTE EXACERBATIONS OF COPD IN THE PILGRIMS FROM JAKARTA EMBARKATION DURING HAJJ YEAR OF 2001 AND 2012

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Background: Chronic Obstructive Pulmonary Disease (COPD) is currently a global health problem in the world and becomes a significant health problem during pilgrimage for moslems. Data from Indonesian ministry of Health from Pilgrims in 2008 showed that acute exacerbation of COPD (AECOPD) ranked second in causes of death with a mortality proportion of 12.3%. To date, no publication known to have reported the proportion and risk factors associated with AECOPD in pilgrims in Indonesia.

Objective: To obtain data on the characteristic COPD in the pilgrims and the proportion and risk factors for AECOPD in the pilgrims from Jakarta Embarkation during hajj year of 2011 and 2012.

Methods: This is a cohort prospective study which was conducted during pilgrims seasons during hajj year of 2011 and 2012.

Results: Ninety-seven COPD patients were identified and subsequently recruited to this study. General characteristics of the subjects were as follows: male (95%), under 60 years of age (54%), low education status (72%), from DKI Jakarta (80%), current smokers (54%), without co-morbidity (60%), not known to have COPD prior to pilgrim's health examination (98%), moderate COPD severity (79%). The proportion of AECOPD during Hajj 2011–2012 was 48% ($n = 47$). General characteristics of the subjects were as follows: elderly (53%), not current smokers (53%), with co-morbidity (55%), having suffered from acute respiratory tract infection (98%) and moderate COPD severity (83%).

Conclusion: This study found a high proportion of AECOPD in the pilgrims from Jakarta Embarkation. Acute respiratory tract infection were commonly found in the pilgrims with AECOPD.

P-F-051

CASE OF EMPHYSEMA DETECTED IN A PILOT

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Background: A fundamental change in the lung parenchyma seen in COPD is emphysema. An abnormal and permanent enlargement of air spaces distal to the terminal bronchioles, with damages occurring in the wall is defined as Emphysema. Due to pilots' exposure to sudden changes in altitude and G-force during executing their job, they are more at risk of hypoxia and pneumothorax compared to other occupational groups. Therefore, we present our case.

Case: 33 years old male pilot applied in our clinic during periodic examinations. He had a smoking history of 12 packages year. He had no symptoms or complaints. Pulmonary auscultation and pulmonary functions test (PFT) were normal (VC: 5.69 (%97), FVC: 5.44 (%97), FEV1: 4.48 (%97), FEV1/FVC: %82)). Complete blood count values and routine biochemistry were normal. Chest X-Ray showed hyperdense and reticular pattern. Paraseptal emphysema and bleb formation on the apical segment of both lungs were observed in the thorax HRCT.

Conclusion: Permanent damage to the wall of terminal distal bronchial airways and alveoli are present in emphysema. Ascending to high altitude causes air expansions in volume and pilots executing sudden manoeuvres in the air subject to G-forces up to 9 times of gravity. These physical changes affect the lungs, as a result of; there is a significant increase in the risk of pneumothorax. Dead space in the lung in patients with emphysema is increasing. This leads to disruption of the blood oxygenation. Again during high G-forces the blood flow to the brain is reduced significantly. Emphysema is increasing hypoxia occur in the brain during exposure to high G-forces, may lead to syncope. For all these reasons, regulation does not allow pilots with emphysema to flying duties. Our case has been also decided to be permanently grounded.

P-F-053

FORCED OSCILLATION TECHNIQUE MEASUREMENTS WITH AND WITHOUT CHEEK SUPPORT IN COPD

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Background: Forced oscillation technique (FOT) is a useful method to assess respiratory resistance and reactance during tidal breathing. The support of the cheeks with the palms of both hands is recommended to reduce upper airway shunting according to the FOT guideline published by the European Respiratory Society. However, the influence of cheek support on FOT measurements in specific diseases is unclear.

Methods: Eighty COPD patients and 19 healthy subjects who attended the outpatient clinics of our hospital from 2013 to 2014 were enrolled in this study. They all gave informed consent and underwent FOT (MostGraph-01) with or without cheek support. Conventional pulmonary function tests were also performed on the same day.

Results: In healthy subjects, the values of R20 increased with cheek support ($p < 0.05$), but there were no differences at R5, X5, and X20 between the two protocols. In COPD patients, the values of R5, R20, X5 and X20 with cheek support were higher than those without support ($p < 0.05$). The frequency-dependence of resistance and reactance were revealed in both protocols in COPD patients. The differences between inspiratory and expiratory phase in X5 ($\Delta X5$) which was used as expiratory flow limitation (EFL) were not affected by support protocols in healthy and COPD patients. The values of R5, X5, X20, R5-R20, resonant frequency (Fres), and low-frequency reactance area (ALX) were significantly associated with FEV1%predicted as well as the slope of phase III($\Delta N2$) in both protocols in COPD patients. These correlations were stronger with cheek support than without cheek support.

Conclusions: Cheek support may help the precise assessment for mechanical inhomogeneities and peripheral airway obstruction in COPD patients.

P-F-052

PROFILE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS WITH IN-FLIGHT HYPOXIA SYMPTOMS AND DISTRIBUTION OF FACTORS THAT INFLUENCED FITNESS TO FLY IN COPD PILGRIMS

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Background: The decreased pressure in aircraft cabins may cause hypoxia symptoms in patients with Chronic Obstructive Pulmonary Disease (COPD). Currently, no publication known to have reported the profile in-flight hypoxia symptoms and pre-flight medical screening in COPD pilgrims.

Objective: To obtain profile of in-flight hypoxia and pre-flight assessment for fitness to fly without oxygen supplementation based on pulmonary function test, oxygen saturation, and the ability to walk more than 50 meters among pilgrims with COPD.

Methods: This is a descriptive study which was conducted during the pilgrimage season haji 2011.

Results: Thirty three COPD patients were identified and subsequently recruited to this study. Pre-flight medical assesment concluded that 33 subject were fit to fly without supplemental oxygen. Nevertheless, three subject developed in-flight hypoxia symptoms i.e. two of them were fit to fly without supplemental oxygen, while another subject was recommended to have supplemental oxygen. Characteristics of subjects with in-flight hypoxia were as follows: (10.5%) current smokers, (8.8%) not known to have COPD prior to health examination, (9.5%) moderate COPD category, (5.3%) above 60 years of age, and (4.2%) with comorbidity.

Conclusion: Most pilgrims with COPD were fit to fly without oxygen supplementation.

P-F-054

P-F-055

THE RELATIONSHIP BETWEEN COPD ASSESSMENT TEST (CAT) AND MODIFIED MEDICAL RESEARCH COUNCIL (MMRC) DYSPNOEA SCALE WITH FORCED EXPIRATORY VOLUME (FEV1) AND EXACERBATION IN STABLE COPD PATIENTS

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Background: COPD is considered a complex disease and global problem that is predicted to be the third most common cause of death by 2030. The 2014 GOLD (Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease [COPD]) consensus report uses symptoms, exacerbation history, and forced expiratory volume (FEV1)% to categorise patients according to disease severity and guide treatment.

Aims: To assess both the influence of symptom instrument choice on patient category assignment and prospective exacerbation risk by category combined COPD assessment.

Methods: We evaluated 100 patients with COPD stable were recruited from 2 centres in the North of Sumatera. Eligible patients were aged 45–80 years, had smoked for 10 pack-years or more, and had an FEV1/forced vital capacity (FVC) <0.7. Categories were defined with the modified Medical Research Council (MMRC) dyspnoea scale (score 0–1 vs ≥2) and the COPD Assessment Test [CAT] ≥ 10 vs <10) in addition to COPD exacerbations in the previous year (<2 vs ≥2), and lung function (FEV1% predicted).

Result: On the basis of the MMRC scale 1, 11 (73,3%) patients were assigned to category A, MMRC scale 2, 16 (61,5%) to category B. MMRC scale 1, 21 (65%) to category C, and MMRC scale 3,14 (51,9%) to category D. On the basis of the CAT < 10, 13 (86,7%) patients were assigned to category A. CAT ≥ 10, 27 (100%) to category D. The correlation between MMRC and the FEV1 % predicted was significant ($p = 0.002$, ANOVA test). There was a significant association between the FEV1 % predicted and total CAT score ($p = 0.002$, ANOVA test). The correlation between MMRC and exacerbation frequency was statistically significant ($p < 0.027$ ANOVA test). Significant heterogeneity in prospective exacerbation rates (exacerbations/person-years) were seen, especially in the D subcategories (70,4%, $N = 11$, chi-square test)

Conclusion: The relationship between CAT score and FEV1% predicted suggests that CAT is linked to severity of airflow limitation and GOLD classification in stable COPD patients. The GOLD classification emphasizes the importance of symptoms and exacerbation risk when assessing COPD stable. The choice of symptom measure influences category assignment. Exacerbation rates for patients in the highest risk category D were seen depending on whether risk was based on lung function, exacerbation history, or both.

TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT (TIOSPIR): ANALYSIS IN ASIA

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Introduction: The primary results from the global, multicentre Tiotropium Safety and Performance In Respimat (TIOSPIR) trial showed that tiotropium Respimat and HandiHaler once daily have a similar safety and exacerbation efficacy profile in patients with chronic obstructive pulmonary disease (COPD). We present here the results for the subgroup of patients in the Asia geographical region in TIOSPIR.

Methods: TIOSPIR, a large-scale ($n = 17,135$), 2–3 year, randomized, double-blind, parallel-group, event-driven trial, compared safety and efficacy of once-daily tiotropium Respimat 5 and 2.5 µg vs HandiHaler 18 µg in patients with COPD. Primary endpoints were the time to death (non-inferiority of Respimat 5 µg or 2.5 µg vs HandiHaler) and the time to first COPD exacerbation (superiority of Respimat 5 µg vs HandiHaler). Safety and, in particular, cardiovascular (CV) safety, including in patients with stable cardiac disease, was assessed.

Results: Overall, 2356 patients ($n = 774$, $n = 788$ and $n = 794$, respectively for tiotropium Respimat 5 µg, 2.5 µg and HandiHaler 18 µg) within Asia were randomized and treated for a mean duration of 691 days (mean follow-up duration of 786 days). Across groups, there was similar risk of death (measured as time to death): Respimat 5 µg vs HandiHaler hazard ratio (HR) (95% confidence interval [CI]) 0.96 (0.67,1.38); Respimat 2.5 µg vs HandiHaler HR (95% CI) 1.23 (0.87,1.73) for patients in Asia based on the vital status analysis. The HRs (95% CI) for the on-treatment analysis were 0.89 (0.60,1.34) for Respimat 5 µg vs HandiHaler and 1.06 (0.72,1.56) for Respimat 2.5 µg vs HandiHaler. Risk of exacerbation (measured as time to first exacerbation) showed no relevant difference between Respimat 5 µg and HandiHaler (HR [95% CI]: 0.99 [0.85,1.15], $p = 0.85$); however the risk was significantly increased with Respimat 2.5 µg vs Respimat 5 µg or vs HandiHaler (HR [95% CI]: 1.18 [1.02,1.38], $p = 0.03$; and 1.17 [1.004,1.35], $p = 0.04$, respectively). Risk of a major adverse CV event (MACE) was similar for Respimat 5 µg vs HandiHaler (HR [95% CI]: 1.02 [0.59,1.76], $p = 0.96$) and for Respimat 2.5 µg vs HandiHaler (HR [95% CI]: 1.20 [0.71,2.02], $p = 0.50$). The data did not indicate differences between groups in causes of death.

Conclusions: Analogous to the global analysis, similar safety and exacerbation efficacy profiles are observed for tiotropium Respimat 5 µg and tiotropium HandiHaler 18 µg in patients with COPD in the Asia region. Despite similar safety, the risk of exacerbations might be increased with the lower Respimat dose (2.5 µg once daily).

P-F-056

EFFECT OF AZYTHROMYCIN TO COPD ASSESMENT TEST (CAT) SCORES OF STABLE COPD OUTPATIENTS AT DR. M. DJAMIL HOSPITAL PADANG

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Background: Azythromycin is a macrolide that has effect as antibiotic and anti inflammation. This effects decrease progresivity of COPD. CAT is a simple questionnaire, useful and sensitive for assessing effect of COPD in daily life. The aim of this study is to evaluate impacts of 8 weeks azythromycin to CAT scores.

Method: A trial clinical study analyze 25 stable COPD outpatients who had given azythromycin 250 mg three times a week for 8 weeks. CAT scores was evaluated before and after treatment. Data was analyzed by using paired t test.

Result: The mean of age in this study is $69 \pm 6,9$ years, degree of COPD predominantly was severe (64%) and CAT score was moderate (96%). Azythromycin decrease CAT score from 14,52 to 12,48 ($p = 0,019$). Cough, sputum and tightness of chest were variables of CAT that have significant changes.

Conclusion: Eight weeks azythromycin 250 mg decreased CAT scores, particularly for three variables; cough, sputum production and tightness of chest.

P-F-057

TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT (TIOSPIR): GEOGRAPHICAL ANALYSIS OF ASIA VERSUS REST OF THE WORLD

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Introduction: The TIOtroprium Safety and Performance In Respimat (TIOSPIR) trial showed that tiotropium Respimat and tiotropium HandiHaler have a similar safety and exacerbation efficacy profile in patients with chronic obstructive pulmonary disease (COPD). We sought to determine whether geographical region affected outcome, and present here results for the Asia geographical region comparison with the rest of the world (RoW).

Methods: TIOSPIR, a large-scale (n = 17,135), 2–3 year, randomized, double-blind, parallel-group, event-driven trial, compared safety and efficacy of tiotropium Respimat 5 and 2.5 µg once daily with HandiHaler 18 µg once daily in patients with COPD. Based on the similar efficacy and safety results between treatment arms in the primary analysis, treatment arms were pooled, and results determined for the Asia versus RoW regions.

Results: A total of 2356 and 14,779 patients were randomized and treated within Asia and RoW, respectively. Risk of death (time to death) was similar between Asia and RoW: hazard ratio (HR) [95% confidence interval (CI)]: 1.15 [0.99,1.35] for data including vital status follow up and for all treatment groups pooled by region. The risk of exacerbation (time to first exacerbation) was lower in Asia vs RoW (HR [95% CI]: 0.84 [0.78,0.89]; p < 0.0001), as was the annual exacerbation rate (rate ratio [RR] [95% CI]: 0.83 [0.77,0.89], p < 0.0001). However, severe exacerbations occurred more often in Asia (RR [95% CI]: 1.62 [1.43,1.83], p < 0.0001). Although the overall mortality was similar for both regions (RR [95% CI]: 1.14 [0.98,1.33]), deaths due to cardiac disorders was numerically less frequent (RR [95% CI]: 0.44 [0.16,1.20]) and those due to respiratory, thoracic and mediastinal disorders were commoner (RR [95% CI]: 1.81 [1.41,2.32] in Asia; most respiratory deaths were due to COPD exacerbations. The risk of major cardiovascular adverse event (MACE) or fatal MACE was similar for both regions (HR [95% CI]: 0.95 [0.75,1.20] and 1.04 [0.76,1.43]).

Conclusions: Patients with COPD treated with tiotropium Respimat 5, 2.5 µg or HandiHaler 18 µg within Asia present different adverse event and exacerbation efficacy profiles to those in the RoW. Although the total mortality rate was similar for both regions, the causes of death differed with less cardiac and more respiratory causes in Asia. Patients in Asia reported fewer exacerbations overall, but a higher share of severe exacerbations than in the RoW. Geographical differences in patient recruitment may impact the likelihood of particular outcomes in trials of COPD treatment.

P-F-058

LONG-TERM EFFECT OF HOME NURSING INTERVENTION ON COST AND HEALTHCARE UTILIZATION FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim of Study: As the disease progresses, COPD patients suffer gradual decreases in lung function, exercise tolerance, and health-related quality of life (HRQOL). Home nursing is one of the interventions that may maintain the patient's optimal respiratory state and health status. The present study aimed to examine the long-term effects of a home nursing intervention on healthcare utilization and costs among patients with chronic obstructive pulmonary disease (COPD).

Methods: Eleven COPD patients who had received home nursing intervention after hospital discharge were enrolled. Our home nursing intervention consisted of regular home visits and the components of the home nursing intervention included the following: (1) a check of the patient's status, disease prognosis and mental health, (2) education on the management of acute exacerbations, (3) drug consultation and education on inhalation techniques, (4) maintenance of a healthy lifestyle (smoking cessation, nutrition, sleep habits), and (5) confirmation of and education about home exercise. We retrospectively investigated their healthcare utilization and costs for 1 year before the intervention and during 2 years of the intervention. Normal distribution variances were analyzed using one-way repeated measures ANOVA, while non-normal distribution variances were analyzed using Friedman's ANOVA by ranks. The Bonferroni test was used as the post hoc test.

Results: The number and length of hospitalizations decreased gradually from the preintervention period through the 2nd year (p < 0.05). The number of hospital and home nursing visits increased from the pre-intervention period through the 1st and 2nd years (p < 0.05). The hospitalization costs were decreased by approximately half from the pre-intervention period through the 1st year (p < 0.05) and from the 1st year through the 2nd year (p < 0.05). The total medical cost did not change significantly. Lung function, arterial blood gas measurements, exercise tolerance, and HRQOL did not change significantly from before the intervention through the 2nd year of intervention.

Conclusions: Our home nursing intervention decreased the number and length of hospitalizations and the hospitalization costs; however, it did not affect the total medical cost. It is possible that the continuation of home nursing interventions may decrease the number of hospitalizations, number of home nursing visits, and the total medical cost by maintaining the health condition of patients.

P-F-059

P-F-061

RELATIONSHIP BETWEEN EXERCISE-INDUCED DESATURATION AND DYSPNOEA DURING THE 6-MINUTE WALKING TEST IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim of Study: The 6-minute walking test (6MWT) is used to evaluate exercise tolerance in patients with chronic obstructive pulmonary disease (COPD). Compared to the amount of research on the relationship between 6MWT and disease severity or probability of survival, few studies have analyzed exercise-induced desaturation (EID) and exertional dyspnea in relation to 6MWT. The purpose of this study was to investigate whether 6MWT leads to dyspnea and EID in patients with COPD.

Methods: We enrolled 73 stable COPD outpatients at our hospital. We measured the body mass index, forced expiratory volume in 1 second (FEV₁), %FEV₁, diffusing capacity of lung for carbon monoxide (%DLco), %DLco/alveolar volume (%DLco/VA), 6-minute walking distance (6MWD), modified Borg scale, and oxygen saturation by pulse oximetry (SpO₂) during 6MWT. We applied the following exclusion criteria: 1) ongoing long-term oxygen therapy, 2) more than a fortnight difference between the dates of a lung function test and 6MWT, and 3) right ventricular systolic pressure >50 mmHg. Pearson's product-moment correlation coefficient or Spearman's rank-correlation coefficient was used for statistical analysis according to the variable characteristics.

Results: We included 21 patients with stable COPD (2 females). COPD was mild (The Global Initiative for Chronic Obstructive Lung Disease stage; GOLD I) in 19.0%, moderate (GOLD II) in 28.6%, severe (GOLD III) in 38.1%, and very severe (GOLD IV) in 14.3% of cases. There was a significant correlation between the minimum value of SpO₂ and %DLco ($r = 0.66$, 95% confidence interval [CI]: 0.16 to 0.81, $p = 0.001$) and DLco ($r = 0.51$, 95% CI: 0.05 to 0.76, $p = 0.01$). The maximum value of the modified Borg scale correlated with FEV₁ ($r = -0.50$, 95% CI: -0.77 to -0.08 , $p = 0.02$) and %FEV₁ ($r = -0.65$, 95% CI: -0.85 to -0.30 , $p = 0.001$). 6MWD results correlated with FEV₁ ($r = 0.55$, 95% CI: 0.15 to 0.80, $p = 0.009$) and %FEV₁ ($r = 0.50$, 95% CI: 0.08 to 0.78, $p = 0.02$).

Conclusion: Our results suggest that EID during 6MWT is related to %DLco and %DLco/VA. Exertional dyspnea and 6MWD may be related to FEV₁ and %FEV₁. It is important to examine EID and exertional dyspnea in patients with COPD. When used in conjunction with spirometric evaluation, 6MWT can aid in early detection of combined pulmonary fibrosis and emphysema (CPFE). Further research of EID during 6MWT is warranted.

P-F-060

RECOVERY PROCESS AFTER 6-MINUTE WALK TEST IN STABLE COPD PATIENTS

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Aim: The purpose of this study was to examine the recovery process after a 6-minute walk test (6MWT) in stable COPD patients.

Methods: Twelve patients with stable COPD (11 male, age; 72.5 ± 6.0 years old, BMI; 20.7 ± 4.7 , FEV_{1.0}/FEV; 53.2 ± 20.2 %) took part in this study. Throughout the 6MWT, oxygen uptake, carbon dioxide production, minute ventilation, and heart rate were measured using a portable cardiopulmonary exercise system (MetaMax 3B, Cortex, Germany). Dyspnea and oxygen saturation were recorded at the end of each 2 minute during the 6MWT. Dyspnea was measured using the Borg CR-10 dyspnea scale. oxygen saturation was measured using the pulse oximetry.

Results: This study showed that the distance walked in the 6MWT was 524.2 ± 58.9 m, the peak oxygen uptake was 15.1 ± 2.9 ml/min/kg, oxygen saturation showed 90.4 ± 4.4 %, and the Borg CR-10 dyspnea scale at the end of the 6MWT was 5.0 ± 2.7 , respectively. In the 6MWT, oxygen uptake and oxygen saturation changed significantly during the first 2 minutes, then showed a steady-state profile. The dyspnea scale increased gradually. After 6MWT was finished, all measurements were significantly restored. The oxygen uptake was restored after 4 minutes, and oxygen saturation was restored after 2 minutes.

Conclusions: We focused on the recovery of the 6MWT in stable COPD patients, and suggested that there were differences in oxygen uptake, oxygen saturation, and the dyspnea.

P-F-062

ASSOCIATION OF TUMOUR NECROSIS FACTOR ALPHA (TNF α) LEVEL WITH SEVERITY OF AIRFLOW LIMITATION IN STABLE COPD PATIENT IN ADAM MALIK GENERAL HOSPITAL

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Background: Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation that is usually progressive resulting from chronic inflammation, mainly due to tobacco exposure. Tumour necrosis factor alpha (TNF α) is a pro-inflammatory pleiotropic cytokine primarily produced by activated macrophages that plays a significant role in pathophysiology of COPD.

Objective: The purpose of this study was to measure serum TNF α levels in stable COPD patients and to investigate the association of serum TNF α levels with severity of airflow limitation.

Materials and Methods: A descriptive study was conducted on 40 stable COPD patients at Pulmonary Clinic Adam Malik General Hospital from October to November 2013. Eligible patients were patients aged 40–80 year, current smoker or ex-smoker with smoking history of ≥ 200 Brinkman index (IB), and have been confirmed by spirometry test with FEV1/FVC < 0.7 . Classification of airflow limitation severity was defined with GOLD 1 (mild: FEV1 $\geq 80\%$ predicted), GOLD 2 (moderate: $50\% \leq$ FEV1 $< 80\%$ predicted), GOLD 3 (severe: $30\% \leq$ FEV1 $< 50\%$ predicted), GOLD 4 (very severe: FEV1 $< 30\%$ predicted). Serum TNF α levels were assessed by ELISA.

Result: From the 40 subjects enrolled, there was no significant differences between serum TNF α levels with various parameters (Body mass index (BMI) and Brinkman Index) with p value of 0.149 and 0.313. Serum TNF α levels were 7.034 ± 7.88 pg/ml in patients with GOLD 2, 6.123 ± 6.06 pg/ml in patients with GOLD 3, and 4.865 ± 1.67 pg/ml in patients with GOLD 4 ($p = 0.757$). There was no significant association of serum TNF α levels with severity of airway limitation.

Conclusion: This study indicates that there was no significant association of serum TNF α levels with severity of airflow limitation in stable COPD patients.

P-F-064

META-ANALYSIS ON STATINS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Research Question: Among patients with chronic obstructive pulmonary disease, how effective are statins in improving exercise tolerance and pulmonary function indices in a randomized control trial?

Background: Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease characterized by progressive airflow limitation. Statins have anti-inflammatory and immunomodulating properties that could alter inflammation of the airways. The objective of this study is to systematically evaluate the effectiveness of adjunct statin therapy in improving exercise tolerance and pulmonary function indices in patients with chronic obstructive pulmonary disease.

Search Strategy and Inclusion Criteria: A thorough search was done using Medline and PubMed, with limits set on studies involving humans in a randomized control trial in English that examined the effect of statins in COPD.

Study Manoeuvre: All the articles retrieved were appraised separately and independently by two reviewers for its applicability and validity. We evaluated the methodological quality of the randomized control trials by assessing allocation, blinding, and if follow up rate was adequate. Disagreements between the reviewers were resolved by consensus. Randomized, double-blinded, single-blinded or placebo controlled studies were included.

Statistical Analysis: Data collected were analyzed using Review Manager Version 5.2.

Results: A total of two articles met the selection criteria. Outcome shows improvement in exercise time (treadmill test) at 95% CI, with statistically significant benefit with mean difference of 335.18 [253.93, 416.43] favouring Pravastatin group. The studies show inconclusive results for Pravastatin in improving FEV1(%) with 95% CI with mean difference of 0.05 [–4.61, 4.7]. The outcome in total lung capacity shows inconclusive results but shows a trend towards benefit with 95% CI with mean difference of –0.08 [–0.46, 0.30]. Inspiratory capacity results at 95% CI with mean difference of 0.13 [–0.06, 0.32] showed an inconclusive outcome but has a trend towards benefit. Improvement in the Borg dyspnoea score at 95% CI, showing statistically significant benefit with mean difference of –2.91 [–3.19, –2.63] favouring the Pravastatin group.

Conclusions: Statins already have an established role in treating cardiovascular patients because of their cholesterol-lowering ability, but also have anti-inflammatory and immunomodulatory effects that are beneficial in airway inflammation in COPD. Statin administration to COPD patients showed amelioration in exercise tolerance, improvement in dyspnoea scores and augmentation in pulmonary function indices. Thus, statins may be useful as adjunct to currently available therapies as well as improvement in lipid status.

P-F-063

RELATIONSHIP BETWEEN PLATELETS, C-REACTIVE PROTEIN AND DEGREE OF SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: The stable COPD is associated with low grade systemic inflammation as demonstrated by an increase in blood leukocytes, acute phase proteins such as C-reactive protein (CRP), and inflammatory cytokines. Indicator of systemic inflammation, levels of TNF- α , IL-8 and IL-6 are measured frequently. Examination of the platelet count as an indicator of systemic inflammation in COPD is still underrated and less attention to be investigated. Whereas examination of platelet easy, inexpensive and can be done in any centre. So for these reasons researchers assess the importance of doing research. The aims of study is to determine the value of platelets and levels of CRP as a marker of inflammation and indicators of severity of COPD.

Objective: This study was conducted to investigate the relationships between platelet, CRP and the degree of severity of COPD.

Methods and Patients: This study was a cross-sectional observational analytic. Subjects were COPD patients, which at the outpatient Pulmonary clinic of Dr. Soetomo Hospital and meet the inclusion and exclusion criteria.

Result: The correlation between the platelets with COPD subject groups amounted to 0.159 with a significance level of 0.341, the correlation between the MPV with COPD subject groups amounted to 0.067 with a significance level of 0.689, while the correlation between CRP group of subjects with COPD patients was 0.464 with a significance level of 0.003.

Conclusion: The higher the CRP levels, the higher the degree of severity of COPD patient subjects. But there is no significant relationship between Platelets and MPV with a group of patients with COPD subjects.

P-F-065

P-F-067

RAISED CRP LEVELS ASSOCIATED WITH MUSCLE WASTING IN PATIENTS WITH COPD

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COPD is no more just an airway disease, but due to the chronic inflammatory state of this disease there is an increase in the prevalence of muscle wasting in patients with COPD. As C-reactive protein (CRP) is a marker of systemic inflammation, we tried to correlate CRP levels with presence of muscle wasting in patients with COPD.

Methods: We evaluated 50 cases with COPD (both male and female, age ranging 45 to 65 year) for muscle wasting, with clinical observation of muscle mass, muscle tone, and measurement of muscle girth 15 cm. above the upper border of patella. We also performed quantitative CRP levels of all the patients included in study. Obtained results analyzed statically to find out correlation between raised CRP titre and muscle wasting in patients with COPD.

Results: In our study we found total 13 patients (26%) has muscle wasting. out of these 13 only one patient had normal CRP levels (<.66 mg/dl), rest 12 patients had raised CRP levels. We found that raised CRP levels had significant positive correlation with muscle wasting ($\chi^2 = 6.842$; $p = 0.008$) in patients with COPD.

Conclusion: Raised CRP titre had positive correlation with muscle wasting in COPD patients.

Reference:

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P-F-066

P-F-068

COMPARISON OF THE EFFECTS OF SINGLE INHALATIONS OF FORMOTEROL AND TIOTROPIUM BROMIDE ON EARLY-PHASE PULMONARY FUNCTION AND SYMPTOMS IN A RANDOMIZED CROSSOVER STUDY

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Aims: To compare the improvements in early-phase pulmonary function and symptoms induced by single inhalations of formoterol (FOM) dry powder (DPI) and tiotropium bromide (TIO) DPI in patients with chronic obstructive pulmonary disease (COPD).

Methods: Fifty-two outpatients with COPD (GOLD stage 2 or 3) were enrolled in this study and assigned either to groups that initially received a single inhalation of FOM DPI (9 µg via Turbuhaler®) or of TIO DPI (18 µg via a HandiHaler® device), and were then switched to the other group in a randomized, open-label, crossover study. Pulmonary function testing was performed before and 15, 60, and 120 min after single administrations of each drug. Various indexes of pulmonary resistance (assessed with a Mostgraph®) were also measured before and 3, 7, 10, 15, 30, 60, and 120 min after treatment. The subjective effects of the drugs were assessed on a visual analog scale (VAS) completed by the patients before and 120 min after each treatment.

Results: FEV1 values had significantly improved 15 min after single inhalations of either FOM ($p = 0.002$) or TIO ($p = 0.026$) and remained so 120 min after each treatment. R5 values, an index of pulmonary resistance on the Mostgraph®, had significantly decreased 10 min after inhaling FOM ($p = 0.007$) and were still improved at 120 min, whereas those after TIO did not. Resonant frequency indexes, which mainly reflect peripheral airway resistance, had significantly decreased 3 min after inhaling FOM ($p = 0.034$) and remained improved at 120 min, whereas those after TIO did not. Low frequency reactant indexes, which also reflect peripheral airway resistance, had significantly decreased 30 min after inhaling FOM ($p = 0.005$) and remained improved at 120 min, whereas those after TIO did not. VAS scores significantly improved in both FOM and TIO groups ($p < 0.001$ and $p < 0.001$, respectively).

Conclusion: The findings of this randomized crossover study suggest that FOM better improves early-phase pulmonary function and symptoms in patients with COPD than TIO.

A SURVEY ON COPD DIAGNOSIS AMONG PRIMARY CARE PHYSICIANS IN MALAYSIA

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Background and Objectives: Chronic obstructive pulmonary disease (COPD) remains underdiagnosed due in part to limited access or under-utilization of spirometry. This survey aimed to explore the approach and knowledge of primary care physicians (PCP) on COPD diagnosis in Malaysia.

Methods: This is a nation-wide, multiple-choice-questionnaire-based COPD survey that was carried out from September 2013 to October 2013 among PCP working in private and public healthcare settings who attended the “Managing Asthma and COPD Effectively (MACE)” workshop conducted in various parts of Malaysia.

Results: 200 PCP was surveyed during this programme. The results of the survey showed that a large proportion of PCP in the private healthcare setting (40.2%) diagnosed COPD based solely on symptoms and signs as compared to those in the public setting (25.0%). Similarly, the proportion of PCP who had never used spirometry in COPD diagnosis was significantly higher among the PCP in the private setting compared to those in the public setting (53.7% vs 28.0%, $P = 0.001$). Besides, PCP who were ≥ 10 years of service were more likely to skip spirometry completely in COPD diagnosis compared with those who practise less than 10 years (49.0% vs 28.8%, $P = 0.009$).

Conclusion: The survey identified significant differences in diagnostic approach for COPD between the PCPs in the private and public settings; and between the senior and less senior PCPs. Notwithstanding, 28 – 53.7% of the PCPs had never used spirometry in their diagnosis of COPD despite national and international COPD guidelines recommendations.

EFFICACY OF INDACATEROL VERSUS LONG-ACTING BETA-ADRENECEPTOR AGONISTS IN DECREASING DYSPNOEA AND EXACERBATION IN MODERATE TO SEVERE COPD: A META-ANALYSIS

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Background: Indacaterol, a novel once daily inhaled ultra long-acting beta-2 agonist marks a significant therapeutic development in COPD by simplifying management especially in terms of reduction in dosing frequency, and possibly increasing compliance and adherence to treatment.

Objectives: To compare the efficacy of indacaterol with formoterol or salmeterol in reducing acute exacerbations and improving dyspnoea in patients with moderate to severe COPD.

Methods: A computerized search was done in MEDLINE, NICE, and CENTRAL for relevant articles. Other publications were searched and authors were contacted for additional information. Randomized controlled trials of 12 weeks or longer duration comparing indacaterol with salmeterol or formoterol were included for this meta-analysis. Primary outcomes were reduction in daily as-needed salbutamol use and increase in the number of days with no-use of salbutamol. Secondary outcomes included improvement in TDI score and the likelihood of achieving MCID for TDI score.

Results: Three eligible RCTs of low-risk bias employed a total of 3855 patients. Indacaterol was superior to long-acting beta agonists in decreasing the number of salbutamol puffs per day (WMD = -0.21, 95% CI: -0.35, -0.06) and increasing baseline Transitional Dyspnea Index (TDI) score (WMD = 0.55, 95% CI: 0.35, 0.75). It significantly increased the percentage of days without salbutamol use (WMD = 5.59, 95% CI: 2.83, 8.35, $P < 0.0001$), while patients using indacaterol had a higher likelihood of achieving minimum clinically important difference (MCID) in their TDI scores (OR = 1.36, 95% CI: 1.18–1.55, $P < 0.0001$). The difference was not significant between doses in terms of all outcomes, and higher doses provided marginal benefits.

Conclusion: Indacaterol showed comparable efficacy compared to salmeterol and formoterol in decreasing daily as-needed salbutamol use and increasing TDI score from baseline. It was clinically superior to both LABAs in achieving the minimum clinically important difference of TDI scores.

P-F-069

OSTEOPOROSIS IS ADDING PAIN TO THE LIFE OF PATIENT WITH C.O.P.D.

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COPD is no more just an airway disease, but due to the chronic inflammatory state of this disease there is an increase in the prevalence of osteoporosis in patients of COPD1. We investigated the proven case of copd2 for prevalence of osteoporosis.

Methods: We evaluated 65 cases with COPD (both male and female, age ranging between 45 to 65 year) with the help of dual energy radiography absorptiometry (DEXA SCAN) of A.P. spine. Then we analyzed bone mineral density, young adult T score, and age matched z-score.

Results: In our study we found that 61.54% patients are having a decrease in bone mineral density. In addition, 67.80% patients have osteopenia³ and 35.40% patients have osteoporosis³. While 72.31% patients were suffering from backache. We also found out that 3 out of 65 patients have pathological fractures.

Conclusion: Osteoporosis is highly prevalent in patients with COPD and early intervention is required to prevent it and its consequences like back pain and pathological fractures.

P-F-071

POLYVALENT MECHANICAL BACTERIAL LYSATE IN ADVANCED COPD; A RANDOMIZED CONTROLLED TRIAL

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Introduction: COPD exacerbation is a common complication that significantly contributes to the high morbidity, mortality and costs associated with COPD, especially in advanced disease. Bacterial immunostimulation has been advocated as a management strategy in COPD for the purposes of preventing acute exacerbations. Polyvalent Mechanical Bacterial Lysate (PMBL) is believed to nonspecifically increase the immune response or augment innate defense mechanisms.

Methods: We conducted a randomized controlled double blinded trial at Respiratory clinic at Teaching Hospital, Kandy. All COPD patients with moderately severe or severe disease staging, presenting during May-September in 2012 were assessed. Out of them we recruited patients who are stabilized on combined salmeterol/fluticasone and tiotropium inhaler treatment for minimum of three months, not on long-term oxygen and who had minimum of three infective exacerbations over the preceding one year. They were randomly allocated to treatment or control arms. Treatment arm was given sublingual PMBL daily on first ten days of three successive months. All were followed up for six months.

results: We recruited 24 patients to treatment arm and 21 patients to control arm. All were males in the age range of 50–85 years. In the treatment arm initial COPD Assessment Test (CAT) score was 18.92 \pm 0.62 (mean \pm SD). At six months mean CAT score was 14.5 \pm 2.0. The mean improvement was 4.42 which was non-significant ($p = 0.1050$). In the control arm the initial and end mean CAT scores were 20.9 \pm 2.12 and 18.09 \pm 2.17 respectively. The improvement was 2.81 ($p = 0.3603$). Both treatment and control groups had a similar number of infective exacerbations requiring antibiotic treatment over the study period. They were 3.58 \pm 0.62 and 3.62 \pm 0.57 respectively ($p = 0.9670$).

Conclusion: We observed a larger, albeit non-significant, improvement of CAT score among patients receiving PMBL compared to controls, over a six month follow up. However the study did not demonstrate a reduction in infective exacerbations with PMBL in advanced COPD.

P-F-070

EVALUATION OF THE PULMONARY FUNCTION TESTS OF THE PATIENTS WHO WERE REFERRAL FROM PRIMARY CARE DOCTORS FOR THE CHRONIC COUGH

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Background: Diagnosis of pulmonary disease in primary care is complex in some cases. Although diagnosed as asthma or chronic obstructive pulmonary disease (COPD), the pulmonary function test may not be undergone. We examined whether diagnosis and medical treatment would have an advantage by hospital and clinic cooperation.

Methods: The subjects were 30 consecutive patients who presented to Respiratory Disease Center, Chiba Hokusoh Hospital, Nippon Medical School, Chiba, Japan between October 2013 and June 2014. All the patients were referral from primary care doctors for a checkup of the lung condition. Chest X-ray, blood tests and pulmonary function tests were performed at our hospital. Parameters of pulmonary function tests were measured according to the American Thoracic Society guidelines using a pulmonary function instrument with computer processing (CHESTAC-9800; CHEST Co., Tokyo, Japan). FEV1 was measured again 10–15 minutes after a short-acting beta2-agonist is given. Chest computed tomography and bronchoscopy were performed, if needed.

Results: The mean age was 56.2 \pm 18.4. 15 males and 11 females. The diagnosis were 2 COPD, 3 bronchial asthma, 4 cough variant asthma, 2 interstitial pneumonia, 2 rhinitis, 2 tumours and 1 sarcoidosis. The case considered to be asthma COPD overlap syndrome (ACOS) also existed.

Conclusion: The undiagnosed patient was found by hospital and clinic cooperation. It was suggested in diagnosis and medical treatment that construction of a regional network was important. We will publish details of the study results at the 19th congress of the Asian Pacific Society of Respirology (APSR).

P-F-072

ANTIBIOTIC EFFECTS AGAINST INTERLEUKIN 8 (IL-8) SPUTUM AND DYSPNOEA SCALE IN STABLE COPD

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammation of the airway that is persistent and progressive. Patient with stable COPD frequently have bacterial colonization in lower respiratory tract and become potential trigger for airway inflammation. Bacterial colonization stimulates the expression of IL-8 in epithelial cells and increases the rate of IL-8 in sputum. Antibiotics treatment can reduce the rate of IL-8 sputum significantly thereby reducing the symptoms of shortness of breath.

Methods: Pre and post prospective study of patients with stable COPD that had potential bacterial pathogen in sputum from Pulmonary Clinic in M. Djamil Hospital, Center for Pulmonary Disease Treatment (BP4 Lubuk Alung). Subject was given antibiotics for 7 days according to the results of sputum culture and sensitivity. Twenty two subjects fulfilled the criteria for inclusion. Sputum IL-8 rate and MMRC scale before and after the administration of antibiotics were examined.

Results: Twenty two sample was observed, 100% were male and ex-smokers with hypertension comorbid disease (18,18%). COPD grade 3 is the most (50%) with 14 subjects MMRC scale 3 (63,34%). IL- 8 before administration was 766.64 \pm 193.24 and after administration was 438.46 \pm 135.38, and it is significant. There is no difference in MMRC scale before and after administration antibiotic.

Conclusion: Antibiotic reduce IL- 8 rate significantly and not affect MMRC scale.

P-F-073

P-F-074

COMPARISON OF MONOTHERAPY WITH A LONG-ACTING MUSCARINIC ANTAGONIST VERSUS COMBINATION THERAPY WITH A LONG-ACTING MUSCARINIC ANTAGONIST PLUS A LONG-ACTING BETA2-AGONIST IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim of the Study: To investigate the time-course effects of long-acting muscarinic antagonist (LAMA) monotherapy versus LAMA plus long-acting beta2-agonist (LABA) combination therapy in patients with chronic obstructive pulmonary disease (COPD).

Methods: Patients newly diagnosed with COPD at Chiba Hokusoh Hospital were randomized to receive either LAMA monotherapy or LAMA/LABA combination therapy. During the 1-year follow-up period, changes in the pathological condition were analyzed based on pulmonary function test values; COPD Assessment Test (CAT) scores; modified Medical Research Council scores; total (R5), central (R20), and peripheral (R5-R20) airway resistance values; and airway resistance by the interrupter technique (Rint).

Results: Twenty patients (all were male [year], 69.96 ± 9.97 [mean \pm SD]) were analyzed. Of the twenty patients, 10 patients were in the LAMA/LABA combination therapy group, and other 10 patients were in the LAMA monotherapy group. In the entire patient population of this study, none of the analyzed variables showed a significant change over time. In the LAMA/LABA combination therapy group, %FEV1.0/predicted FEV1.0 and FEV1.0 showed significant improvement at Month 1 (%FEV1.0/predicted FEV1.0: 61.25 ± 30.51 vs. 65.31 ± 32.63 , $p = 0.014$; FEV1.0: 1.32 ± 0.56 vs. 1.40 ± 0.56 , $p = 0.0055$), but showed no significant change from baseline at Month 2 and later. CAT scores showed no significant improvement throughout the observation period in the combination therapy group compared with the LAMA monotherapy group. Increases in R5 and R20 are considered to reflect peripheral airway disease. In this study, R5 and R20 in the expiratory phases showed significant improvement in the combination therapy group up to Month 1 (R5 in the expiratory phase: 4.43 ± 1.89 vs. 5.18 ± 2.00 , $p = 0.018$; R20 in the expiratory phase: 3.22 ± 1.16 vs. 3.72 ± 1.28 , $p = 0.036$), but no significant improvement at Month 2 and later.

Conclusion: LAMA/LABA combination therapy, as compared with LAMA monotherapy, improved pulmonary function test values and Airway resistance measurements only for a short period. We will publish details of the study results at the 19th congress of the Asian Pacific Society of Respirology (APSR).

RATIONALIZED MEDICATION PRESCRIBING FOR COPD PATIENTS FOLLOWING GOLD GUIDELINE IN RAMATHIBODI HOSPITAL

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Introduction: The main driver of treatment cost in COPD is exacerbation requiring hospitalization. Since GOLD recommended COPD medications based on patient symptoms and future risks include lung function. Undertreated COPD is not uncommon. However, over-treatment is associated with adverse effects.

Objective: To identify the appropriateness of medication for COPD patients who were treated at Ramathibodi according to GOLD guideline, and the association with exacerbation.

Study Design: This retrospective cohort study in 2013 reviewed the electronic medical records of 1608 COPD patients. Further computer generated ratio yielded a ratio of 2:1 to 804 patients. Final 109 cases with completed lung function test were selected. Exacerbation was defined by Anthonison criteria. Prescribed medication appropriateness was according to GOLD 2013.

Results: There were 109 enrolled COPD patients with completed data. Mean age was 71.0 years having mean post bronchodilator FEV1 $63.6 \pm 20.3\%$. COPD with post BD FEV1 $\geq 50\%$ predicted (GOLD 1 and 2) were 77.1% and those with post BD FEV1 $< 50\%$ predicted (GOLD 3 and 4) were 22.9% at index dates. Hence patients experienced exacerbations in the past year after index dates were noted in 22 cases (26.1%) in GOLD stage 1 & 2, and 20 cases (80%) in GOLD stage 3 and 4. The mean frequency of GOLD stage 1 & 2 exacerbation in the past year was 1.36 (95% CI: 1.1–1.6) while GOLD stage 3 & 4 had mean frequency of 2.5 (95% CI: 1.59–3.4). Patients were classified as being treated with appropriate and inappropriate COPD medications based on GOLD stages. Accordingly, 43.1% of patients received appropriate medications for their COPD stages. Nevertheless, 54.1% received overtreatment and 2.8 received undertreated regimens according to their GOLD stages. There was a significant association between being prescribed appropriate or inappropriate medication, and the presence or absence of exacerbation ($p = 0.002$). Of the total 42 patients who experienced exacerbations, 9 among 13 patients in GOLD stage 1 and 2 received inappropriate medications. Despite receiving appropriate medications, 19 among 20 patients in GOLD stage 3 and 4 suffered from exacerbation after the indexed date of treatment commencement.

Conclusion: More frequent exacerbation was noted in patients with severe airflow obstruction. Inappropriate medications in the less severely obstructed, were associated with exacerbation. Despite receiving appropriate drugs, COPD exacerbations in severely obstructed COPD patients, were common.

P-F-075

IMMUNE INFLAMMATION IN PATIENTS WITH OBESITY-ASSOCIATED ARTERIAL HYPERTENSION DEPEND ON BRONCHIAL OBSTRUCTION PRESENCE

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Objective: Recent evidence suggests close obesity and arterial hypertension association. Both pathological states are characterized by low-grade inflammation which result in adipokines dysfunction: increased activity of proinflammatory cytokines, such as tumour necrosis factor - α (TNF- α), interleukin-6 (IL-6), C-reactive protein (CRP) and decreased activity of anti-inflammatory cytokines - interleukin-10 (IL-10). The aim of our research was study the relationships between serum TNF- α , IL-10, IL-6 concentrations and external breathing function disorders in hypertensive patients with obesity.

Design and Methods: 55 patients with arterial hypertension (AH) were examined. Serum TNF- α , IL-10, IL-6, CRP levels by ELISA were detected. All patients underwent anthropometry, office BP measurement, and spirometry. Patients were divided into 3 group, depending on body mass and FEV1 means: 1st Group - hypertensives with normal body mass; 2nd Group - obesity-related hypertensives without bronchial obstruction (FEV1 > 80%); 3rd Group - obesity-related hypertensives with bronchial obstruction (FEV1 < 80%).

Results: Serum TNF- α (1st Group 3.32 \pm 1.3 pg/ml, 2nd Group 6.37 \pm 0.6 pg/ml, 3rd Group 13.78 \pm 4.1 pg/ml; $p < 0.05$ in all cases); IL-6 (1st Group 10.27 \pm 3.2 pg/ml, 2nd Group 18.29 \pm 1.4 pg/ml, 3rd Group 25.42 \pm 2.9 pg/ml; $p < 0.05$ in all cases) and CRP (1st Group 1.73 \pm 1.3 mg/ml, 2nd Group 5.21 \pm 0.3 mg/ml, 3rd Group 7.87 \pm 1.1 mg/ml; $p < 0.05$ in all cases) levels increasing were found in relation to obesity and bronchial obstruction development. IL-10 serum levels decrease depended on obesity progression to attain minimum means in AH patients with obesity and bronchial obstruction syndrome (1st Group 9.25 \pm 1.8 pg/ml, 2nd Group 6.57 \pm 0.5 pg/ml, 3rd Group 4.05 \pm 0.9 pg/ml; $p < 0.05$ in all cases).

Conclusion: Obtained data demonstrate that TNF- α , IL-6, CRP level elevated and IL-10 levels reduced with maximum changes in obesity-associated arterial hypertension with obstructive disorders of external breathing function. Our results suggest a possibility of TNF- α , IL-6, CRP and IL-10 involvement in the development of obstructive type of ventilation disorder in patients with AH and obesity.

P-F-076

THE PREVALENCE OF AIRWAY OBSTRUCTION AMONG JAPANESE HIV-POSITIVE MALE PATIENTS COMPARED WITH GENERAL POPULATION: A CASE-CONTROL STUDY OF SINGLE CENTER ANALYSIS

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Background and Objective: Previous studies have suggested that human immunodeficiency virus (HIV) infection and/or the airway colonization of *Pneumocystis jirovecii* (Pcj) impact on the progression of airway obstruction, such as chronic obstructive pulmonary disease (COPD). This study was aimed to evaluate the relationship between HIV infection, airway colonization of Pcj and airway obstruction in Japanese male patients.

Methods: Case-control study of 49 HIV-positive and 257 HIV-negative men were enrolled in this study. Airway obstruction was determined by spirometry. Cigarette smoking was determined by a self report. Laboratory data were obtained from medical records. Among HIV positive patients, the airway colonization of Pcj was evaluated by induced sputum using the real time polymerase chain reaction method.

Results: Forty-eight out of 49 (97.9%) HIV-positive patients received antiretroviral therapy, and their median CD4 cell counts were 491/mL (79–935). The prevalence of airway obstruction as determined by spirometry was 10.2% (5/49) in HIV-positive subjects and 2.4% (5/208) in HIV-negative subjects ($p = 0.024$). Compared with the control group, HIV-positive patients were significantly younger (median age 44 vs 40, $p = 0.019$). After adjusting for age, pack-years of smoking, HIV infection was an independent risk factor for airway obstruction (OR; 10.93, 95%CI 1.99e60.1, $p = 0.006$). None of patient was detected the airway colonization of Pcj.

Conclusions: HIV infection was an independent risk factor for airway obstruction regardless of airway colonization of Pcj. Health-care provider should be aware of the increased likelihood of airway obstruction among HIV-positive patients.

P-F-077

DIAGNOSIS AND QUANTIFICATION OF EXCESSIVE DYNAMIC AIRWAY COLLAPSE (EDAC) IN COPD USING DYNAMIC 320-SLICE CT

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Background and Objectives: Expiratory tracheal narrowing causing obstruction may contribute to dyspnoea in chronic obstructive pulmonary disease (COPD). Airflow limitation can result from excessive dynamic airway collapse (EDAC) or tracheobronchomalacia (TBM). Both conditions require accurate quantification and diagnosis but normative data and quantitative diagnostic criteria are lacking.

Methods: We used dynamic 320-slice computed tomography to quantitatively characterize the trachea during tidal breathing. 15 healthy volunteers were assessed to define normal luminal area, lateral and antero-posterior size. Measurements were compared between expiration and inspiration and a ratio calculated. The normative data obtained was applied to 14 age-matched individuals with stable COPD.

Results: During expiration, healthy individuals demonstrated only mild tracheal cross-sectional area narrowing (expiration/inspiration percentage; 72 \pm 8%; mean \pm SD). There was similar lateral (80 \pm 10%) and anterior-posterior (76 \pm 8%) distance reduction. Narrowing was greater in patients with stable COPD (61 \pm 23%, $p = 0.047$). There was significantly greater anterior-posterior area reduction (76 \pm 14%, $p = 0.039$), but no difference in lateral wall change (76 \pm 14%, $p = 0.341$). Visual inspection confirmed that posterior membrane movement was responsible for the majority of narrowing in this group. Four patients with stable COPD had EDAC as defined by maintaining less than 50% tracheal area on expiration: this mainly resulted from anterior-posterior distance (40 \pm 4%) reduction.

Conclusions: This study used a novel imaging modality to provide the first validation of criteria conventionally used to diagnose EDAC. The findings indicate that greater than 50% reduction in tracheal area can discriminate and diagnose EDAC. Further studies are needed to establish EDAC prevalence in stable COPD as well as during disease exacerbations.

P-F-078

P-F-079

BIOMASS RELATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE IS ASSOCIATED WITH HIGHER INFLAMMATORY RESPONSE THAN HEALTHY SMOKERS

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Background: Smoking-related chronic obstructive pulmonary disease (COPD) is known to be an inflammatory state. However, similar information regarding COPD in biomass exposed non-smoking subjects is sparse. We compared the serum levels of Interleukin-6 (IL-6) and Interleukin-10 (IL-10) in biomass-related COPD patients, with that of healthy smokers.

Methods: Non-smoking subjects with COPD and significant history of biomass exposure as well as healthy smokers were recruited over a three year period. They were categorized into two groups with 75 subjects in each: Group I – COPD due to biomass exposure and Group II – Smokers without COPD. Detailed history including smoking status and dyspnea by modified medical research council (MMRC) was recorded. Six minute walk test (6MWT) was done according to ATS guidelines. Nutritional assessment included Skin fold anthropometry using calipers (Holtain Ltd., Crymch, U.K.) and Fat-free mass index (FFMI) was calculated using Durnin and Womersley and Siri equations. Lung function was assessed by spirometry as per ATS/ERS recommendation. Serum IL – 6 and IL – 10 levels were estimated by ELISA technique using kits from Diaclone (France) as per the manufacturer's instructions.

Results: Both the groups had similar age distribution [56.03 ± 10.03 years vs. 55.29 ± 10.3 years ($p = 0.6612$)]. Group I comprised entirely of females and group II predominantly comprised of males [75 females vs. 71 males and 4 females]. Group I patients were significantly more dyspnoeic [MMRC grading 3 (0–4) vs. 0 (0–4)], had poorer lung function [% pred FEV1 51.02 ± 20.26 vs. 78.28 ± 17.98 ($p < 0.0001$)], had poorer exercise tolerance [6MWD 295.03 ± 105.5 m vs. 418.54 ± 93.01 m ($p < 0.0001$)] and had poorer nutritional status [FFMI 15.35 ± 2.72 kg/m² vs. 17.49 ± 2.5 kg/m² ($p < 0.0001$)] as compared to Group II. They also had statistically significant higher circulating IL-6 [0.82 (0–175.98) pg/ml vs. 0.00 (0–267.01) pg/ml ($p = 0.0276$)] and lower IL-10 [3.49 (0–88.01) pg/ml vs. 8.62 (0–37.62) pg/ml ($p = 0.0273$)]. (All values are compared Group I vs. Group II; data with normal distribution are expressed as Mean \pm SD and those with non-normal distribution are expressed as Median (range); 6MWD: Six Minute Walk Distance).

Conclusion: COPD due to biomass exposure is associated with higher pro-inflammatory cytokines in the circulation and impaired anti-inflammatory responses compared to smokers without COPD.

BACTERIOLOGICAL PROFILE IN CASES OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE, AT TERTIARY CARE CENTRE IN INDIA

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Introduction/Background: Acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD) is a significant cause of hospital admissions, morbidity and mortality. The study was conducted to determine the microbiological aetiology of acute exacerbation of COPD considering the paucity of microbial data from developing countries.

Aims and Objective: Bacteria are responsible for causing 30–50% exacerbation. As only few studies are available from India, the present study was undertaken to see the bacteriological profile of the isolates from cases diagnosed with acute exacerbation of COPD.

Methods: The study comprises of 65 patients (46 treated as in-patients and 19 treated as out-patients), sputum samples and pharyngeal aspirates were obtained within 48 hours and were subjected to microbiological studies. The associations between various patient characteristics, their outcome and the type of organism isolated were assessed.

Results: The mean age of the patient was 58 ± 10 years with male predominance (92%); growth of pathogens were obtained from 48.84% of samples, in cases of in-patients and 67.28% in out-patients. All bacterial isolates were gram negative bacilli, with viruses showed wide spectrum. *Pseudomonas aeruginosa* 34.48% was predominant organism in hospitalized patients; whereas *Klebsiella pneumoniae* and *Streptococcus pneumoniae* together (29.21%) was isolated from out-patients. Mortality was higher in patients with chest X-Ray (CXR) infiltrates on initial presentation, elevated liver enzymes and higher leukocyte count. Baseline variables such as age, smoking status, duration of exacerbation and CXR infiltrates were not associated with isolation of organism.

Conclusions: (1) Gram negative bacteria especially beta-lactamase producers were more frequently isolated in our patients. (2) The more the severity of acute exacerbation, the more is the chance of isolating *Pseudomonas aeruginosa* as causative organism. (3) There is no association between microbial isolation and patient outcome.

P-F-080

THE ASSOCIATION BETWEEN ENVIRONMENTAL EXPOSURES AND PATTERNS OF BRONCHODILATOR RESPONSE IN PATIENTS WITH CHRONIC OBSTRUCTIVE LUNG DISEASE IN DUSTY AREA NEAR CEMENT PLANTS

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Background: Patients with COPD show various responses to reversibility test using short acting bronchodilators. Positive responders to reversibility test are presented with significant changes of FEV1, FVC or both. However, the associations between environmental exposure and the patterns of reversibility test have not been studied.

Objective: To describe the pattern of reversibility tests in patients with COPD lived near cement plants and elucidate the association between dusty exposure and patterns of response to reversibility test.

Methods: Among a participants in a health survey on six Korea's administrative districts of Korea near cement plants which has been performed since 2007, symptomatic patients with airflow limitation defined as a post-bronchodilator forced expiratory volume in 1s (FEV1) over forced vital capacity (FVC) value of less than 0.7 were recruited. Bronchodilator response (BDR) test was performed as recommended by the American Thoracic Society/ European Respiratory Society. Positive responder was defined when FEV1% or FVC% increased by more than 12% and 200 mL after inhalation of 400 ug salbutamol. According to the patterns of BDR test, we classified as isolated flow responders (FR), isolated volume responders (VR), or dual responders (DR). Using a systemized questionnaire, data of demographics, history of disease, habitant area, and environmental exposures were collected.

Results: Among 237 patients with COPD, 87 patients (36.7%) showed positive BDR. Patients with positive BDR showed higher body mass index than non-responders (23.6 ± 3.3 vs. 22.4 ± 3.1 kg/m², $p = 0.005$). VR (31.2%) were more common than FR (16.9%) or DR (11.4%). Female were more common in VR (31.9% in VR, 15.4% in FR, and 7.4% in DR). DR has lower pre-bronchodilator FVC comparing with that of VR or FR (71.7 ± 15.3 vs. 78.7 ± 18.4 vs. $87.5 \pm 16.5\%$, $p = 0.026$) whereas post-bronchodilator FVC% or FEV1% are not different between groups. Change of maximum mid expiratory flow (FEF25–75%) was greatest in VR ($7.2 \pm 13.1\%$, $p < 0.001$). Severity or duration of cough, wheeze, and dyspnoea were not different in groups. Density and duration of exposure to dusts and biomass were not associated with patterns of BDR.

Conclusions: Isolated volume response to reversibility test was most common in this study cohort with the risk of regional environmental dust exposures. However, the associations between environmental exposures and patterns of bronchodilator responses were not identified.

P-F-081

UNDERSTANDING THE SEVERITY, RISK FACTORS AND COMORBID CONDITIONS IN NEWLY DIAGNOSED SMOKING AND NON-SMOKING COPD PATIENTS: THE SCOPE STUDY

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Introduction: Survey of newly diagnosed COPD Patients (SCOPE) aimed to gain insights on presenting symptoms, severity, exacerbation history, risk factors and treatment practices in newly diagnosed Indian chronic obstructive pulmonary disease (COPD) patients.

Method: This survey was conducted in 7 cities of India from 1st May to 30th June 2014 and involved 47 pulmonologists. Each pulmonologist filled a respiratory health questionnaire capturing information on symptoms, risk factors, lung function, previous respiratory ailments, use of inhalers, history of exacerbations, hospitalizations, comorbid conditions and recorded COPD assessment test (CAT) score for consecutive newly diagnosed COPD patients.

Results: COPD patients comprised 35% of all patients attending the chest physician's clinic. Data was obtained on 247 newly diagnosed COPD subjects, mean age (\pm SD) 59.91 ± 11.53 years, majority 209 (84.6%) males with current or past history of smoking reported in 187 (75.7%). Of the 60 non smokers, (24.29%) reported exposure to biomass. The average FEV1% predicted was $50.30 (\pm 18.96)$ [$n = 178$] and average FEV1/FVC% was $60.38 (\pm 20.30)$ [$n = 231$], indicating a higher degree of airflow limitation at first diagnosis. Presenting symptoms included cough (97.57%), dyspnoea (95.45%), sputum (92.41%), wheezing (82.51%) and chest tightness (85.59%). Approximately, 31%, 28% and 22% of all patients reported biomass exposure, living close to highway/ industrial areas and work related exposure (cotton mills/ chemicals industry etc.), respectively. 29.96% patients had earlier been diagnosed with asthma, 15.38% with tuberculosis and 5.73% with allergic rhinitis. 45.9% of the patients were using inhalers, 67.44% did not have a good inhaler technique and 59.77% had average to poor compliance with therapy. On an average, there were 1.96 exacerbations and 0.79 hospitalizations for respiratory conditions in the last 1 year. The average CAT score (\pm SD) for these newly diagnosed COPD patients was $21.26 (\pm 7.68)$. Hypertension, diabetes mellitus, osteoporosis, depression was reported in 33.2%, 17.81%, 7.69% and 6.88% of the COPD patients. There was no significant difference between the symptoms, clinical presentation, co-morbidities, number of exacerbations and CAT assessment in smokers and non-smokers.

Conclusion: The SCOPE survey highlights that newly diagnosed COPD patients attending a chest physician's clinic in India, are at an advanced stage of COPD, with history of exacerbations and comorbid conditions with a significant number being non-smokers. Non-smoking COPD appears to behave similar to smoking COPD in terms of symptoms, co-morbidities and exacerbation frequency.

P-F-082

P-F-084

THE ACCURACY OF A PORTABLE COPD SCREENING DEVICE IN DETECTING OBSTRUCTIVE AIRWAY DISEASES

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Background: Conventional spirometry as screening tool for early case finding of obstructive airway disease may be difficult and impractical. The Vitalograph COPD-6® is a portable spirometer that can help in the early diagnosis and could improve the clinical management of obstructive airway disease. It is the aim of this study to validate the use of Vitalograph COPD-6® spirometer in the out-patient department and in a community-based setting to facilitate the need for further testing with standard spirometry.

Methods: A cross-sectional validation study of a portable COPD screening device in detecting obstructive airway disease, done at the Philippine Heart Center from March 2013 to December 2013. We screened 131 individuals with occupations deemed at higher risk of developing COPD (i.e. policemen, firemen, traffic enforcers, and/or jeepney drivers). Upon random selection one group underwent spirometry using the Vitalograph COPD-6® followed by standard spirometry, then the other group tested with standard spirometry prior to the portable spirometer. The following lung function parameters were measured FVC, FEV1, FEV6, FEV1/FVC ratio, and FEV1/FEV6 ratio with airflow limitation was clinically confirmed when the FEV1/FVC ratio value is <70 and FEV1/FEV6 ratio value is <0.70.

Results: Standard spirometry diagnosed 43 subjects (32.82%) with an obstructive ventilatory defect with FEV1/FVC ≤ 70. Vitalograph COPD-6® diagnosed 38 subjects (29%) with FEV1/FEV6 ratios ≤ 0.70. In detecting an obstructive ventilatory defect or COPD with the Vitalograph COPD-6®, it has an 81.40% specificity and 96.59% sensitivity with a positive predictive value (PPV) of 92.11 and a negative predictive value (NPV) 91.40.

Conclusion: The portable spirometer, Vitalograph COPD-6®, is a simple yet accurate device for the detection of obstructive airway diseases and may aid in the early detection of COPD hence early management.

DIFFERENTIAL CHANGES OF COMPONENTS IN QUALITY OF LIFE OVER 5 YEARS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background: Health-related quality of life (QOL) is being recognized as an important outcome when evaluating COPD patients. There have been few studies focusing on the longitudinal change in components of quality of life. The St George's Respiratory Questionnaire (SGRQ) is a standardized, self-completed questionnaire for measuring impaired health, perceived well-being, and 'quality of life' in chronic airways disease. The total score of the SGRQ consists of three components (domains): Symptoms, Activity, and Impacts.

Methods: In the Hokkaido COPD cohort study, 279 adequately-treated patients were prospectively followed over 5 years. The annual changes in SGRQ total score and its three components were evaluated in relation to annual change in forced expiratory volume in one second (Δ FEV1/year).

Results: Overall, the annualized change in the SGRQ total score had a weak, but significant correlation with Δ FEV1/year. The activity score deteriorated in general and the annualized decline was the greatest in those who experienced rapid decline in FEV1. On the other hand, total and symptom scores improved significantly in those who had sustained FEV1 over 5 years. When looking at baseline data, predictors for total SGRQ worsening were older age and lower FEV1. And those for the activity component were older age and lower body mass index, whereas larger reversibility was related with future improvement of symptom component. When looking at data during the follow-up period, the most remarkable predictor was rapid annual decline in FEV1 for worsening of total score and its components of SGRQ. Interestingly, another predictor for worsening in the activity component was continuous smoking, whereas improvement in the symptom components over time was related with use of beta agonists.

Conclusion: Annualized change in the SGRQ total score over 5 years weakly but significantly reflects that of pulmonary function decline. Component scores, however, may change differentially and independently over time.

P-F-083

COPD MANAGEMENT IN A GOVERNMENT HEALTH CARE SYSTEM IN THAILAND: A RETROSPECTIVE OBSERVATIONAL STUDY FROM COPD REGISTRY DATABASE

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Introduction: COPD management guideline were published in Thailand since 2005 following GOLD recommendations. Thoracic society of Thailand use a lot of efforts implementing the guidelines. However the data on COPD management in Thailand were not available. We have COPD registry in Easy COPD clinic Network since 2004. This study aim to provide the data on COPD management in Thailand using data from COPD registry.

Method: COPD clinics have been set up in the general hospitals throughout Thailand since 2004. COPD patients were registered at each hospitals and data was uploaded to on-line web database. On registered date we asked about the onset of COPD, the burden in the previous year, treatment, mMRC and CAT.

Results: There were 583 hospitals participated in this programme. There were 70,003 patients registered. 79.77% were male. GOLD guideline indicate that spirometry is required to diagnose COPD but only 20.75% of the patients ever had spirometry done. 49.30% of the patients was visited to the Emergency Department because of COPD exacerbations in the previous year and 33.94% of the patients was admitted in the hospitals in the previous year. Most of the patients received short acting bronchodilators (51.74% received SABA, 51.36% receive SABA/SAMA) and 53.12% received ICS monotherapy. Only 14.06 % received ICS/LABA. When classified patients using MRC or CAT scores and exacerbation history, 28.23%, 26.75%, 17.92% and 27.11% were classified in groups A, B, C and D respectively.

Conclusions: The burden of COPD is high in Thailand and guidelines are not being followed. Encouraging greater use of spirometer and greater use of long-acting bronchodilators will be important steps towards improving COPD control in Thailand.

P-F-085

EFFICACY AND SAFETY OF NEBULIZED FORMOTEROL/BUDESONIDE (FB NEB) COMPARED WITH FORMOTEROL/BUDESONIDE PMDI (FB PMDI) IN PATIENTS WITH SEVERE TO VERY SEVERE COPD

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Background: Many patients, especially those with advanced COPD, find it difficult to use handheld inhaler devices which leads to suboptimal disease control. Nebulized therapy due to its convenience has been shown to be of benefit to such patients. A novel formulation containing formoterol and budesonide in combination, to be delivered through a nebulizer has recently been developed.

Objective: To evaluate the efficacy and safety of 20 mcg/1 mg of FB neb with 6/200 mcg of FB pMDI in patients with severe to very severe COPD.

Methods: This was an open-label, prospective, active-controlled, parallel group, 6 weeks, multicentre study, with 2 weeks run-in period during which patients were treated with a combination of ipratropium 40 mcg & levosalbutamol 50 mcg, 2 puffs, thrice daily. Eligible patients were then randomized (2:1) to receive either FB neb or FB pMDI (2 puffs) with a non-static spacer, twice daily. Levosalbutamol 50 mcg pMDI was provided as rescue medication. Primary efficacy parameter was difference in mean change in trough FEV1 at the end of 6 weeks. Others included FVC, FEF25–75 and subject diary assessment at the end 2, 4 and 6 weeks.

Results: 113 patients (96.43% males) were randomized, with a mean age 62 ± 9.11 years. Data of 94 patients with a mean baseline post bronchodilator (PB) FEV1% predicted 35.91% with reversibility 10.44% was analyzed. At the end of 6 weeks, the difference in the change in trough FEV1 between FB neb and FB pMDI was not significant (30 ml, 95% CI (-0.05 L, 0.11 L) (p = 0.42)). Similar results were seen for PB FEV1, FVC and FEF25–75. There was a trend towards significance in the PB FEF25–75 at week 6 vs baseline in FB neb group (p = 0.05) but not in the FB pMDI group. Use of rescue medication and adverse events were similar in both groups.

Conclusion: FB neb is as efficacious and well tolerated as FB pMDI and can serve as an alternative treatment option in patients with severe to very severe COPD who are unable to use handheld inhalers.

P-F-086

CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH CARDIOVASCULAR DISEASE – REVIEW OF 3 CASES

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Chronic obstructive pulmonary disease (COPD) affects more than 600 million people in the world and 10% found at age >40 years. World Health Organization (WHO) predicts that at 2020 the prevalence of COPD will be the third cause of mortality in the world's population. COPD is often accompanied by multiple comorbid of extrapulmonary manifestations that contributes to disease severity, and affects prognosis. Comorbidities include cardiovascular diseases (ischemic heart disease, chronic heart failure and hypertension). Several studies have shown an increased risk of cardiovascular disease three times in patients with COPD as compared with the general population. The Towards a Revolution in COPD Health (TORCH) study reported causes of death in COPD patients as cardiovascular disease (27%), pulmonary disease (35%), and cancer (21%). In this report, there were three cases of COPD patients with comorbid cardiovascular disease, i.e. heart failure, ischemic heart disease, and hypertension. One of the cases has developed secondary pulmonary hypertension and arrhythmias. COPD is a complex disease that is often accompanied by multisystem comorbid disease that affects the symptoms, exacerbation, hospitalization and mortality. Systemic inflammation has a major role in COPD and the comorbid. Mannoni et al reported the prevalence of cardiovascular disease in COPD patients to be 20–22%, as compared with 9% of patients with non-COPD. The prevalence of heart failure increases with age, at the rate of eight out of 1000 people age >50 years and 10% after the age of 80 years. COPD as a comorbid cardiovascular disease occurs due to pulmonary and systemic inflammatory processes, which often affects the prognosis and management of patients with COPD. Therefore, it is necessary to screen for comorbid diseases in patients with COPD.

P-F-087

P-F-089

ALTERNATIVE OPTIONS TO IDENTIFY AT-RISK COPD PATIENTS MORE EASILY: THE UTILITY OF PEAK EXPIRATORY FLOW AND COPD ASSESSMENT TEST

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Background and Objective: Standard spirometry to diagnose chronic obstructive pulmonary disease (COPD) is skill-dependent, expensive and not easily available. In contrast, measurement of peak expiratory flow rate (PEFR) is a simple, cheap, easily-performed procedure to detect airway obstruction. COPD assessment test (CAT) provides short, simple and sensitive attributes to assess and monitor COPD. We aim to investigate the utility of PEFR and CAT as an alternative diagnostic tool for at-risk COPD patients.

Methods: This prospective, observational study enrolled participants if they aged between 40 to 90 years, presented with at least one of the chronic airway symptoms (cough, phlegm, or dyspnoea) and had smoking history greater than 20 pack-years. All eligible participants completed CAT questionnaire and measurement of PEFR, followed by pre- and post-bronchodilation (BD) spirometry for standard COPD diagnosis (post-BD FEV1/FVC < 70%).

Results: A total of 305 consecutive at-risk participants were enrolled, including 160 (52.5%) non-COPD subjects, 39 (12.8%) COPD GOLD stage I (post-BD percentage of FEV1 predicted value [%FEV1] ≥ 80), 79 (25.9%) stage II ($50 \leq \% FEV1 < 80$) and 27 (8.9%) stage III to IV ($\%FEV1 < 50$). For total CAT scores, the mean values in non-COPD and GOLD stage I were similar (6.5 & 5.5, respectively), but significantly higher in stage II and III-IV (10.7 & 12.3, $P < 0.001$, ANOVA with post-hoc test, vs. non-COPD and stage I, respectively). CAT scores significantly and negatively correlated with %PEFR, post-BD percentage of FVC predicted value, and post-BD %FEV1 ($r = -0.421$, -0.261 , and -0.413 , respectively; all $P < 0.001$). Using %PEFR and CAT scores to predict the diagnosis of COPD, the best cut-off value for %PEFR and CAT was 79 and 7, and in which the diagnostic accuracy presented by sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, area under the receiver operating characteristic curve was 78.1% and 65.5%, 82.3% and 51.7%, 79.1% and 83.7%, 81.3% and 28.3%, 4.4 and 1.4, 0.802 and 0.608, respectively. Combined assessment by %PEFR and CAT did not exert greater diagnostic value than % PEFR alone.

Conclusions: For at-risk patients, PEFR can be a simple and effective alternative to predict the diagnosis of COPD in settings where spirometry is unavailable. CAT scores alone provide lower diagnostic accuracy and add no additional diagnostic value to %PEFR alone. However, higher CAT scores might indicate more severe airflow obstruction.

P-F-088

SACCULAR BRONCHIECTASIS WITH SEVERE PULMONARY HYPERTENSION IN A 15-YEAR-OLD MALE

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Bronchiectasis is an abnormal, chronic enlargement of the bronchi, the passageways from the trachea to the alveoli that are the air-exchanging parts of the lungs. The prevalence and incidence of bronchiectasis are not known accurately because the symptoms are variable and the diagnosis is often not made. Bronchiectasis generally occurs as a result of infection, although non-infectious factors may contribute to the development of this condition. There have been few reports about patients affected by saccular bronchiectasis with severe pulmonary hypertension. This report presents a 15-year-old male with progressive dyspnoea, cough, sputum production, and fever. The clinical and laboratory examination revealed that the patient had a respiratory infection due to bronchiectasis. Chest x-ray and high resolution of thoracic CT-scan showed bilateral infected bronchiectasis saccular type and bilateral pleural effusion. Echocardiography revealed severe pulmonary hypertension. Abdominal ultrasound revealed a congestive liver. The patient's treatment included antibiotics, diuretics, bronchodilators, mucolytics, oxygen, chest physiotherapy and a regular exercise programme. Although not resolve completely, the patient condition regained improvement, and he continue with his cardiopulmonary treatment programme.

COMPARING THE QUALITATIVE AND QUANTITATIVE VOLUMETRIC COMPUTED TOMOGRAPHY FINDINGS AND SPUTUM INFLAMMATORY PROFILE IN TOBACCO SMOKE AND BIOMASS SMOKE ASSOCIATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: 50% of world's population uses biomass fuel for cooking and heating purposes and exposure to biomass smoke is a known risk factor for COPD. There are studies reporting the similarities in the clinical presentation of tobacco smoke and biomass smoke associated COPD. However little is known about the radiological and sputum inflammatory profile of these two groups. MDCT scanners have revolutionized the way the CT images of lungs can be studied and induced sputum studies are simple and easy way to study airway inflammation. Therefore the aim of our study was to compare the radiological and airway inflammation profile in tobacco smoke and biomass smoke associated COPD.

Methods: We enrolled 81 COPD patients visiting a respiratory hospital outpatient clinic, males and females ≥ 40 years and COPD was diagnosed by GOLD guidelines 2009 with post bronchodilator FEV1/FVC < 70%. We excluded patients with COPD exacerbation within 4 weeks of enrollment, bronchial asthma, tuberculosis and pulmonary fibrosis. Spirometry was performed as per ATS/ERS 2005 guidelines. Volumetric Computed Tomography was performed using Siemens Somatom Definition AS multidetector CT, using low radiation protocol in full inspiration. Images were read qualitatively by 2 radiologists blinded to clinical details of the patients and quantitatively by Pulmo CT software using density mask method, where emphysema was defined as percentage of voxels < -950 Hounsfield Units. Bronchiectasis was diagnosed by Naidich criteria. Sputum induction was performed as per Medical evaluation Unit(U.K).

Results: We had 57 tobacco smoke associated COPD (TS – COPD) and 24 biomass smoke associated COPD (BS – COPD). Mean age was 64.5 (7.6), 62.54 (7.8) respectively. 98.1% of males were smokers and 85.2% women were non smokers. Mean FEV1 in both groups did not differ significantly 55.9 (17.0), 61.4 (20.8), $p = 0.22$. Qualitative evidence of emphysema (centrilobular emphysema and paraseptal emphysema) was statistically significantly high in TS-COPD compared to BS-COPD and quantitatively, % emphysema was 27.8 (11.2), 20.0 (13.0), $p = 0.04$. Bronchiectasis was similar in both groups 29.8%, 33.3%, $p = 0.755$ and induced sputum inflammatory profile was also similar (neutrophil% 84.6, 87.3, $p = 0.5$. eosinophils% 7.1, 9.6, $p = 0.40$. macrophages% 6.3, 2.4, $p = 0.16$. lymphocytes% 2.01, 0.66, $p = 0.31$. total cells per gram of sputum = 3.33×10^6 , 3.95×10^6 , $p = 0.31$).

Conclusions: BS-COPD had less centrilobular and paraseptal emphysema and less percentage emphysema (%LAA) compared to TS – COPD. There was no statistically significant difference in CT evidence of bronchiectasis and induced sputum inflammatory profile in both these groups. Thus BS-COPD had lesser emphysema but similar sputum cellular inflammatory profile.

P-F-090

A MULTI-CENTRE NON-INTERVENTIONAL STUDY OF PERCEPTION OF SYMPTOM VARIABILITY IN COPD PATIENTS IN CHINA

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Purpose: The present study aimed to assess the perceptions of daily symptom variability of patients with Chronic Obstructive Pulmonary Disease (COPD) in China.

Methods: A multiple-centre, observational cross-section study conducted in 11 centers of China. Participants were outpatients ≥ 40 years old with a history of COPD ≥ 6 months, post-bronchodilator forced expiratory volume in 1s (FEV1) $< 80\%$ predicted and no exacerbation in the previous 3 months. The perception of the patients on the symptom variation and their impact on daily life activities were recorded. Multivariate analyses were performed to identify factors associated with symptom variability.

Results: A total of 1032 (97.5%) eligible patients out of 1058 provided data that were valid for analysis. The mean age of patients was 64.9 years old; 80.9% of the patients were male. Mean post-bronchodilator FEV1 was 46.5% predicted. According to Global Initiative for Chronic Obstructive Lung Disease (GOLD 2011) spirometric grading systems, 40.1%, 42.8% and 17.1% of the patients were at moderate, severe and very severe stages, respectively. Inhaled corticosteroids in combination with long-acting beta-2 agonist drugs (53.0%) and inhaled long-acting anti-cholinergic drugs (32.5%) were the most commonly used medications. Cough, sputum production and dyspnea were the most common symptoms (73.6%, 68.8% and 61.4%, respectively). Daily symptom variability was reported by 518 (50.2%) patients. Among these 518 patients "on waking" (39.3%) and "at night" (21.3%) were the most likely occurring time and the most troublesome time. The morning activities that were most affected by COPD symptoms were morning exercises, having breakfast, washing, dressing and getting out of bed. 72.7% of 308 patients who didn't have a good sleep were caused by COPD. As regarding to the patient's perception on COPD treatments, 445 (45.1%) patients took medicine only when symptoms occurred or worsened and 275 (27.9%) patients didn't know about how and when to use their medications. Only 3.2% of the patients followed the doctor's instruction to take medicine before getting up. Multivariate analyses indicate that CAT scores was the only factor associated with symptom variability (OR = 0.463, $p < 0.0001$). However, gender, smoking index, Body Mass Index (BMI), co-morbidities, severity of airflow limitation and frequency of exacerbation in previous 12 months were not associated with symptom variability.

Conclusion: Coughing and sputum production are currently the most common symptoms presenting in Chinese COPD patients. Patient-perceived COPD symptoms vary over the day and have impact on daily activities. Morning and night were the worst time of the day. This variation in the perception of symptoms in COPD patients should be put into consideration in the long-term COPD management in China.

POSTER PRESENTATION – CRITICAL CARE MEDICINE

P-G-002

THE SECRETORY IMMUNOGLOBULIN A IN THE EARLY ONSET-VENTILATOR ACQUIRED PNEUMONIA AND ARDS BASED ON ANALYSIS OF SPECIMENS FROM THE BRONCHOALVEOLAR LAVAGE

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Background: Secretory immunoglobulin A (s-IgA) is the major humoral immunoglobulin of the respiratory system, the most important for lung defense, consisting 65–80% of total. Along with innate immunity system, s-IgA protects the lung from infection. In ARDS, s-IgA will be destructed, due to the damage of the environment surrounding the alveoli. The aim of this study is to prove that s-IgA in the lung maintain immunity in patients on mechanical ventilators, early-onset VAP, and s-IgA in ARDS.

Method: The study was a prospective analytic observation cohort on s-IgA from BAL, the VAP(-/+) with a scores of CPIS > 6 is VAP(+). Basic subjects' data are collected on the first day, and will later be used as an internal comparison with samples taken on the third day. Bronchoscopy techniques and BAL: FOB using a large channel bronchoscope was inserted through the endotracheal or tracheotomy tubes via sterile connector to maintain ventilation during procedure. BAL commonly performed on left subsegment lingula or right middle lobe, selected based on chest radiograph or according to the presence of direct inflammatory signs (purulent secretions, mucosal oedema, and hyperemia) with protected BAL Balloon Catheter. Finally fluid from BAL was immediately delivered to microbiology laboratory for quantitative bacterial culture, cytological, and serological analysis.

Results: Subjects observed were 61 people, with initial diagnosis consists of 37 head trauma, 10 strokes, 8 post operative, 6 encephalopathies, and no pneumonia. On the third day of the study, subjects are divided into two groups, group VAP(-) with CPIS scores ≤ 6 (± 2.86), 28 subjects, and group VAP(+) with CPIS scores > 6 (± 7.94), 33 subjects. On the first day of bronchoscopy BAL s-IgA was ± 54031.562 , whereas on the third day, s-IgA BAL in VAP(-/+) were ± 78144.029 and ± 96778.818 , significant ($p < 0.05$). By Mann-Whitney test, s-IgA VAP(-/+) did not differ significantly ($p > 0.05$), because s-IgA in VAP(+) has a larger SD. S-IgA in the VAP(+) and VAP(+) with ARDS is different significantly ($p < 0.05$). Average s-IgA in VAP(+) is ± 140181.884 , higher than the s-IgA in VAP(+) with ARDS which is ± 37874.657 .

Conclusion: S-IgA of BAL has a role in maintaining local immunity in the lung, but in VAP(+) with ARDS, when the alveoli environmental destructed, the s-IgA was also destroyed.

P-G-003

P-G-004

EFFICACY OF RECRUITMENT MANOEUVRE WITH OR WITHOUT ANTIDERECRUITMENT STRATEGY IN ARDS PATIENTS: A PROSPECTIVE STUDY

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Background: In acute respiratory distress syndrome (ARDS), adequate positive end-expiratory pressure (PEEP) may recruit collapsed alveoli and reduce repetitive opening and closing that causes shear stress. Recruitment manoeuvre (RM) opens up collapsed segments of the lung in many patients with ARDS whereas some patients do not respond to RM. In responders, the collapse may reappear once the RM is complete and the patient is returned to his pre-RM PEEP level. Oxygenation benefit achieved by RM may be partially lost soon after the RM. The level of PEEP, i.e., an antiderecruitment strategy in mechanical ventilatory support, could be important in preserving the effect of the ARM.

Objective: To evaluate the outcome of setting the PEEP using decrement PEEP titration after an alveolar recruitment manoeuvre and its effects on the clinical outcome in patients with ARDS.

Methods: Twenty four patients with early ARDS were assigned in this study. Initially, recruitment manoeuvre was given using pressure control ventilation to determine the responders vs non-responders. Responders were randomly assigned to 'antiderecruitment RM' (ADRM) group and 'only RM' group. The 'antiderecruitment RM' group received RM using volume control ventilation and optimal PEEP was set after RM using the decremental PEEP titration method. The 'only RM' group patient was put on baseline ventilator settings after manoeuvre.

Results: Out of the total of 24 patients, 12 showed an improvement in oxygenation (P/F) in response to the initial recruitment manoeuvre by more than 20% from baseline. When the change in P/F ratio was correlated with survival, it suggests that a P/F ratio <90 at admission (baseline) is associated with mortality.

Conclusion: Only half of the patients with ARDS respond to recruitment manoeuvres with an improvement in oxygenation. In most responders, the improvement is sustained irrespective of whether RM only or ADRM was used.

OBSERVATIONAL STUDY OF OUTCOME ACCORDING TO ANTICOAGULATION STRATEGY IN ADULT EXTRACORPOREAL MEMBRANE OXYGENATION PATIENTS

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Introduction: During ECMO, anticoagulation is critical to avoid the thrombotic complications. But, bleeding complications contribute significantly to morbidity and mortality. Previous data suggests that haemorrhagic complications are more common than thromboembolic ones and lower doses of anticoagulation may be safe and effective. Therefore, we assess the clinical outcomes according to anticoagulation strategy.

Method: We reviewed a retrospectively obtained ECMO database and patients' medical records between December 2008 and March 2014. We divided into two groups with a standard anticoagulation strategy and a conservative anticoagulation strategy. The conventional anticoagulation strategy was a commonly used protocol during ECMO, the target activated coagulation time (ACT) was between 180 and 220 seconds. And the conservative strategy was designed for reducing bleeding risk by low dose heparin, the target activated partial thromboplastin time (aPTT) was between 50 and 70 seconds. We reviewed the incidence of bleeding events and transfusion requirements, mortality according to anticoagulation strategy. Major bleeding was defined requiring blood transfusion and resulting in hemodynamic compromise.

Result: Total 626 ECMO days were studied in 58 patients. VA ECMO (67%) was twice as common as VV ECMO (33%) with a median duration shorter than for VV ECMO (8 days versus 16 days). The primary indications for ECMO support were respiratory failure 47% and cardiogenic shock 31%, CPR 22%. 59% of the ECMO patients were successfully weaned and the overall mortality was 50%. The mean hourly heparin dose was 12 unit/kg. Median aPTT was 109 seconds and median ACT was 181 seconds. Major bleeding occurred 37.9% and bleeding related death occurred 22.4%. Of all patients, 62% (n = 36) used the conventional anticoagulation strategy and 38% (n = 22) used conservative anticoagulation strategy. The mean aPTT and ACT in conventional group were higher than conservative group (116 versus 98, 201 versus 147). Incidence of major bleeding and bleeding related death were significantly lower in the conservative group, respectively (53% versus 14%, p = 0.003 and 33% versus 5%, p = 0.011). The mean daily number of transfused RBC unit and FFP and cryoprecipitate were higher in the conventional group (2.9 ± 2 versus 1 ± 1.1, p = 0.017, 1.5 ± 2 versus 0.6 ± 0.9, p = 0.015, 0.9 ± 1.5 versus 0.8 ± 1, p = 0.047). However, hospital mortality and successful weaning did not differ between the two groups.

Discussion: In this study, conservative anticoagulation strategy showed acceptable results in terms of major bleeding event, transfusion dose and thromboembolic complications. Based on this study, conservative anticoagulation strategy could be expected to reduce bleeding complications without serious thrombotic complication.

P-G-005

VALIDATION OF SIMPLE MODEL SCORE IN PREDICTING SEVEN DAY IN HOSPITAL MORTALITY OF NONSURGICAL EMERGENCY PATIENTS AT CIPTO MANGUNKUSUMO HOSPITAL

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Background: Patients who came to emergency department (ED) had different diagnosis and severity spectrums. Scoring system could stratify the risk of ED patients and predict their mortality. Simple Model Score (SMS) utilizing age and laboratory data as variables was already proven as a instrument with good performance. Nevertheless, the application of SMS in different characteristic population, should be validated.

Objective: To evaluate calibration and discrimination of SMS in predicting seven day in hospital mortality of nonsurgical ED patients at Cipto Mangunkusumo Hospital.

Methods: This was a retrospective cohort study of nonsurgical patients who attended to ED of Cipto Mangunkusumo Hospital in October–November 2012. The data of age, haemoglobin, platelet count, white blood count, ureum, sodium and blood glucose level when the patient was admitted to emergency room used to perform the calculation of SMS. The primary outcome was seven day in hospital mortality. Calibration was evaluated with calibration plot and Hosmer-Lemeshow test while discrimination was evaluated with area under the curve (AUC).

Results: There were 701 patients who met the criteria were recruited to this study. Mortality was observed in 92 patients (13.12%). Calibration plot of SMS showed $r = 0.639$ and Hosmer-Lemeshow test showed $p = 0.749$. Discrimination was shown by ROC curve with AUC 0.665 (CI 95% 0.610; 0.719).

Conclusion: Simple Model Score showed a good calibration despite less satisfying discrimination in predicting seven day in hospital mortality of nonsurgical ED patients at Cipto Mangunkusumo Hospital.

P-G-007

MODIFIED SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE AND STRESS HYPERGLYCEMIA ON ADMISSION AS PREDICTORS OF 28 DAYS MORTALITY IN NON-DIABETIC CRITICALLY ILL PATIENTS

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Background: Modified Sequential Organ Failure Assessment (MSOFA) has been developed as critical care triage in centres with limited resources. MSOFA's performance has been validated in Indonesia but limited only in surgical critically ill patients which showed a low precision in predicting mortality. Addition of another variable to improve MSOFA's performance merits further investigation. Hyperglycemia in critically ill patients without previous history of diabetes (stress hyperglycemia) has been shown to be an independent risk factor of mortality.

Objective: To evaluate MSOFA scoring system's performance and addition of admission blood glucose test to predict mortality in critically ill patient without previous history of diabetes.

Methods: This was a prospective cohort study recruiting medical and surgical critically ill patients admitted to Cipto Mangunkusumo Hospital during a period of August to December 2013. History taking, physical examination, peripheral oxygen saturation, Glasgow Coma Scale, creatinine, blood glucose and A1C were obtained within 24 hour of admission. The outcome was mortality within 28 days. Performance of MSOFA was evaluated using the Hosmer-Lemeshow goodness of fit test and by measuring the Area Under Curve (AUC).

Results: 150 patients completed the study protocols. Mortality was observed in 52 patients (34.67%) with sepsis being the most prevalent diagnosis. Calibration of MSOFA showed a Hosmer-Lemeshow test $\chi^2 = 13.748$ ($p = 0.056$). Receiver Operating Characteristic (ROC) of MSOFA showed an AUC of 0,83 (95% CI 0,76–0,89). Stress hyperglycemia was evident in 79 patients (52,67%) recruited in this study. Addition of blood glucose to MSOFA scoring system did not show improvement in MSOFA's performance.

Conclusion: We have validated MSOFA in this study which showed good calibration and discrimination in both medical and surgical critically ill patients. Adding blood glucose to MSOFA scoring system did not improve MSOFA's performance.

P-G-008

THE SURVIVAL OF ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN PATIENTS WITH COMORBIDITY: EXPERIENCE AT RUMAH SAKIT CIPTO MANGUNKUSUMO (RSCM) HOSPITAL

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Background: Acute respiratory distress syndrome (ARDS) is an emergency case in pulmonology field that contribute to high mortality rate. The mortality rate of ARDS patients with comorbidity is usually higher than patients without comorbidity, because patients with comorbidity show worse response to treatments. Most of the ARDS patients that are hospitalized in RSCM have comorbidity because RSCM is the national reference hospital. So we need to study about the survival rate of admitted ARDS patients who had comorbidity. The result of the study is expected to be a reference for patient treatment.

Aim: To know about the survival of ARDS patients with comorbidity, that were hospitalized in RSCM hospital.

Method: This is the survival analysis study of ARDS patients with comorbidity that were hospitalized in RSCM in 2008–2012. Data about clinical condition, laboratory, chest X-ray, and outcome of hospitalization were all collected from medical records. The Survival Analysis were performed to know the survival of ARDS patients with comorbidity, that were hospitalized in RSCM. The result of the study is presented as survival rate and Kaplan Meier Curve.

Result: As many as 368 patients were included in this study. As many as 236 (64,%) patients have comorbidity. Immunocompromise is the most common comorbidity, occurring in as many as 148 (62,7%) patients, diabetes mellitus in 71 (30%) patients, chronic kidney disease in 58 (24,5%) patients, stroke in 51 (21,6%) patients and sirrochis hepatitis in 14 (5,9%) patients. The survival of ARDS patients with comorbidity is ARDS 3 (CI; 2,58–3,43) days, and the survival of ARDS patients without comorbidity that hospitalized in RSCM is 8 (CI ; 3,05–12,94) days.

Conclusion: The survival of ARDS patients with comorbidity that re hospitalized in RSCM is shorter than patients without comorbidity.

P-G-009

THE FAILURE OF HIGH FLOW NASAL CANNULA THERAPY MAY CAUSE DELAYED INTUBATION AND MORTALITY

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Background: High flow nasal cannula (HFNC) provides a high flow of humidified and heated oxygen. The use of HFNC allows respiratory failure patients who require mechanical ventilation, a chance to delay intubation.

Objectives: We compared the outcomes of critically ill patients with HFNC therapy, for early failure or late failure.

Methods: We performed a retrospective observational study of patients receiving HFNC therapy in a tertiary hospital between January 2013 and March 2014. We selected intubated patients for the failure of HFNC therapy and classified the patients into two groups depending on the timing of intubation – intubation before and after 48 hours.

Results: A total of 615 patients receiving HFNC therapy were enrolled in our study. Among them, 175 patients clinically deteriorated despite HFNC therapy and finally received endotracheal intubation. Before 48 hours, 130 patients (74.3%) were intubated and after 48 hours, 45 patients (25.7%) were intubated. There were no significant differences in baseline characteristics between two groups except higher diabetes mellitus (33.85% vs. 15.56%, $p = 0.02$) and Sequential Organ Failure Assessment (SOFA) score day 1 (9.81 ± 3.82 vs. 8.07 ± 3.85 , $p = 0.009$) in the patients with intubation before 48 hours. The patients with intubation before 48 hours had higher extubation (37.69% vs. 15.56%, $p = 0.006$) and ventilator weaning rate (55.38% vs. 28.89%, $p = 0.002$), lower ICU mortality (39.23% vs. 66.67%, $p = 0.001$), and longer ventilator free days (8.58 ± 10.06 vs. 3.62 ± 7.48 , $p = 0.011$).

Conclusions: In patients with clinical deterioration during the HFNC therapy, delayed failure may be harmful and cause bad outcome.

P-G-010

P-G-011

THE EFFECT OF SORAFENIB ON PULMONARY FIBROSIS INDUCED BY LIPOPOLYSACCHARIDE

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Introduction: Acute respiratory distress syndrome (ARDS), the most severe form of Acute lung injury (ALI) is characterized by increased permeability of the alveolar-capillary barrier after epithelial and endothelial injury induced by a variety of stimuli. After early acute inflammatory phase, fibroproliferative and progressive fibrotic phase follow. As the overall mortality of ARDS has decreased and beneficial effects of anti-inflammatory agent such as glucocorticoid were not demonstrated in previous trials, the importance of fibroproliferative response for the long term outcome of ARDS are being emphasized. In bleomycin-induced pulmonary fibrosis, sorafenib, an oral multikinase inhibitor, antagonized TGF-beta1-mediated epithelial mesenchymal transition (EMT) and reduced the proliferation and collagen synthesis in fibroblasts.

Objectives: We evaluated whether the sorafenib has the antifibrotic effect and antagonize the TGF-beta1-mediated EMT on lipopolysaccharide (LPS) induced lung fibrosis.

Methods: The eight-week-old male mice were instilled with LPS intratracheally and the control mice were instilled with normal saline only. The LPS-treated mice were randomized into three groups that received low dose sorafenib (10 mg/kg), high dose (100 mg/kg) or phosphate buffered saline (PBS). Mice were sacrificed 7 days after LPS instillation. The bronchoalveolar lavages (BAL) were done and the lungs were harvested for histologic examination, real time polymerase chain reaction (RT-PCR), and western blot analysis.

Results: Treatment of sorafenib inhibited the fibroproliferative morphologic changes induced by LPS in both low-dose and high-dose groups in 1 week. Moreover, RT-PCR and western blotting data showed the loss of epithelial markers E-cadherin, ZO-1, and β -catenin; and an increase in the mesenchymal markers N-cadherin, Vimentin, Snail, Slug, TCF8/Zeb1, Fibronectin, α -SMA in both the BAL fluids and lung tissue lysates of sorafenib-treated mice compared to PBS group. We also found by ELISA that sorafenib reversed the secretion of IL-6, IL-8, VEGF, TGF- β 1, TNF- α , and MCP-1 induced by LPS in both BAL fluids and tissue lysates.

Conclusions: We found that sorafenib inhibited the activity for EMT via pro-inflammatory cytokines signaling and attenuated LPS-induced lung fibrosis. So, sorafenib might be one of the potential therapeutic candidates for ALI.

ASSOCIATION BETWEEN TRACHEOSTOMY TIMING ON ICU MORTALITY IN MECHANICALLY VENTILATED PATIENTS

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Background: Tracheostomy is a common procedure in the intensive care unit. Tracheostomy can reduce airway resistance, the usage of sedation and ventilator-associated pneumonia. Based on these advantages, tracheostomy can potentially reduce ICU mortality and morbidity. But the timing to perform a tracheostomy in critically ill patients who are predicted to require long-term ventilatory support is still under debate, because previous studies showed different results.

Objective: Investigating the association between tracheostomy timing with intensive care unit mortality. Knowing the incidence of ICU mortality between early and late tracheostomy in patients with mechanical ventilation in intensive care unit.

Methods: Retrospective cohort study design was conducted on 162 critically ill patients in mechanical ventilation. These patients also underwent tracheostomy procedure during intensive care treatment in Cipto Mangunkusumo during period from January 2008–December 2012. The timing to tracheostomy, clinical, laboratory, and radiological data were collected. Patients were observed for the incidence of mortality during intensive care. Chi Square test was used to analyze the relationship between tracheostomy timing with intensive care unit mortality. Multivariate analysis with logistic regression was used to calculate adjusted odds ratios (and 95% confidence intervals) between early and late tracheostomy group to the intensive care mortality by including confounding variables as covariates.

Results: There is no significant association between early and late tracheostomy with the intensive care unit mortality ($p = 0.07$) with a risk ratio (RR) of 0.67 (CI 95% 0.51 to 1.05). The incidence of mortality in early and late tracheostomy was 28.4% and 42%.

Conclusion: Early tracheostomy group tended to have a lower mortality incidence compared with late tracheostomy. Association between timing to tracheostomy with the intensive care unit mortality was not statistically significant.

P-G-012

ASSOCIATION BETWEEN TRACHEOSTOMY TIMING WITH MECHANICAL VENTILATION DURATION IN CIPTO MANGUNKUSUMO HOSPITAL INTENSIVE CARE UNIT

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Background: Tracheostomy is a common procedure in the intensive care unit and can potentially reduce the duration of mechanical ventilation. Outcome between tracheostomy timing in critically ill patients, who are predicted to require long-term ventilatory support, on the duration of ventilator is still debatable, with previous studies showing different results. The aim of this study is to see the association between tracheostomy timing with the duration of ventilatory support after tracheostomy.

Methods: A retrospective cohort study was conducted on 162 critically ill patients in mechanical ventilation. These patients also underwent tracheostomy procedure during intensive care treatment in Cipto Mangunkusumo from January 2008–December 2012. Patients were divided into two groups; early tracheostomy (<10 days mechanically ventilated) and late tracheostomy (≥ 10 days). Patients were observed for the duration of mechanical ventilation post tracheostomy. Mann Whitney test was performed to analyze association between tracheostomy timing with the duration of mechanical ventilation.

Results: Median for total mechanical ventilation duration was 11 (3–68) and 21 (11–62) days in the early and late tracheostomy group. The median duration of mechanical ventilation post tracheostomy was shorter in early tracheostomy group 5 (1–62) days over late tracheostomy group 7 (1–14) days. No significant association were found between the 2 groups with the duration of mechanical ventilation ($p = 0.064$).

Conclusion: Early tracheostomy group tend to have a shorter mechanical ventilation duration compared with late tracheostomy. Association between time to tracheostomy with the duration of mechanical ventilation was not statistically significant.

P-G-013

A SURVEY FOR HEAD OF BED ELEVATION IN A TERTIARY INTENSIVE CARE UNIT

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Introduction: During ventilator care, the bundle care would be recommended for prevention of ventilator associated pneumonia (VAP). Head of bed elevation (HOBE) more than 30 degree, oral care with chlorhexidine and hand washing are included in the bundle care. In several studies, compliance of HOBE were variable from 15% to 76% of study time. We assessed the health care worker's perception and performance of HOBE.

Methods: Critical care workers answers four questions: What were made of ventilator bundle care? What degree of head of bed elevation for prevention of ventilator-associated pneumonia? During care how frequently do you determine the head of bed elevation? Clinicians were requested to elevate head of bed up to 30 degree.

Results: The participants for survey were 38 doctors and 46 nurses who worked in ICU. In October, 2013, the survey was performed in the ICU and HOB was checked with actual ICU bed and monitor of HOBE. The doctors were residents who consisted of medical, surgical, and service departments. The nurses worked in medical, surgical ICU and operating rooms. Thirty three percent of doctors and 49% of nurses correctly answered HOBE is associated with VAP prevention. ICU nurses checked HOBE more frequently rather than doctors. The performance of HOBE 30 degree was more accurate in nurses than in doctors ($p = 0.014$).

Conclusion: Education for sepsis and ventilator bundle care would be needed in participants of ICU.

P-G-014

THE PROGNOSIS OF PATIENTS WITH CANCER ADMITTED TO THE MEDICAL INTENSIVE CARE UNIT

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In the past, many studies showed the prognosis of cancer patients who were admitted to the Intensive Care Unit (ICU) was poor, especially lung cancer. These patients were usually refused admission to ICU. Lung cancer is still the leading cause of cancer-related death. Previous studies also showed the outcome of lung cancer patients who admitted to ICU was extremely poor. Despite their poor outcome, patients with advanced lung cancer were increasingly admitted to the medical ICU for management of critical illness. However, advances in the cancer management and critical care help improve the survival of these patients. The benefit of ICU care for these advanced cancer patients still remains controversial. This is a retrospective analysis of the adult patients with advanced cancer who were admitted to the medical ICU. 1396 patients were admitted to the medical ICU between January 2012 and December 2013. 577 patients were diagnosed with advanced cancer. However, in cancer patients, 75 patients were diagnosed with lung cancer and 502 with the other cancers. The ICU mortality rate of non-cancer patients and cancer patients was 17.6% (144/819) and 6% (35/577) [lung cancer and the other cancers were 8% (6/75) and 5.8% (29/502)]. In the survival group, the ICU stay time of non-cancer patients and cancer patients was 8.05 days and 9.77 days ($p = 0.001$) (lung cancer and the other cancers was 8.62 days and 9.94 days). In the mortality group, the ICU stay time of non-cancer patients and cancer patients was 9.58 days and 15.74 days ($p = 0.02$) (lung cancer and the other cancers was 13 days and 16.31 days). Although the length of ICU stay of the cancer patients was more than the non-cancer patients, the ICU mortality rate of the cancer patients was not higher, even in the lung cancer group. In conclusion, our data showed the medical ICU outcome of cancer patients including lung cancer is improving. Advances in intensive care and better selection of cancer patients help improve the survival of these patients in the ICU. Further studies are necessary to access long-term mortality, quality of life, ability to continue chemotherapy and cost-effectiveness.

P-G-015

INCIDENCE AND OUTCOME OF WEANING FROM MECHANICAL VENTILATION IN MEDICAL WARDS AT THAMMASAT UNIVERSITY HOSPITAL

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Background: Weaning from mechanical ventilation (MV) is classified as simple, difficult or prolonged weaning according to weaning process. This classification has not been identified in Thailand.

Objective: To determine the incidence, causes of weaning failure and outcome of weaning from MV in medical wards.

Material and Methods: A prospective observational study was performed between June and December 2013. All patients who required MV with endotracheal intubation in medical intensive care unit, cardiac care unit, stroke unit, and general medical wards were recruited. Patient's data including sex, age, co-morbid diseases, illness severity, admission wards, intubation, weaning, causes of weaning failure, extubation, re-intubation, tracheostomy, ventilator-free days, length of stay, and mortality were analyzed.

Results: A total of 164 patients who required MV. One-hundred ten patients started weaning, 7 of these were excluded (4 patients died during weaning and 3 patients received tracheostomy). Of these 110 patients, 103 patients were eligible for final analysis. The cumulative incidences of simple, difficult and prolonged weaning group (3 weaning groups) were 48 (46.6%), 38 (36.9%) and 17 (16.5%), respectively. The mortality rate of 3 weaning groups were 0 (0%), 4 (10.5%) and 4 (23.5%) ($p = 0.006$), respectively. Prolonged weaning was associated with risk of death (odds ratio [OR] 6.3; 95% confidence interval [CI] 1.4–28.3, $p = 0.016$) when compared with simple and difficult weaning. The re-intubation rate of 3 weaning groups were 0 (0%), 7 (18.4%) and 4 (23.5%) ($p = 0.004$), respectively. The tracheostomy rate of 3 weaning groups were 0 (0%), 3 (7.9%) and 4 (23.5%) ($p = 0.004$), respectively. The median (interquartile range) of number of ventilator-free days within 28 days of 3 weaning groups were 25.0 (23.2–26.0), 20.0 (13.5–22.0), and 13.0 (0–20.0) days ($p < 0.0001$), respectively. The hospital length of stay of 3 weaning groups were 12.0 (5.2–20.7), 17.0 (13.7–26.0), and 26.0 (19.5–51.0) ($p < 0.0001$), respectively. Multivariate logistic regression analysis, causes of prolonged weaning group compared with non-prolonged weaning group were respiratory (OR 16.3; 95% CI 1.8–150.7, $p = 0.014$), nutritional (OR 6.2; 95%CI 1.2–30.0, $p = 0.023$), and metabolic problems (OR 5.1; 95%CI 1.2–22.7, $p = 0.031$).

Conclusion: Non-simple weaning was association with increased mortality, re-intubation, tracheostomy rate, hospital length of stay, and decreased ventilator-free days. Respiratory, nutritional, and metabolic problems were significant causes of prolonged weaning which need to be emphasized on these problems and provide early intervention.

P-G-016

P-G-017

FACTORS AFFECTING MORTALITY OF ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) PATIENTS HOSPITALIZED IN RUMAH SAKIT CIPTO MANGUNKUSUMO (RSCM) HOSPITAL

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Background: Acute respiratory distress syndrome (ARDS) is an emergency in pulmonology field that contributes to high mortality rate. But the recent studies showed that the survival of ARDS patients improved by time to time because the improvement management of ARDS patients is very good right now. There is still no comprehensive study about the survival of ARDS patients in Indonesia especially in RSCM hospital.

Aim: To know the survival of ARDS patients that hospitalized in RSCM hospital and factors affecting it.

Methods: This study was a retrospective cohort on ARDS patients who were hospitalized in Cipto Mangunkusumo hospital from 2008 to 2012. Data about clinical condition, laboratory, chest X-ray, and outcome of hospitalization were all collected from medical records. The Survival Analysis were performed to know the survival of ARDS patients. on age, ARDS aetiology, comorbidity Charlson index, PaO₂/FIO₂ ratio, APACHE II score, and ventilator use in the first 48 hours since ARDS diagnosed. Multivariate with logistic regression would be done to variables that fulfilled the condition.

Results: As many as 368 patients were included in this study. Inhospital mortality was 75.3%. On bivariate analysis we found that age, ARDS aetiology, comorbidity Charlson index, PaO₂/FIO₂ ratio, APACHE II score, and ventilator use in the first 48 hours since ARDS diagnosed were variables that had significant associations with inhospital mortality. From multivariate analysis, we found variables that had associations with mortality were sepsis as ARDS aetiology (RR 1.26; 95% CI 1.20–1.32; $p < 0.001$), the high APACHE II score (RR 1.19; 95% CI 1.04–1.30; $p = 0.019$), and no ventilator use in the first 48 hours since ARDS diagnosed (RR 1.37; 95% CI 1.25–1.43; $p < 0.001$).

Conclusion: Sepsis as ARDS aetiology, the high APACHE II score, and no ventilator use in the first 48 hours since ARDS diagnosed were independent factors affecting ARDS patients' mortality.

FLUID MANAGEMENT FOR SHOCK IN THE FIRST 24 HOURS OF INTENSIVE CARE UNIT STAY: IMPACT OF A SIMPLE CLINICAL PROTOCOL

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Accurate fluid delivery during hemodynamic optimization for shock is critical for patient survival. However, guiding fluid therapy and assessing fluid responsiveness is challenging. This study assesses the clinical impact of a simple Medical Intensive-Care Unit (MICU) fluid management protocol using intra-arterial blood pressure (IABP) readings to assess fluid-responsiveness, prompting nursing staff to administer fluids if patients are responsive. It uses minimal equipment and can be readily implemented in other ICUs and resource-limited countries. Cohort study of mechanically ventilated patients admitted to MICU from the Emergency Department, from 2010–2013, in shock on 1st admission (Systolic Blood-Pressure < 90 mmHg/vasopressor requirement within 24 h of MICU admission). Conditional logistic regression was performed controlling for age, gender, APACHE-II score, and diagnosis (sepsis vs non-sepsis). 813 patients were analyzed, with mean (+standard deviation) age 62 ± 16.6 years, and 332 (40.8%) females. Mean APACHE-II score was 28.4 ± 8.9 . ICU mortality and hospital mortality were 34.7% and 40.2% respectively. Median ICU length-of-stay (LOS) was 4 days (IQR 2–7), and hospital LOS 8 days (IQR 4–16). Sepsis was diagnosed in 477 (58.7%) patients on admission. Patients with protocol-use differed significantly from “no protocol-use” for APACHE-II score and sepsis diagnosis. The protocol was used for 223 patients (27.4%) 455 times, with 244 (53.6%) fluid-responsive episodes. The protocol reduced both ICU [odds ratio 0.57, 95% CI 0.40–0.82; $p = 0.002$] and hospital mortality (odds ratio 0.65, 95% CI 0.46–0.91; $p = 0.012$). This remained significant on subgroup analysis of ICU mortality for septic and non-septic patients. Comparing protocol and non-protocol use, net fluid balance showed no significant difference at baseline, but increased at 6, 12, and 24 h after admission. Larger net balance at 24 h was not associated with improved survival. Ventilator days, ICU LOS, and hospital LOS all increased with protocol use. The protocol was used on patients who were more ill, with poorer expected survival (higher APACHE II score). Protocol use was associated with significantly improved ICU and hospital survival, possibly owing to appropriate fluid resuscitation. This was facilitated by clear documentation of patients' IABP readings with fluid therapy, enhancing physician-nurse cooperation. It allows fluid responsiveness to be assessed objectively, and can help optimize the benefits of fluid therapy, while reducing associated complications.

P-G-018

SURVIVAL RATE OF ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) PATIENTS HOSPITALIZED IN CIPTO MANGUNKUSUMO HOSPITAL (RSCM) WITH VENTILATOR

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Background: Acute respiratory distress syndrome (ARDS) is an emergency in pulmonology field that contributes to high mortality rate. The evidences show that the correct use of ventilator is the only medical intervention that can decrease ARDS mortality. In RSCM not all of ARDS patients had been taken care of with a ventilator, due to limited facilities. So we need to study the survival rate of ARDS patients who were hospitalized and were given ventilator, in order to evaluate the treatment procedure of ARDS patients that are hospitalized in RSCM.

Aim: To know the survival of ARDS patients who were hospitalized in RSCM with ventilator.

Methods: This research is a survival rate study of ARDS patients who were hospitalized in RSCM between 2008–2012. Clinical data, laboratorium, thorax expertise photo, outcome status (living or dead) and time of death, during treatment are drawn from medical records. Results of this research are presented as survival rate and Kaplan Meier Curve.

Results: As many as 368 ARDS patients were hospitalized in RSCM between 2008–2012. From that count, 304 patients (82.7%) used ventilators during treatment. Survival rate of ARDS patients that were using ventilators is 4 (IK; 2,54–5,47) days. Whereas the survival rate of ARDS patients in RSCM without ventilators is 2 (IK; 1,66–2,34) days.

Conclusion: Most of the patients are treated with ventilators in RSCM. The survival rate of ARDS patients in RSCM with ventilators is still low (4 days), though this is still higher than those treated without ventilators.

P-G-019

NONINVASIVE VENTILATION KNOWLEDGE AND PRACTICE AMONG JUNIOR SAUDI DOCTORS

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Introduction: Non-invasive mechanical ventilation using a face mask has revolutionized respiratory support for patients presenting in type II hypercapnic respiratory failure. It reduces mortality, hospital stay and need for intubation. A prerequisite for its success is to initiate as early as possible and the familiarity of the in charge physician of its use. Junior doctors are the front line physician for sick patients and so they need to have the knowledge and skills of using NIV. In this paper we assess the knowledge and practice of the junior doctors in King Fahad Hospital of the University (KFHU) of NIV.

Methods and Results: A questionnaire based survey was done in KFHU. It included recollection of taught courses or clinical training in the use of NIV and actual cases to test factual knowledge. It was distributed to 36 junior staff, one form was incomplete and so excluded. 63% of responders were interns, 20% were specialists and the rest were residents (R1-R3). Of the responders 48.5% describe their undergraduate education of NIV as poor whereas only 25% think the postgraduate training in NIV is poor. 34% consider their NIV postgraduate education as good which reflects improvement due to clinical rotation and patient exposure. 72% of those who had postgraduate training describe it as informal. When asked to use a score of ten to assess their NIV skills, 40% scored as 1 which is the lowest part of the scale. 17/33 Feel worried when confronted with a patient on NIV. 40% of the responders worked either in ICU or Pulmonary Medicine during their rotation. In the questions related to factual knowledge it was clear that there is significant gap between what is known by the responders and what is known from clinical evidence. The questionnaire reveals significant gap in the knowledge of junior doctors in the use of the NIV and hence the use of this therapy for those in need.

Conclusion: There is no standardization of NIV education for both undergraduates and postgraduates in Saudi Arabia. Exposure in the wards improved staff perception of the knowledge of NIV. Knowledge and clinical competence in the use of NIV is an essential skill which need to be acquired by junior staff. There exists a gap which needs to be addressed through both under- and postgraduate education. There should exist a formal training curriculum for the postgraduates when they join their hospitals which should include factual knowledge and training in the available ventilators in the hospital.

P-G-020

PROGNOSTIC FACTORS OF THE PATIENTS WHO WERE ADMITTED TO INTENSIVE CARE UNIT WITH HEALTHCARE-ASSOCIATED PNEUMONIA

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Introduction: Healthcare-associated pneumonia (HCAP) is a respiratory infection acquired through outpatient contact with the health system. Limited studies have been identified about HCAP requiring intensive care unit (ICU) admission. We evaluated HCAP patients who were admitted to the ICU, to identify their clinical characteristics and prognostic factors.

Materials and Methods: We reviewed the clinical characteristics and microbiological distributions of HCAP patients admitted to ICU of tertiary hospital from January 2008 to December 2012. HCAP was separated from A to D according to nursing-home residence, previous hospitalization, physically disabled, and continuously receiving outpatient endovascular therapy. The severity of pneumonia was assessed by using the pneumonia severity index (PSI) and CURB-65. The 30-day mortality was evaluated as a primary endpoint.

Results: Of the 1056 patients, 428 patients (men, 67.1%) were enrolled. The median age was 73.0 year-old. Median APACHE II and PSI score were 23.0 (19 – 27) and 144.0 (130 – 158) respectively. Thirty-day mortality was 25.5% and duration of ICU stay was 9.0 days. Mortality ($P = 0.349$) had no significant difference among four groups although the duration of ICU stay ($P = 0.008$) was significantly longer in group C and D. When we performed multivariate logistic analysis using significant variables, PSI score (odds ratio (OR) 1.011 95% confidence interval (CI) 1.000–1.022, $P = 0.040$), serum HCO₃- level (OR 0.956 95% CI 0.920–0.993, $P = 0.022$), multidrug-resistant (MDR) pathogens including ESBL-producing *Klebsiella pneumoniae* (OR 2.688 95% CI 1.237–5.840, $P = 0.016$), MDR *Acinetobacter baumannii* (OR 3.081 95% CI 1.504–6.311, $P = 0.002$) and polymicrobial pathogens (OR 4.161 95% CI 1.414, 12.547, $P = 0.011$) were significantly associated with 30-day mortality.

Conclusion: ESBL-producing *K. pneumoniae* and MDR *A. baumannii* were significantly associated with 30-day mortality in HCAP in ICU patients, therefore these MDR pathogens as well as PSI score should be considered as prognostic factors in HCAP.

P-G-021

WOULD CUFF LEAK TEST LEAD TO DELAYED EXTUBATION?

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Introduction: Cuff leak test is used as clinical method to predict laryngeal oedema after extubation. In literature review and clinical practice, positive finding of cuff leak test did not necessarily predict post-extubation laryngeal oedema and may be delayed of extubation. This study is designed to evaluate the relationship between positive cuff leak test and post-extubation laryngeal oedema.

Method: From April 2012 to December 2013, we prospectively included 192 patients who were admitted to a teaching hospital in Taiwan. The inclusion criteria were adult patients who received intubation and ventilator support for more than 3 days. Cuff leak test was performed when the patient was considered suitable for entering extubation protocol. The test was standardized to evaluate cough reflex, tracheal sound, air leakage amount and the change of airway pressure. Air leakage amounting more than 110 ml is defined as having passed the cuff leak test.

Result: In the total of 192 patients, 158 patients passed the cuff leak test and 34 patients did not. After extubation, 28 patients had stridor and 164 patients were without stridor. In the non-stridor group, the predictive factors to pass the cuff test or not are females (100% vs. 27.1%; $P < 0.001$), shorter body height (153.3 ± 6.1 vs. 163.7 ± 7.8 cm; $P < 0.001$) and ever tracheostomy (16.7% vs. 0%; $P = 0.020$).

Conclusion: In our study, the correlation of cuff leak test and post extubation laryngeal oedema is low. Female, shorter body height and history of receiving tracheostomy may decrease the air leakage and result in false positive in cuff leak test. We suggest adjusting the amount of air leakage when performing cuff leak test, to avoid delayed extubation.

P-G-022

P-G-023

PROFILE OF PATIENTS WITH RESPIRATORY FAILURE WHO NEED TRACHEOSTOMY IN INTENSIVE CARE UNIT PERSAHABATAN HOSPITAL, JAKARTA, INDONESIA

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Introduction: Respiratory failure is a syndrome in which the respiratory system is unable to perform its basic function of gas exchange. The incidence and prevalence of respiratory failure are difficult to determine, as respiratory failure represents a syndrome rather than a single pathological process. Tracheostomy is also one of the most commonly performed operative procedures in the modern intensive care unit (ICU). Tracheostomy is generally indicated for respiratory failure requiring prolonged mechanical ventilation (MV), airway protection in disease states leaving patients unable to protect the airway. The aim of this study is to know the indication, timing, and duration of tracheostomy in patients with pulmonary problem who admit to our ICU.

Methods: We collected data from our ICU registry. Patients with pulmonary problems who were admitted to our ICU with respiratory failure were involved in this study. We noted all patients who had tracheostomy performed at our ICU, also we measured the length of stay (LOS), and day when the tracheostomy was performed.

Results: One hundred sixty seven patients were admitted to our ICU from 2012 until 2013 with variety problems and diagnosis. Among them, 4 patients with respiratory failure due to respiratory problems underwent tracheostomy. Indication for ICU admission was respiratory failure (3 patients) and unconsciousness. There were 2 male patients (50%) and 2 female patients (50%). Average age were 53.5 years old (34, 54, 79, 47 years old, respectively). Diagnosis were bronchiectasis (patient 1), COPD (patient 2), lung oedema (patient 3), and tuberculosis (patient 4). Duration of MV was 18.75 days (average) (18, 16, 25, 16 days, respectively). Length of stay (LOS) in ICU was 21.5 days (average) (19, 19, 26, 22 days, respectively) with LOS in hospital was 27.25 days (23, 37, 29, 30 days, respectively). Days when tracheostomy performed were 16.5 days (15, 15, 22, 14 days, respectively). APACHE II was 25.25 (average) with prediction 54.105 (average). Patient 1 and patient 3 died due to sepsis.

Conclusion: This study shows that tracheostomy reduced mortality in patients with prolonged mechanical ventilation, even though this study only involved several patients as our subject.

OUTCOME AND PROGNOSTIC FACTORS IN PATIENTS WITH CARBON MONOXIDE POISONING ADMITTED TO MEDICAL INTENSIVE CARE UNIT (MICU): A 10 YEARS RETROSPECTIVE STUDY

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Objective: Carbon monoxide poisoning (COP) causes cognitive sequelae. However, there is a paucity of prognostic factors for mortality in COP patients admitted to intensive care unit (ICU).

Methods: A retrospective study of COP adults admitted to a university affiliated hospital ICU between July 2001 and December 2010 was performed. Outcomes were survival to ICU discharge and to hospital discharge. Data for the survival and non-survival groups were compared, univariate and multivariate logistic regression analyses were performed, and odds ratios (OR) were calculated. A multivariate logistic regression model was applied using Acute Physiology and Chronic Health Evaluation II scores and variables that were significantly associated ($P < 0.001$) with survival in the univariate analysis.

Results: Seven hundred and eighty-seven COP patients admitted to our hospital and 140 patients (17.8%) admitted to ICU. The overall hospital mortality rate was 14.3% (20/140). Univariate analysis indicated that non-surviving CO poisoning patients were more likely to have had no HBO therapy ($P < 0.001$), initial COHb level over 30% ($P = 0.026$), shock ($P < 0.001$), endotracheal intubation ($P = 0.04$), APACHE II score ($P < 0.001$), GCS score ($P < 0.01$), acute renal failure ($P = 0.024$) and pH level of blood ($P = 0.001$). Multivariate logistical regression analysis identified HBO intervention [$P = 0.021$, relative risk (RR) 0.13, 95% CI 0.022–0.733] and APACHE II score ≥ 25 [$P = 0.005$, relative risk (RR) 12.02, 95% CI 2.13–67.91] had significant effect over mortality of CO poisoning in ICU.

Conclusion: In conclusion, we observed that APACHE II score over 25 on ED admission was associated with a significant mortality risk in patients with CO poisoning admitted to the ICU. Moreover, HBO intervention could reduce mortality in patients with CO poisoning admitted to the ICU.

P-G-024

THE ROLE OF NEUTROPHILS IN EARLY ONSET-VENTILATOR ACQUIRED PNEUMONIA AND ARDS BASED ON ANALYSIS OF SPECIMENS FROM BRONCHOALVEOLAR LAVAGE

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Background: Neutrophils are part of the innate immunity that protects lung from infective pathogens, transmigration circulation plays an important role in the immune system. Neutrophils in patients using mechanical ventilator is $\pm 60\%$, with two distinct functions, one of which is as a defense component. On the contrary, excessive inflammation, damage of lung tissue, and worsening of pulmonary function take place when neutrophils amounts increased. This may lead to acute respiratory distress syndrome (ARDS). The aim of the study is to seek for evidence that neutrophils in the lung maintain immunity in patients using mechanical ventilators.

Method: The study was a prospective cohort and analytic observation of neutrophils from BAL, VAP(-/+) with a CPIS scores >6 considered as VAP(+). Basic subjects' data are collected on the first day, and will later be used as an internal comparison with samples taken on the third day. Bronchoscopy techniques and BAL: FOB using a large channel bronchoscope was inserted through the endotracheal or tracheotomy tubes via sterile connector. BAL commonly performed on left subsegment lingula or right middle lobe, selected based on chest radiograph or according to the presence of direct inflammatory signs (purulent secretions, mucosal oedema, and hyperemia) with protected BAL Balloon Catheter. Finally fluid from the BAL was immediately delivered to microbiology laboratory for quantitative bacterial culture, cytological, and serological analysis.

Results: Subjects observed were 61 people, with initial diagnosis consists of 37 head trauma, 10 strokes, 8 post operative, 6 encephalopathies, and no pneumonia. On the third day of the study, subjects are divided into two groups, group VAP(-) with CPIS scores ≤ 6 (± 2.86), 28 subjects, and group VAP(+) with CPIS scores >6 (± 7.94), 33 subjects. Neutrophils on the first day are $\pm 63.5361\%$. On third day, neutrophils in VAP(-) is $\pm 66.5650\%$, which is not significant ($p > 0.05$), while in VAP(+) is $\pm 85.4000\%$ (significantly $p < 0.05$). Neutrophils on both groups also differ significantly ($p < 0.05$). Analysis of the correlation between neutrophils and CPIS scores strongly correlate (0.595). By Spearman correlation, a strong correlation between neutrophils and the incidence of ARDS was found.

Conclusion: Neutrophils of BAL was significantly correlated with CPIS scores, contributed to the incidence of early onset-VAP, and a strong correlation between neutrophils and the incidence of ARDS was found.

P-G-025

DEVELOPMENT OF A pH/pO2 DUAL-PARAMETER FLUORENSOR

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The accurate measurement of blood pH and PO₂ is often critical in the clinical assessment of patients with severe illness. Continuous intra-arterial blood gas and pH monitoring by use of optical sensors offer certain advantages over other types of sensors. Miniaturization is vital for the continuous intravascular blood gas monitoring probes. But the most recent devices had withdrawn from market partly due to the bundled probes. The present study aimed at preparing and evaluating a pH / PO₂ dual-parameter fluorosensor by use of a single optic fibre. We fabricated a fibre-optic pH fluorosensor based on a proton-sensitive fluorescent dye AMPN firstly. A PO₂-sensitive filming, in which the PO₂-sensitive indicator Ru(dpp)3(PF6)2 was immobilized, was coated to the upper section over the pH sending membrane. The fluorescent intensity at 510 nm and 615 nm was recorded separately when the fabricated dual-parameter probe was excited at 395 nm. Its selectivity and accuracy were analyzed when the probe was exposed to the buffers with different pH or bubbled by 100% N₂ or O₂ in turn. The sensor emitted green and red dual-colour fluorescence simultaneously when excited at 395 nm. Both the two fluorescence intensity peaks at 510 nm and 615 nm changed separately with different pH or PO₂ values and weren't almost interfered each other. The pH / PO₂ dual-parameter fluorosensor can determine accurately the two signals simultaneously, making the two signals transmitted through a single optic fibre and miniaturizing the multi-parameter sensor.

P-G-026

ANTI-INFLAMMATORY EFFECTS OF LACTOFERRIN ON HYPEROXIA-INDUCED LUNG INJURY USING NF-KB/LUCIFERASE TRANSGENIC MICE

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High levels of oxygen are used for mechanical ventilation and extracorporeal membrane oxygenation (ECMO) in critically ill patients. However, exposing to hyperoxia may induce production of reactive oxygen species (ROS) and lung injury. Lactoferrin (LF) is an iron-binding glycoprotein found in milk, saliva, tears, airway secretion, and granules of neutrophils. It has many biological functions, including antimicrobial, anticancer, antioxidant, and anti-inflammatory effects. The present study used NF- κ B/luciferase transgenic mice, which carrying the luciferase gene under the control of NF- κ B, to investigate the hypothesis that oral administration of LF could attenuate the inflammatory response and injury of lungs after hyperoxia (FiO₂ $> 95\%$) for 72 hours. When NF- κ B was activated by hyperoxia, luciferase protein would have more expression. Luminescence excitation could be observed by non-invasive in vivo imaging system (IVIS) after injection of luciferin. The transgenic mice were assigned to four groups for treatment: (1) treated with water and room air, (2) treated with water and hyperoxia, (3) treated with 150 mg/kg LF and hyperoxia, (4) treated 300 mg/kg LF and hyperoxia. The therapeutic effects of LF for lung injury were measured by IVIS, bronchoalveolar lavage, lung histology, and cytokines in lungs. The groups treated with LF had lower luciferase expression and less injury in lungs. The decayed ratio of κ B decreased significantly. The ROS, MAPK and pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) expression also decreased significantly ($p < 0.01$). Our results suggest that LF via oral administration decrease the production of ROS and attenuates the severity of inflammation and injury of lungs after hyperoxia.

P-G-027

THE EFFICACY OF PHYSIOTHERAPY USING RTX RESPIRATOR AGAINST PATIENTS WITH PNEUMONIA

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Background and Aim of Study: The RTX respirator is a biphasic cuirass ventilator. Recently, it has been reported that its secretion clearance mode is effective for the treatment of atelectasis or obstructive pneumonia. We retrospectively investigated the efficacy and safety of RTX respirator against patients with pneumonia.

Patients and Methods: A total of 16 patients treated with RTX respirator between April 2011 and April 2014 were included in the study. We classified the patients into two groups; effective and ineffective, according to the degree of improvement in their radiologic findings in the chest X-ray and decrease of CRP levels.

Results: The effective group consisted of 8 community acquired pneumonia (CAP) patients and 2 nursing-healthcare associated pneumonia (NHCAP) patients. The average serum CRP level was 28 mg/dl and their chest X-ray showed prominent consolidations. Their consolidations disappear within 5 days in 6 patients. The ineffective group consisted of 2 CAP patients and 4 hospital associated pneumonia (HAP) patients. The average serum CRP level was 6.9 mg/dl. There was no adverse event.

Conclusion: This study indicates that RTX respirator should be introduced to patients with CAP, the prominent consolidation in the chest X-ray, high serum CRP level and moderate to severe pneumonia, as an additional therapy to encourage airway clearance.

P-G-028

P-G-030

EPIDEMIOLOGICAL PROFILE OF TRACHEOSTOMY PATIENTS WITH MECHANICAL VENTILATION IN CIPTO MANGUNKUSIMO HOSPITAL INTENSIVE CARE UNIT

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Background: Tracheostomy is a common procedure in intensive care units but the epidemiological profile of tracheostomized patients with mechanical ventilation has not been published yet, especially in Cipto Mangunkusumo, a national public referral hospital in Indonesia. The aim of this study is to describe the epidemiological profile, Charlson Index for evaluating comorbidity, indication and type of ICU admission and MSOFA for evaluating patient's severity, tracheostomy complication and ICU outcome.

Methods: A retrospective cohort study was conducted on 162 critically ill patients in mechanical ventilation. These patients also underwent tracheostomy procedure during intensive care treatment in Cipto Mangunkusumo from January 2008–December 2012.

Results: The clinical and epidemiological analysis of 162 patients showed majority of patients was male (58%) and mean age 50.2 (SD 16.7). Majority of cases were neurologic problems (40.1%). Most common comorbidity were malignancy (23.5%). Median time of endotracheal intubation before tracheostomy was 9.5 days. Median MSOFA score before and after tracheostomy was 6. No severe complication post tracheostomy procedure were identified. ICU mortality rate was 35.2%. Median ICU length of stay and duration of mechanical ventilation after tracheostomy were 7 (0–62) and 5.5 (1–62) days.

Conclusion: Tracheostomy was more often performed in neurology cases. The median time to tracheostomy was 9.5 days.

P-G-029

P-G-031

POST THYMECTOMY MYASTHENIA GRAVIS IN PATIENT DIAGNOSED WITH THYMIC CARCINOMA

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Thymic carcinoma is a rare type of thymus gland cancer, thymic epithelial tumour that exhibits clear-cut cytologic atypia and histologic features no longer specific to the thymus. Thymic carcinomas are rare and have been reported to account for only 0.06% of all thymic neoplasms. Commonly myasthenia gravis is associated with thymoma and a few thymoma patients without myasthenia gravis have been observed to develop MG after total removal of the thymoma with an incidence of 1.5% (5) but association of thymic carcinoma with autoimmune disorders are very rare like MG, only 3 cases have been documented (8), no local and international data on incidence and prevalence of post thymectomy MG in patient diagnosed with Thymic carcinoma.

Objective: To present a rare case of post thymectomy myasthenia gravis in patient with thymic carcinoma who presented with Osserman III from its symptomatology to diagnosis and treatment.

Case: A 54 year old female who complained of shortness of breath. The present condition started 2 months prior to admission she complained of persistent fever and shortness of breath, workups revealed a pulmonary mass on the left apical region by Chest Ct scan, underwent further work ups, which on histopath revealed high grade malignant potential favouring thymic carcinoma. She was advised to undergo radiotherapy but due to persistent shortness of breath hence she was admitted after 52 days post operatively. On the second hospital day patient had severe dyspnoea and was intubated, no associated fever nor cough, initial consideration of pneumonia with pleural effusion was entertained, which was ruled out due to negative effusion on Chest ultrasound. She was started on antibiotics and was referred to medical oncology for possible chemotherapy. On the 5th hospital day patient noted to have bilateral ptosis. Repetitive nerve stimulation test was done and findings were compatible with Myasthenia gravis. Pyridostigmine and Prednisone started. Plasmapheresis was done for a total of 5 sessions, and patient was extubated after the 4th session of plasmapheresis, patient was discharged improved.

Conclusion: We reported a case of post thymectomy Myasthenia gravis Osserman III in patient with thymic carcinoma and described its symptomatology, diagnostic work ups and treatment. Awareness of this disease entity would enhance one's clinical suspicion when confronted with a similar patient with presentation of respiratory crisis and ptosis with the aim to prevent serious complications such as prolong intubation and probably nosocomial infections and start immediate and appropriate treatment.

ACUTE RESPIRATORY DISTRESS SYNDROME AS THE INITIAL CLINICAL MANIFESTATION OF AN ANTISYNTHEASE SYNDROME

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Antisynthetase syndrome has been recognized as an important cause of autoimmune inflammatory myopathy in a subset of patients with polymyositis and dermatomyositis. It is associated with serum antibody to aminoacyl-transfer RNA synthetases (anti-Jo1) and is characterized by a constellation of manifestation, including fever, myositis, interstitial lung disease, mechanic's hand like cutaneous involvement, Raynaud phenomenon, and polyarthritis. The lung disease is the presenting feature in 50% of cases. We report a patient with an antisynthetase syndrome, revealed by an acute respiratory distress syndrome (ARDS). The patient described in the present case study was a 59-yr-old female, and she was admitted to hospital for ARDS and diagnosed with anti-Jo-1 antibody positive polymyositis (antisynthetase syndrome). The patient's condition improved when she was given high-dose corticosteroids. She was successfully weaned from the ventilator on day 11 after intubation. We think that given that steroids are not greatly beneficial in the treatment of ARDS, it is likely that the improvement of the respiratory symptoms in this patient also resulted from the prompt suppression of the inflammatory systemic response by corticosteroids.

SEVERE PULMONARY HYPERTENSION AND INFECTED BRONCHIECTASIS IN TWIN PREGNANCY

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Introduction: Pulmonary hypertension (PH) is a rare pathology encountered in pregnant woman, which carries a high risk of maternal mortality. Anaesthetic management of parturient with PH undergoing cesarean section is a challenge as maternal mortality rate remains 30 – 50% irrespective of adequate medical care. We report the case of patient with severe PH and infected bronchiectasis who successfully underwent an emergency cesarean section under epidural anaesthesia (EA).

Case Report: A 29-year-old primigravida female presented with increasing dyspnoea at 30 weeks of pregnancy. Her past medical history revealed that she had a tuberculosis treatment and history of chronic cough with mucoid expectoration for a period of six months. She was admitted with symptoms and signs of right heart failure. On examination she had a clubbing finger and could only sleep in a semi-setting position. Arterial blood gas showed hypoxia with partially compensated metabolic alkalosis (pH 7.466, pCO₂ 56.2 mmHg, pO₂ 76.9 mmHg, HCO₃ 40.9 mmol/l). On auscultation she had an accentuated pulmonary component of the second heart sound and a systolic murmur of tricuspid regurgitation. Electrocardiography showed right heart strain, and a chest radiograph showed a honeycomb appearance in right mid lung. Computed tomography of her chest showed a signet ring appearance in the both of lungs, suggesting a bilateral bronchiectasis. An echocardiogram showed a dilated right heart chambers with D-shaped of left ventricle, impaired right ventricular systolic function, tricuspid regurgitation, and a pulmonary artery systolic pressure of 131.4 mmHg, suggesting severe PH. On obstetric examination, the height of fundus was about 28 weeks in size, ultrasound scan showed a twin intra uterine pregnancy with an estimated gestational age of 28–30 weeks. Sputum culture positive for *Pseudomonas aeruginosa*. Based on relatively stable maternal and good fetal condition, our multiprofessional team decided to extend the gestation to 34 weeks under close fetal and maternal monitoring and to schedule an elective cesarean section. She was treated with meropenem for infected bronchiectasis, furosemide for right heart failure, and phosphodiesterase type-5 inhibitor for her pulmonary hypertension. But she had a worsening dyspnoea at 32 weeks of gestational age, so she underwent an emergency cesarean section under EA. Twin pre-term female neonates were born (weight 1380 gram and 1330 gram, respectively; Apgar score 7/9 and 7/9 at 1 and 5 minutes, respectively). Postoperatively the parturient was transferred to intensive care unit with stable hemodynamics.

P-G-032

TOXICITY OF INTRAVENOUS COLISTIN AS A FACTOR INTERFERING WITH WEANING FROM MECHANICAL VENTILATION

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Introduction: The use of colistin, which is the most commonly used agents for *Acinetobacter* isolates resistant to first-line agents, is associated with considerable toxicity, mainly nephrotoxicity and neurotoxicity, including neuromuscular blockade. We report a case of neurotoxicity of intravenous colistimethate sodium (CMS) manifesting as a potential factor interfering with weaning from mechanical ventilation.

Case: A 71-year-old woman visited the hospital with aggravated dyspnea and purulent sputum, who has been managed with low dose macrolide for bronchiectasis. Laboratory was significant for leukocytosis and elevated C-reactive protein. A chest radiograph showed newly appeared infiltration on right lung field. She was intubated and admitted to the intensive care unit (ICU) for type 2 respiratory failure and received empirical antibiotics including piperacillin/tazobactam and levofloxacin for pneumonia. On day 10 after her admission, sputum culture grew *acinetobacter baumannii* resistant to all antimicrobials except for colistin. Therapy was instituted with intravenous CMS (2.5 mg/kg every 12 h) and imipenem (500 mg every 6 h), which were administered for 2 weeks. On day 28 after intubation, we tried weaning from mechanical ventilation because the consolidation was nearly resolved on the chest radiograph with much improved clinical aspects and PaO₂/FiO₂ ratio became more than 200. However, it was failed to wean off the mechanical ventilator for 4 days consecutively even after all analgesics and sedatives were completely discontinued. There were no additional risk factors that may potentially trigger the development of neurotoxicity including the use of muscle-relaxants or corticosteroids. So the possibility of CMS-induced neuromuscular toxicity was suspected, and therapy with CMS was withheld. One day later, she became tolerable with T-piece (FiO₂ 0.4). She was extubated within 48 hours after discontinuation of CMS and was then transferred to the floor.

Conclusion: Patients receiving colistin could be exposed to the potential risk of neurological toxicity. As the use of colistin in ICU continues to increase, its neurotoxicity should be considered when weaning from mechanical ventilation is difficult.

P-H-003

FACTORS AFFECTING SUCCESS IN SMOKING-CESSATION THERAPIES USING NICOTINE PATCHES AND VARENICLINE

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Background: In 2006, smoking-cessation therapies using nicotine replacement therapy and varenicline became available for health insurance coverage in Japan. However, smoking-cessation success rates cannot yet be considered satisfactory.

Objective: To examine the factors affecting success in smoking-cessation therapies.

Subjects and Methods: The subjects were 109 patients who received outpatient smoking-cessation treatment at our hospital (set at a total of 5 visits) from January 2007 to November 2013. Concerning these cases, factors affecting the success of smoking cessation were analyzed using logistic regression.

Results: Forty-four patients (40.37%) successfully stopped smoking, while 65 patients (59.63%) were unsuccessful, dropped out, or stopped visiting. The success rate with a nicotine patch was 28.6% and that with varenicline was 50.0%, with varenicline achieving a higher success rate ($p = 0.031$). Of the 57 patients (52.2%) who attended the final examination at the 5 outpatient smoking-cessation visits, the success rate for nicotine patch was 66.7% and that for varenicline was 88.3%, showing that patients who strictly followed the outpatient smoking-cessation protocol tended to have higher success rates. In the nicotine patch group, adverse effects occurred in 7 cases (14.29%). In the varenicline group, adverse effects occurred in 23 cases (38.33%). Varenicline use was particularly associated with gastrointestinal adverse effects. Factors affecting success that exhibited statistical significance were Brinkman index (per 1 sd) (OR 0.651, $p = 0.049$) and fractional exhaled nitric oxide at the first examination (per 1 sd) (OR 0.618, $p = 0.031$). In cases where patients completed the outpatient examinations, Tobacco Dependence Screener (per 1 score) (OR 1.809, $p = 0.031$) exhibited statistical significance.

Conclusion: The smoking-cessation success rate was higher in the varenicline group than the nicotine patch group. Our results suggest that a lower Brinkman index and fractional exhaled nitric oxide at the first examination are associated with success. Moreover, patients who received examinations according to the prescribed protocol were observed to have higher success rates.

P-H-004

POSTER PRESENTATION – ENVIRONMENTAL & OCCUPATIONAL HEALTH AND EPIDEMIOLOGY

P-H-001

THREE CASES OF DENTAL TECHNICIAN'S PNEUMOCONIOSIS

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Dental technician's pneumoconiosis has recently been defined as a distinct group of pneumoconiosis. It develops as a result of exposure to alloys, acrylic plastics, quartz, carbon, and metal dust used by dental technicians and abundant in the ambient air inspired by them. CASE REPORT: Three men aged 38, 45, and 53 years presented to our clinic. They had been working as dental technicians in separate dental laboratories for 16, 25, and 31 years, respectively. Past history of all revealed a smoking history only. Diffuse pulmonary infiltrates were present on chest X-rays of all of them. One of them had mild obstruction and restriction in lung function test and a decrease in diffusion capacity. He had been working as a dental technician for a longer time. They were all diagnosed with dental technician's pneumoconiosis and were followed clinically and radiologically. In conclusion, dental technician's pneumoconiosis (DTP) is a preventable occupational pneumoconiosis that is related with the exposure time. Providing adequate information about occupational lung diseases and taking adequate technical prevention measures are necessary for saving dental technicians from this disease.

THE ROLE OF DIABETES MELLITUS AGAINST LUNG FUNCTION DECLINE RATE (FVC & FEV1) IN THE PRESENCE OF WORKERS WITH DUST EXPOSURE HISTORY

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Introduction: Developments in the industry today, has changed the pattern of existing disease. Pulmonary disease, which was formerly dominated by infectious diseases, today is influenced not by infectious diseases, such as exposure to airborne dust but is also affected by metabolic diseases suffered by the individual. The purpose of this study was to determine the role of diabetes mellitus on the rate of decline in lung function with a history of dust exposure.

Methods: The study design was cross-sectional comparative use of data from 494 periodic health examinations in 2012 and 2013. The data was collected using secondary data from periodic health examination period in 2012 and 2013.

Results and Conclusions: The mean difference between FVC and FEV1 impairment in 2012 and 2013 respectively in subjects with permanent status in DM (499 ml & 553 ml), normal to DM (192 ml & 253 ml), controlled DM (102 ml & 190 ml), and remained normal (143 ml & 213 ml). The results of the statistical test p -value <0.0001, significant at the 5 % alpha can be concluded there is difference in the rate of lung function decline in the average value of FVC and FEV1 on all study subjects.

Suggestion: There needs to be control over the workers who suffer from diabetes, by making appropriate treatment and prevent complications. Promotive and preventive activities to prevent workers from diabetes.

P-H-005

P-H-006

INTENTION OF NURSES TO RECEIVING INFLUENZA VACCINATION BEFORE THE FORTHCOMING SEASON

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Introduction: Influenza A (H1N1) pdm09 virus (pH1N1) has been shown to affect the influenza vaccine uptake rate. As pH1N1 has become the dominant strain and with its incorporation into the seasonal vaccine, the impact might have changed.

Objectives: To determine the influenza vaccine uptake rate of nurses in Hong Kong after the pH1N1 epidemic, and explore their intention for vaccination before the next influenza season.

Methods: Self-administered questionnaires were distributed by post through 4 professional nursing bodies of Hong Kong to individual nurses. Multiple choice questions in Chinese explored the reasons of accepting or rejecting vaccination, perceived professional responsibility, personal perceptions towards vaccination, infection and outbreak. All returns were anonymous.

Results: Between March to May 2013, 7% (2050 of 28300) questionnaires were returned. Over 60% of nurses were between 36–55 years old with frequent patient contact in public service. 31% were vaccinated in the season of 2012–13, 5% more than last year. Preventing oneself, friends/family from infection and reducing symptoms were reasons for vaccination in >50% of nurses. Vaccine side effects and failure to prevent infection were reasons against vaccination in >40% of them. About 30.7% accepted and 42% declined vaccination in the forthcoming season (2013–14) while 27.3% remained indecisive. Focusing on indecisive nurses, over 80% had refused vaccination in the last season. Some 18.1% refusing and 9.8% indecisive of vaccination perceived themselves as being “significantly unwell” after past vaccinations, compared to only 1% in the accepted. Odd ratio for future vaccination was 9.3 in nurses who had vaccinated in the last season. Risk of outbreak and individual infection were recognized in 60% and <40% of nurses. Expert opinion/guidelines were identified by only 1/3 of them. Professional responsibility e.g. setting an example for vaccination, vaccination as infection control, vaccinate to prevent outbreak were agreed by >70% of nurses who accepted future vaccination, <55% in those undecided and <40% in those refused.

Conclusion: Flu vaccine uptake rate of the last season has slightly increased compared to previous year. The acceptance in nurses was heavily influenced by one's past experience of side effects in previous vaccinations and perceived vaccine effectiveness. History of past vaccinations and beliefs in professional obligation positively affect the flu uptake rate. Given the high percentage of nurses who remained undecided on vaccination before the next flu season, it is particularly important that they be targeted in enhancing the preparedness among the healthcare profession.

THE ASSOCIATION BETWEEN OCCUPATIONAL AND ENVIRONMENTAL ASBESTOS EXPOSURE AND ASBESTOSIS IN KOREA-ASBESTOS HEALTH DAMAGE RELIEF SYSTEM

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Introduction: Asbestos-Health Damage Relief System have been activated in Korea since 1st Jan 2011. This system is for prompt relieving of patients with asbestos related diseases (ARDs) or bereaved families of patients with ARDs. When reviewing the results, it was noted that patients with asbestosis were exposed to environmental asbestos. In contrast with malignant mesothelioma, asbestosis is related to high exposure of asbestos. Therefore, it is necessary to evaluate details of exposure history in patients with asbestosis.

Objectives: The aim of this study was to evaluate detailed exposure history and to find which components (whether occupational or environmental exposure) is related with asbestosis.

Methods: Using the data derived from “Asbestos Health Damage Relief System” (January 1st 2011 through May 8th 2013), a total of 420 cases with asbestosis were analyzed. The diagnoses of those cases were reviewed and confirmed by specialists who majored in radiology, respiratory medicine, and occupational medicine. Disproved cases were excluded from this study. Occupational specialists evaluated the occupational exposure history in terms of probability and intensity. With probability and intensity of occupational exposure, Job-Exposure Matrix (JEM) was established. Environmental exposure was classified into definitely high exposure (residents near the asbestos mine) or not. The final exposure variables were described as Occu(low)/Envirn(low), Occu(high)/Envirn(low), Occu(low)/Envirn(high), Occu(high)/Envirn(high).

Results: The distribution of occupational & environmental asbestosis exposure were 31 (7.7%) at Occu(low)/Envirn(low) group, 104 (25.7%) at Occu(low)/Envirn(high) group, 62 (15.4%) at Occu(high)/Envirn(low) group, 207 (51.2%) at Occu(high)/Envirn(high) group. Male is more prevalent (n = 278, 71.1%). Familial occupational exposure levels were more frequent (n = 58, 27%) in those group with Occu(high)/Envirn(high) exposure history. The most prevalent group for advanced type of asbestosis was Occu(high)/Envirn(low) (n = 18, 26.5%). However, 6.5% (7 out of 107) of advanced type of asbestosis were also found.

Conclusion: Environmental exposure (residents near asbestos mine) may be a major risk factor for asbestosis. There was an interaction between occupational and environmental exposure. To prevent asbestosis, the evaluation of occupational and environmental exposure should be considered.

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P-H-007

ROUTE OF EXPOSURE ALTERS INFLAMMATION AND LUNG FUNCTION RESPONSES TO DIESEL EXHAUST EXPOSURE

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Introduction: Mice are commonly used in studies investigating the effects of diesel exhaust exposure on respiratory health. A plethora of studies in this field has resulted in a range of exposure protocols, from inhalation of diesel exhaust, to the administration (via various routes) of diesel exhaust particles in solution.

Aims and Objectives: In this study, we compared the physiological consequences of short-term exposure to diesel exhaust via inhalation to those due to exposure to the same diesel exhaust particles suspended in solution and delivered intranasally.

Methods: Adult BALB/c mice were exposed to diesel exhaust via inhalation for 2 hours per day for 8 days. A sample of particles was collected and a second group of mice was exposed to them suspended in saline. A low and a high-dose were studied, with these matched based on respiratory parameters. Six and twenty-four hours after the last exposure we measured bronchoalveolar inflammation, lung volume, lung function and the amount of elemental carbon in alveolar macrophages.

Results: Exposure via either route elicited pulmonary inflammation and changes in lung function. We identified significant differences in response between the two routes of exposure, with mice exposed via inhalation generally displaying more realistic dose-response relationships. Mice exposed via intranasal instillation responded more variably, with little influence of dose.

Conclusions: Our results suggest that selection of the route of exposure is of critical importance in studies such as this. Further, inhalation exposure, while more methodologically difficult, resulted in responses more akin to those seen in humans.

P-H-008

LONG TERM EFFECTS OF THE WILDFIRES SMOKE ON RESPIRATORY SYSTEM IN PEOPLE EXPOSED TO AEROSOLS IN ABNORMAL SUMMER IN MOSCOW 2010

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Our previous study showed the pathogenic role of abnormal heat and wildfires smoke in the development of acute respiratory diseases and exacerbation of chronic illness, leading to increased mortality. The aim of this study was to reveal the long term effects of exposed aerosols in lung function. The study included 59 persons both genders, nonsmokers, exposed to smog in summer 2010.

I group – 10 healthy persons.

II group – 23 with newly diagnoses acute and chronic bronchitis (11), asthma (12) during smoky period.

III group – 12 (7 COPD, 5 asthma) had an exacerbation due to inhalation of dust particles in 2010.

IV group – 14 (7 COPD, 7 asthma) who were absent this time in Moscow. The number of calls for medical aid and duration of exacerbations during 2-year period were registered. All patients were submitted to: physical examination, spirometry before and after bronchodilators, PEF monitoring. The results were analyzed in comparison to previous data. I group registered 60% having upper respiratory tract infection 2–3 times a year, followed by obstructive lung function failure and bronchial hyperreactivity. II group noted 82% with chronic bronchitis of a light stage which transferred to the 2–3 stages; 50% with intermittent asthma transferred to light and mild persistent diseases with frequent exacerbations (2–3 times per year) and FEV1 reduction (15–28% predicted). III group noted 43% with COPD GOLD2 that transferred to GOLD3. 4 persons with asthma from mild persistent moved to moderate (3) and severe persistent (1) stages. In IV group only 1 person with COPD moved from GOLD 2 to GOLD3 stage. Our results suggest a persistent pathogenic effect of the wildfire smoke, leading in one hand to irritative inflammation and development of respiratory disorders and in another, to the severity of chronic lung diseases.

P-H-010

A CASE OF DYNAMITE EXPLODER WITH SILICOSIS

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A 46-year-old male patient who was admitted to our polyclinic with hemoptysis and dyspnea was hospitalized with a suspicion of occupational disease. The patient had worked as a dynamite exploder for 16 years. He had a 20 pocket-year smoking history and recurrent hemoptysis in the last two months. A thorax computed tomography revealed multiple mediastinal lymphadenopathy, extensive parenchymal micronodules and interstitial pattern. Fiberoptic bronchoscopy showed enlargement of all carinas, extensive mucosa trabeculations, oedema and scattered haemorrhagic mucosa. All histopathological specimens were nondiagnostic. A diagnosis of silicosis was made after open lung biopsy. In conclusion, dynamite explosion may be a cause of silicosis as an occupational disease and the case was presented in order to discuss this aspect.

P-H-011

PREVALENCE OF COAL WORKERS' PNEUMOCONIOSIS IN KARADON COAL MINE, ZONGULDAK, TURKEY

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Introduction: Coal workers' pneumoconiosis (CWP) is a paranchymal lung diseases that is caused by inorganic dust exposure. We aimed to investigate CWP in underground coal miners who are employed in one of the biggest coal mining area of Turkey.

Material and Method: During the periodical examination of all coal miners who work in Karadon instution of Zonguldak coal mining area, analog standart posteroanterior (35 × 35 cm) chest radiographies of all coal miners were obtained and were assessed by a chest diseases specialist who had an ILO radiography reader certificate.

Results: Of the 3705 underground coal workers, 181 had pneumoconiosis lesions. 1327 workers that were employed in 2008 were included this numbers and none of them had a pneumoconiosis. 19 workers had a progression when compared with their previous year's radiographies. We detected that all the pneumoconiosis cases have been in employment for at least 10 years. Total prevalence was 4,9% and incidence was 1,9%. All cases of pneumoconiosis were micronodular types. There was no major opacity. In 2009, all areas of Zonguldak had 8705 coal workers, of which 258 had pneumoconiosis (2,9%). **Discussion:** Pneumoconiosis incidence was 1,62% (49/3012) and the prevalence was 4,7% (142/3012) in Karadon instution in 2009. In 2011, the prevalence was 2,7% but in 2012 it increased to 4,9%. The prevalence that we found in Karadon instution is similar to world pneumoconiosis prevalence (3–5%).

P-H-012

ASSESSMENT OF RESPIRATORY HEALTH IN TIMBER MILL WORKERS IN CENTRAL SRI LANKA: A PILOT STUDY

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Background: Respiratory disorders in occupational settings are well established, however there is minimal information related to respiratory health in timber mill workers in Sri Lanka.

Objectives: Our primary objective was to assess the workers in relation to their current respiratory health status, and to identify possible preventive interventions for future protection.

Methodology: In this cross sectional descriptive study, all workers in the mill were enrolled. An interviewer administered questionnaire was used to gather information related to demographic data, respiratory symptoms, type of work, duration, exposure type, and health related other co morbidities. All subjects were clinically examined and each underwent a chest X ray. A basic spirometry was performed using 'Spirolab 111' portable spirometer. The data were analyzed using Microsoft Excel software.

Results: The total number was 65, out of them 62 (95%) were males. Mean age of the workers was 42 years with a range of 21 to 71. None were using protective devices such as goggles, masks, ear plugs or gloves. All the subjects were unaware of health related ill effects of wood dust and noise pollution. Respiratory health-related common symptoms were chest pain (21%), shortness of breath (18%), cough (18%) and wheezing (07%). Majority of the workers (58%) were asymptomatic. 42 (67%) of the male workers were smokers. 26 subjects had co-morbidities with Bronchial Asthma in 7 (10%) and Cardiovascular Diseases in 19 (29%). 15 (24%) had abnormal chest x rays which included emphysema in 11 subjects and reticulonodular pattern in 4. Spirometry was normal in all subjects.

Conclusion: Common respiratory symptoms observed in our study group were chest pain, cough and shortness of breath. Majority of the subjects were asymptomatic and all had normal spirometry. More than 2/3 of the study population was found to be smokers. We would like to address the importance of smoking cessation in this group because they are the economically most productive employees in the community. Also we recommend periodic re evaluation and follow up screening of these workers and emphasize on use of protective devices to preserve the respiratory health of these workers.

P-H-013

ASSESSMENT OF RESPIRATORY HEALTH IN PETROLEUM PUMP WORKERS IN SRI LANKA: A PILOT STUDY

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Background: Petroleum products are known to cause respiratory diseases when patient is exposed to a significant quantity and duration of them. Pump workers at filling stations are a vulnerable group. No systematic studies have been done in Sri Lanka to assess the exposure effects of these products on this group of workers.

Objective: Our primary objective was to assess the pump workers in relation to their current respiratory health status, and to identify possible preventive interventions.

Methodology: In this cross sectional descriptive study, an interviewer administered questionnaire to gather information related to demographic data, respiratory symptoms, type and duration of exposure and co morbidities. All subjects were clinically examined and each underwent a Chest X-ray. Basic spirometry was done using 'Spirolab 111' portable spirometer. The data were analyzed using Microsoft Excel software.

Results: The total number studied was 50. All were male workers with a mean age of 33 years (range 20 y–58 y). Mean duration of exposure was 9 years (range 6 Months to 30 years). 22 (44%) subjects were current smokers. None were using protective devices such as goggles, masks or gloves. All the subjects were unaware of health-related ill effects of exposure to petroleum fumes. Respiratory health-related symptoms were cough in 60.6%, breathing difficulty in 16.6%, and chest pain in 5.5%. Lung function test were normal in 39 (78%) subjects, and 11 (22%) were found to have mild restriction. 33 (66%) had normal chest X-rays and 17 (34%) had abnormal Chest X-rays. 15 had air trapping while 2 had nodular shadows with lower zone predominance. HRCT and other investigations were carried out for abnormal CXR and confirmed abnormalities as COPD and non specific granuloma by tissue biopsy.

Conclusion: Respiratory symptoms were detected in one fifth of the sample. Majority of the study sample were having normal lung function and chest X-Rays. COPD and early stage of possible pneumoconiosis were detected in minority. There is inadequate knowledge about the use of protective devices, and awareness of occupational hazards. We would like to recommend to educate these workers regarding the hazards of the petroleum products and smoking. Continuous surveillance to detect respiratory disorders and timely appropriate management are needed for exposed population.

P-H-014

RESPIRATORY DISORDERS PROFILE AND PULMONARY FUNCTION TESTS ON WOOD-HOUSEWARES MILLS WORKERS IN DELI SERDANG INDONESIA

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Background: Wood dust in low concentrations when inhaled by humans continuously for long periods of time can cause abnormalities in the airways in the form of restriction, obstruction, or a combination. Examination of lung function as a supporting examination in occupational pneumoconiosis is a more sensitive examination to determine the pathological changes of the respiratory tract.

Methods: This study is an analytic approach and using cross sectional data collection. Samples of wood dust workers are all employees working at Wood-Housewares Mills and associated with wood dust were 39 people while office workers samples were 7 people. Then the data collection was done by using a questionnaire and spirometry. The questionnaires are arranged in the form of basic data such as gender, age, work units, height, weight, duration of work, history of smoking. Examination of lung function is using spirometry.

Results: In this study, we found the restriction abnormalities were 9 people (23%). Abnormalities combination were 7 people (18%), the remaining 23 people (59%) were normal spirometry results of the total study subjects were 39 people.

Conclusion: Smoking Factor, years of work, workplace, and use of PPE do not have a significant association with impaired lung function.

P-H-015

INCIDENTALLY DIAGNOSED PULMONARY DIFFUSE STIPPLED CALCIFICATION IN AIRCRAFT LINE MECHANIC

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Background: Chronic exposure to aircraft exhaust gases and many chemicals used in aircraft can lead to occupational diseases in the long term. We report the case of an aircraft technician worker.

Case: A 40-year-old male patient had worked as a line mechanic for 20 years. He had a history of exposure to exhaust gas and the iron powder during landing gear tire replacement while working in the flight line. He had a smoking history of 7.5 pack-year. He did not have pulmonary disease or complaints. Patient underwent T3 and T4 vertebroplasty operation due to trauma two months before. He was referred to our clinic after abnormal findings on chest radiography during postoperative controls.

Results: Pulmonary auscultation, pulmonary function test and oxygen saturation were normal. Complete blood count values and routine biochemistry were normal. Chest X-Ray and thorax CT showed diffuse pulmonary Stippled calcification in both lungs.

Discussion: The patient did not have any known history of respiratory disease. He had not use protective mask while working in the flight line. Patient may have inhaled various micro particles derived from exhaust gas, dust, and aircraft parts during tire replacement of landing gears.

Conclusion: Due to all these factors, the patient's existing lesions was thought to be due to occupational exposure. Patient was informed about his disease and what measures have to be taken. Patient initiated Outpatient follow up.

P-H-017

THE EVALUATION OF OCCUPATIONAL RESPIRATORY DISEASES AND OCCUPATIONAL HEALTH PROBLEMS IN DENTAL LABORATORY TECHNICIANS WORKING IN DENIZLI, TURKEY

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Aim: Dental Laboratory technicians (DLT) are exposed to various risks (dust, noise) while working in laboratories. The aim of this study is to determine the prevalence of occupational respiratory diseases and occupational health problems among DLT working in Denizli, Turkey.

Materials and Method: All the dental technicians participated to the study. A questionnaire which contains demographic characteristics, work conditions and symptoms was applied to all participants. Also spirometric measurements and chest x-rays examinations and if necessary HRCT were performed for evaluation of respiratory system of DLT. Data were analyzed by SPSS 10,0 statistical packet programme.

Results: 166 technicians (23 female, 143 male) who had been working in Denizli city were included to the study. The mean age of technicians was 33.5 years and the mean total working duration was 16.0 years. The mean total working duration was calculated as 36.177 hours. Also 56% of technicians were smokers. When we evaluated the workplaces; it was found that 98.8% of laboratories have a ventilation system, but only 80.2% of them were using them frequently or continuously. The use of protective materials such as mask, vacuum extractor, eyeglasses or gloves was also found to be low (respectively 69%, 63% 47%, 36%). Only 59.69% of technicians have had three doses Hepatitis B vaccination. 21,2% of DLT have respiratory symptoms such as cough, dyspnoea and phlegm expectoration. Also 15% of the them have eye-related symptoms. Ten pneumoconiosis cases (6%) were found among DLT. Pneumoconiosis cases were found higher in male technicians and in technicians working at district government hospitals. Pneumoconiosis cases were found higher at metal leveling department employees. Cases were higher at technicians working more than ten years. These findings were indicating problematic regions of the laboratories.

Conclusion: Insufficient indoor ventilation and insufficient use of protective equipment, smoking was common among the technicians. Ten pneumoconiosis cases indicated that the dental technicians are at risk for occupational respiratory diseases. Occupational health and safety measures such as increasing usage of protective materials, ventilation systems, and vacuum equipment in workplaces should be increased.

P-H-018

HYDATID DISEASE – SHOULD WE SCREEN CLOSE CONTACTS? A SERIES OF 3 CASES OF THE SAME FAMILY WITH MULTIPLE HYDATID CYSTS

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Hydatid disease is caused by larvae of the tapeworm Echinococcus. Four species are recognized and the vast majority of infestations in humans are caused by *E. granulosus* which causes cystic echinococcosis that has a worldwide distribution. In cystic echinococcosis, humans are an accidental host and are usually infected by handling an infected dog. Here we present a series of 3 cases of hydatid disease diagnosed over a period of one year who are family members and lived in the same premises. The first case was symptomatic but the second case with minimal symptoms was diagnosed after 1 yr only because of high clinical suspicion. The third case was totally asymptomatic and was diagnosed on screening after the second case was diagnosed. With this background, we raise an important question, should the members living in same surrounding be screened for possible hydatid disease? As common pet animals and livestock are involved in transmission of the disease, it is likely to affect other individuals sharing the same habitat. Hydatid disease is known to have an insidious course which is largely unrecognized till very late hence chances of it remaining undiagnosed are high. With the progression of the disease the chances of rupture of the cysts increases considerably that may be life threatening. This can be avoided by early diagnosis and treatment of the disease. Moreover the disease can be picked up early by simple, non invasive and inexpensive tests that are easily available across geographies like X Ray Chest and Sonography of the Abdomen.

P-H-019

COMPARISON OF PULMONARY FUNCTION IN TRAFFIC POLICEMEN AND GENERAL POLICEMEN IN PADANG CITY

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Background: Air pollution exposure for long term could cause pulmonary impairment and lower respiratory symptoms such as cough, breathlessness, and chest pain. Traffic policemen who work in field job are exposed to many pollutants. The aim of this study to define the association between traffic-related pollutant exposures and pulmonary function on traffic policemen in Padang.

Material and Methods: In this cross sectional study, we collected demographic data, tenure, body weight, height, pulmonary function, smoking status, the use of mask, and air quality in Padang. Data were analyzed using unpaired T-test alternative Mann whitney test and chi square test, alternative Fisher's exact test and Kolmogorov-Smirnov test, and Spearman Correlation test and eta. P value of <0.05 is considered as significant.

Result: There was a total subject of 146, comprising 73 traffic policemen and 73 general policemen as control. Force Expiratory Volume in one second (FEV1) value in traffic policemen is greater than general policemen with p value = 0,232. Force Vital Capacity (FVC) value in traffic policemen is greater than in general policemen with p value p = 0.045. FEV1/FVC value in general policemen is greater than traffic policemen with p value = 0,084. There were no association between age, Body Mass Index (BMI), tenure and pulmonary impairment (p = 0,370; 0,921; 0,384; 0,095; respectively). There were statistically significant association between smoking status with pulmonary function and the use of mask with pulmonary function (p = 0,038; 0,007; respectively).

Conclusion: The value of FVC in general policemen statistically is lower than in traffic policemen. There were no association between traffic related pollutant exposure and pulmonary function.

P-H-020

P-H-022

THE MEASUREMENT OF URINARY COTININE LEVELS IN PASSIVE SMOKERS ADULT WOMEN EXPOSED TO ENVIRONMENTAL TOBACCO SMOKE AT THEIR RESIDENCE IN PASAR REBO AREA, JAKARTA (PRE-ELIMINARY REPORT)

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Background: About 75.4% (62 million) non-smoking women age more than 15 years old in Indonesia were exposed to tobacco smoke in their house. Studies of the health effects of environmental tobacco smoke (ETS) using cotinine, a nicotine metabolite detected in urine, has been recommended as a quantitative measurement of nicotine intake and as a marker for ETS exposure in humans. The aim of this study was to correlate daily indoor ETS exposure in non-smokers (adult women) at their house by measuring urinary cotinine levels and its health effects.

Methods: In this study, we performed a pre-eliminary, cross-sectional study to 50 ETS-exposed non-smokers adult women in Pasar Rebo area, Jakarta. The urinary cotinine concentrations of 50 subjects who were exposed to environmental tobacco smoke at home were measured and analyzed using ELISA method. In addition, information was collected regarding the smoking habits of the subjects family members at home and health effects to the subjects. The passive smokers adult women completed a series of questionnaire, included number of active smokers at home, quantities and duration of cigarette smoked by family members at home per day, years of exposure to tobacco smoke, and health effects to subjects.

Results: 50 passive smokers adult women aged 18 to 54 years old with a mean age of 39 years old participated in this study. Most of them (92%) were less educated because the highest education they achieved was high school. Urinary cotinine concentrations that we got from ELISA method measurement to these 50 subjects ranged between 2.6 ng/ml until 136 ng/ml with a mean cotinine concentrations level of 35.13 ng/ml.

Conclusion: The mean urinary cotinine concentrations in passive smoking women from various studies around the world ranged between 13.1 ng/ml until 48.5 ng/ml. Although this study is still in preliminary report, our data showed that Indonesian passive smoking adult women have reached higher mean urinary cotinine concentration levels (35.13 ng/ml). Urinary cotinine measurement is a sensitive, noninvasive and effective method to correlate with ETS exposure.

P-H-021

INCIDENT OF SILICOSIS AND RESPIRATORY SYMPTOMS IN LIMESTONE FACTORY'S WORKERS IN BUKIT TUI PADANG PANJANG

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Background: Limestone factories produce dust, smoke, and gases in ptheir roduction process. Long term exposure could cause respiratory symptoms and silicosis. The aim of this study is to determine the association between limestone dust exposure and the incident of silicosis and respiratory symptoms.

Method: In this cross sectional study, we collected data including demographics, limestone dust exposure, respiratory symptoms, and we performed chest X-rays to evaluate silicosis in limestone factory's workers. Data were analyzed using SPSS version 21 and chi square test with p value <0.05 considered as significant.

Result: We found a total 96 eligible subjects. There was an association between respiratory symptoms (no symptom, chronic cough, breathlessness, chest pain, two symptoms and three symptoms) with the application of personal protective equipments (p = 0,032; confident interval 95%) and the application of non standardized personal protective equipments (p = 0,034; confident interval 95%). There were no association between tenure and respiratory symptoms (p = 0,330; confident interval 95%). We found two subjects with silicosis based on ILO chest x-rays (2.08%), in man and woman, 45 and 56 years old. Both of them had different work places (burning vs milling) and tenure (3 years vs 32 years). None of them used standardized mask. Both are smokers with moderate brinkman index and working hour of more than 40 hours a week.

Conclusion: There were no significant association between respiratory symptoms and sillicosis.

THE RELATIONSHIP BETWEEN ENVIRONMENT AND THE PREVALENCE OF ALLERGY RHINITIS IN PRE-SCHOOL CHILDREN IN GUANGZHOU CITY

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Background: In recent decades, the prevalence of allergic rhinitis in many countries has increased, particularly among children. According to previous study, we know that influential factors included individual characteristics (allergic constitution), genetic factor, and environmental factor and so on. Environmental pollution in China is getting worse, we do not know whether the prevalence of children's allergic rhinitis is related to the environment or not. An investigation of the relationship between the prevalence of children's allergic rhinitis and the environment (passive smoking, long-term exposure to plush or bubble toys, long-term exposure to pets and use carpet at home, etc) could present strong evidence for the prevention of allergic rhinitis in children.

Method: The questionnaire was designed based on the internationally accepted International Study of Allergic rhinitis and Allergies in Childhood (ISAAC) questionnaire, in combination with the epidemiological characteristics of local allergic disorder in Guangzhou city. Kindergartens were selected by a random, cluster-sampling method. There are 13 kindergartens, which had 2500 children. Parents of kindergarten children completed the questionnaire after being taught by teachers. Relevant investigators confirmed the effectiveness of the questionnaire by phone call. The results were analyzed by SPSS 17.0. Multivariable logistic regression was used to analyze the associations between parent-reported allergic rhinitis and environment factors that yielded p-values <0.1 in the univariate analyses.

Result: Of the 2500 questionnaires that had been handed out, 2355 were valid and 145 invalid, giving a valid answer rate of 94.2%. The prevalence of allergic rhinitis in children in this survey was 15.5%. Applying the logistic regression analysis of environment factors in children allergic rhinitis, we found that with a home or school near the road, long-term exposure to plush or bubble toys, pet ownership, or passive smoking, the risk of children having allergic rhinitis increased (P < 0.050). Using cotton pillow or quilt was one of the protection factors.

Conclusion: In Guangzhou city, home or school near the road; long-term exposure to plush or bubble toys; pet ownership; and passive smoking can increase the risk of allergic rhinitis in children.

P-H-023

SOCIOECONOMIC AND EDUCATION CONCERNING AWARENESS AND BEHAVIOURS RELATING TO INFLUENZA IN MEXICO

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Background: During the spring of 2009, an outbreak of influenza H1N1pdm09 was identified in Mexico and spread rapidly around the world. However, the rates of severe and fatal cases differed among countries and regions. Although there were several factors associated with the severity and mortality from influenza H1N1pdm09, our previous studies indicated that low socioeconomic conditions and lack of information were one of factors for hospitalized pneumonia with influenza H1N1pdm09, along with the clinical conditions of patients.

Method and Principal Findings: The study was conducted the National Institute for Respiratory Diseases (INER), a national tertiary care organization in Mexico City. We carried out a questionnaire survey to evaluate an educational intervention, conducted in the September of 2013, as well as to collect the clinical and socioeconomic backgrounds of subjects and their health related behaviours. We followed-up subjects if they got influenza or hospitalized due to influenza after the intervention. Total 445 subjects (Male, 172) of whom formally hospitalized in the INER due to influenza during H1N1 pandemic and were allocated into intervention (n = 242) and no-intervention (n = 245) groups. The family income of 58% of total subjects was \$385 (US)/month. 15.1% of total subjects were smoker, 20% had chronic respiratory diseases, and 14% of subjects were obesity. After the educational intervention, the high recognition of four major symptoms of influenza (fever >38°C, cough, headache, shortness of breath) was observed in 86% of intervention group and 7% of no-intervention group. During the October of 2013 and February 2014, 16.9% and 14.3% of subjects in intervention and no-intervention groups got influenza, respectively. However, 2.4% and 42.4% of subjects in intervention and no-intervention groups, respectively, hospitalized due to influenza pneumonia (p < 0.001). Approximately 70% of subjects in intervention group received the vaccination during the observational period.

Conclusion: Health education assisted to reduce disease severity of influenza in Mexico. The educational model of the present study is an opportunity for a tertiary care hospital for maintaining the people's health, especially those facing economic difficulties.

POSTER PRESENTATION – INTERSTITIAL LUNG DISEASE

P-I-001

LEBRIKIZUMAB IDIOPATHIC PULMONARY FIBROSIS TRIAL: A PHASE II RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO ASSESS EFFICACY AND SAFETY (RIFF)

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Objectives: Lebrikizumab – developed by Genentech/Roche – is a humanized monoclonal IgG antibody targeting the protein IL-13. Lebrikizumab binds specifically to soluble interleukin-13 (IL-13) and blocks IL-13 signaling through the interleukin-4R alpha (IL-4Rα)/IL-13Rα1 pathway, thereby preventing the downstream effects of human IL-13 with high potency. The IL-13 and IL-4 pathway have been implicated in normal tissue repair processes and aberrant lung fibrosis. IL-13 and IL-4 are strong inducers of fibrogenic responses in vitro and tissue fibrosis in vivo. Idiopathic pulmonary fibrosis (IPF) is characterized by varying degrees of interstitial fibrosis. It is hypothesized that inhibition of IL-13 by lebrikizumab may reduce disease progression. Based on the importance of IL-13 in the pathogenesis of IPF, inhibition of IL-13 represents a potentially effective approach for the treatment patients with a confirmed diagnosis of IPF across a broad range of disease severity.

Methods: Lebrikizumab idiopathic Pulmonary Fibrosis Trial: A Phase II Randomized, Double-blind, Placebo Controlled Study to Assess Efficacy and SaFety, (RIFF), is designed to evaluate the safety and efficacy of lebrikizumab in patients with Idiopathic Pulmonary Fibrosis. The trial will enroll 250 patients with a diagnosis of IPF based upon the most recent ATS/ERS/JRS/ALAT guidelines (Raghu et al. 2011) randomized 1:1 to lebrikizumab or placebo. Inclusion/Exclusion criteria have been established to include patients across a broad range of disease severity. Enrollment started in October 2013 and recruitment is ongoing. The study will measure clinical, functional, structural and quality of life outcomes over a maximum period of 2.5 years of treatment per patient. The primary outcome measure for the study is Progression Free Survival. A number of design features distinguish this trial from many others, among them are the inclusion of patients across a broader range of disease severities, standardization of lung function including DLco, and assessment of patient activity using biosensor technology. A fully integrated biomarker programme is planned to assess pre-selected serum proteins as candidate biomarkers of disease progression, including periostin, a potential predictive and prognostic serum protein.

Conclusion: Further information on the study including inclusion/exclusion criteria is available at www.clinicaltrials.gov and directly at <http://www.clinicaltrials.gov/ct2/show/NCT01872689>.

P-I-002

SERUM B CELL ACTIVATING FACTOR BELONGING TO THE TUMOUR NECROSIS FACTOR FAMILY (BAFF) IN AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Introduction: Due to the existence of autoantibody against anti-granulocyte/macrophage colony-stimulating factor (GM-CSF) antibody in systemic fluids, autoimmune pulmonary alveolar proteinosis (APAP) has been thought as an autoimmune rare disease. The elevation of B cell activating factor belonging to the tumour necrosis factor family (BAFF) level in serum is reported in some autoimmune diseases, such as systemic lupus erythematosus, Sjögren's syndrome and rheumatoid arthritis. Abnormality of humoral immunity is also suspected in the patients with APAP. Then, we hypothesized that abnormality of humoral immunity in patients with APAP make BAFF level increase prominently in serum.

Subjects and Methods: Thirty patients with APAP (Male: 22, Female: 8, Age: 54 ± 15 y.o.) and 27 healthy controls (Male: 15, Female: 12, Age: 49 ± 8 y.o.) were enrolled in this study. Serum BAFF levels were measured by ELISA using commercially available kit (R&D systems). To clarify the role of serum BAFF level, we compared the data with clinical measures.

Result: We found significant increase in serum BAFF level of the patients with APAP compared to healthy control ($p < 0.05$, respectively). Furthermore, we found a case that serum BAFF level showed remarkable increase with high level of CRP. Serum BAFF level showed correlations with KL-6, surfactant protein (SP)-D, SP-A, and CYFRA in serum ($p < 0.05$, respectively). Serum BAFF level did not correlate with disease severity score as well as autoantibody against GM-CSF. (Inoue Y. AJRCCM, 2008).

Conclusion: We confirmed APAP as an autoimmune disease by significant increase of BAFF and autoantibody against GM-CSF in serum, which may be indicating an abnormality of humoral immunity system. Longitudinal studies are required to determine the role of the BAFF systems in APAP.

P-I-003

NITRIC OXIDE EXERTS PROTECTIVE EFFECTS AGAINST BLEOMYCIN-INDUCED PULMONARY FIBROSIS IN MICE

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Background: Increased expression of several types of nitric oxide synthases (NOS) and increased levels of plasma nitrite and nitrate (NOx) have been reported in patients with pulmonary fibrosis, suggesting that nitric oxide (NO) has important roles in the development of pulmonary fibrosis. However, the roles of the entire system including NO and NOS in the pathogenesis of pulmonary fibrosis has not still being fully elucidated. The aim of the present study was to clarify the roles of NO and NOS in pulmonary fibrosis using the mice lacking all of three NOS isoforms.

Methods: Wild-type, single and triply NOS knockout (*n/i/eNOS*^{-/-}) mice were treated with intraperitoneal administration of bleomycin (BLM, 8.0 mg/kg/day for 10 consecutive days). Two weeks after the last administration of BLM, fibrotic and inflammatory changes of the lung were pathologically evaluated. In addition, the effects of long-term treatment with isosorbide dinitrate, a NO donor, on the BLM-induced pulmonary fibrosis in *n/i/eNOS*^{-/-} mice were studied.

Results: The histopathological findings, collagen content and total cell numbers in bronchoalveolar lavage fluid were the highest in the *n/i/eNOS*^{-/-} mice after BLM treatment. Long-term treatment with supplemental NO donor significantly prevented the progression of these histopathological findings and an increase of collagen contents in the lungs induced by BLM treatment in *n/i/eNOS*^{-/-} mice.

Conclusions: These results provide the first direct evidence that a lack of all three NOS isoforms led to a deterioration of pulmonary fibrosis in a BLM-treated murine model using *n/i/eNOS*^{-/-} mice. We speculate that the entire system of endogenous NO and NOS plays an important protective role in the pathogenesis of pulmonary fibrosis.

P-I-004

TUMOUR NECROSIS FACTOR-RELATED APOPTOSIS-INDUCING LIGAND ENHANCES FIBROSIS AND COLLAGEN PRODUCTION IN IDIOPATHIC PULMONARY FIBROSIS PATIENTS

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Background: Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL/APO-2L) is a member of the tumour necrosis factor family that induces apoptosis. Numerous basic and clinical research studies have explored its evaluation for the treatment of human cancers, however it is unknown whether TRAIL has a role in human idiopathic pulmonary fibrosis (IPF). We therefore studied TRAIL expression in IPF patients.

Methods: Serum samples were collected from 14 IPF patients and 12 controls from 2012.10 to 2013.03 in the Second Affiliated Hospital of Jilin University. Clinical data, including pulmonary function tests, are also collected. ELISA for serum TRAIL was performed to measure protein levels of TRAIL. Primary human lung fibroblasts were cultured, early passaged fibroblasts were cultured with 1 ng/ml recombinant TRAIL for 24 h and qPCR was performed to measure the expression of collagen α (II). All the studies were approved by the Medical Ethics Committee of the Second Affiliated Hospital of Jilin University, Changchun, Jilin, China. All the results were compared using t-tests. Correlations between serum TRAIL levels and total diffusing capacity of the lung for carbon monoxide (DLco) were assessed using Pearson's correlation coefficient.

Results: Serum TRAIL is increased in patients with IPF compared with controls ($P < 0.01$); Serum levels of TRAIL in IPF patients were significantly negative correlate with DLco values ($r = 0.7528$, $P < 0.0001$, $n = 14$). The expression of collagen α (II) in fibroblasts cultured with rTRAIL was higher than in fibroblasts ($P < 0.05$).

Conclusions: These data suggest TRAIL enhances fibrosis and serum levels of TRAIL are negative correlate with DLco in patients of IPF. In addition, rTRAIL can enhance extracellular matrix synthesis in human fibroblasts.

P-I-005

CLINICAL FEATURES OF PATIENTS WITH PLEUROPARENCHYMAL FIBROELASTOSIS (PPFE): OUR EXPERIENCE

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Aim of the Study: Pleuroparenchymal fibroelastosis (PPFE) was first mentioned in the ATS/ERS statement in 2013 but its clinical features have not yet been established. It is difficult to collect a large number of cases of PPFE since it is a rare condition as described in the ATS/ERS statement and few cases are pathologically confirmed.

Objective: To illustrate clinical features of a group of diseases associated with PPFE-like upper lobe-predominant fibrosis on HRCT.

Methods: A total of 11 patients (7 males and 4 females; mean age, 73.9 ± 6.8 years) showing upper lobe-predominant fibrosis on HRCT at Nippon Medical School Chiba Hokusoh Hospital and Ibarakihigashi National Hospital between April 2011 and July 2014 were examined for BMI, smoking history, KL-6, SP-D, room-air arterial blood gas at resting, lung function, and chest expansion defined as the difference between maximal inspiration and expiration in circumference measured by a tape measure at the levels of axilla, xiphoid process, and the tenth rib.

Results: These patients were lean with the mean BMI of 16.4 ± 2.2 . Six patients had no smoking history (never smokers), while 5 patients smoked 15 pack-years in average. Both KL-6 (712 ± 494 U/mL) and SP-D (234.6 ng/mL) were slightly high. Resting arterial blood gas analysis in the stable stage resulted in pH 7.418 ± 0.025 , PaCO₂ 42.6 ± 6.3 mmHg, PaO₂ 81.6 ± 13.3 mmHg and HCO₃⁻ 26.9 ± 3.1 mEq/L, which suggested chronically slight increases in CO₂. Lung function test indicated restrictive ventilator impairment with %VC of $50.2 \pm 20.0\%$ and %TLC of $60.9 \pm 18.3\%$, while many patients showed no obstructive ventilator impairment with FEV₁% of $86.4 \pm 20.0\%$. The mean chest expansion (% chest expansion) was generally small: 0.13 ± 0.12 cm ($0.17 \pm 0.15\%$), 0.73 ± 0.46 cm ($0.90 \pm 0.53\%$) and 0.97 ± 0.47 cm ($1.3 \pm 0.63\%$) at the levels of axilla, xiphoid process and the tenth rib, respectively. A marked restriction of chest extension was noted especially at the level of axilla.

Conclusion: The present findings on BMI, smoking history, markers for fibrosis, arterial blood gas analysis, and respiratory function were consistent with previous reports. The present study additionally revealed a markedly limited chest expansion. There is no report on the chest expansion in patients with PPFE as far as we have searched. Given that upper lobe-predominant fibrosis with PPFE-like histology has been reported in patients with ankylosing spondylitis that is associated with similarly limited chest expansion, such a restriction in chest expansion may be involved in development of PPFE. Further evaluation in more cases is required.

P-I-006

PREVALENCE OF AMRUBICIN INDUCED LUNG INJURY IN OUR HOSPITAL

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Background and Aims: Amrubicin (AMR), a topoisomerase II inhibitor, is an important therapeutic option for lung cancer, especially for small cell carcinoma. Drug induced lung injury is a serious, sometimes fatal, side effect of anticancer drug. We investigated the prevalence of lung injury and clinical characteristics of patients who were treated with AMR in our hospital.

Methods: The subjects of this report were all of the 111 patients with lung cancer (both small cell and non small cell carcinoma) to whom AMR were administered between February 2005 and September 2013 in our hospital. The basic information, histology or cytology, the presence of acute lung injury, the existence of interstitial lung disease before AMR use were reviewed.

Results: Of 111 patients, 100 were male and 11 were female. The average age was 67.3 (38–82) years old. AMR was administered as 2nd–10th line of therapy, to patients with refractory or relapsed disease. The number of small cell carcinoma patients was 56 and non small cell carcinoma was 55. Among them, 12 patients already had interstitial lung disease before initiation of AMR. Lung injury induced by AMR administration occurred in 2 of 99 cases without underlying interstitial lung disease, and 2 of 12 cases with preceding interstitial lung disease. None of the 4 patients with drug induced lung injury was fatal.

Conclusion: AMR-induced lung injury developed in 4 of 111 patients (3.6%). It occurred more often in patients with preceding interstitial lung disease.

P-I-008

THE PREDICTIVE FACTORS FOR THE EFFECT OF PIRFENIDONE IN IDIOPATHIC PULMONARY FIBROSIS

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Background: Pirfenidone and acetylcysteine monotherapy are anti-fibrotic drugs used for the treatment of idiopathic pulmonary fibrosis (IPF). Pirfenidone has been approved in some Asian and European countries recently, but usage experience in practical clinics is still limited.

Methods: We retrospectively analyzed general information and clinical characteristics in 70 consecutive patients with IPF treated with pirfenidone in one university hospital in Japan.

Results: The study comprised 70 patients (77% male) with an average age of 68.1 ± 7.4 years old. The baseline forced vital capacity: FVC and percentage predicted FVC were 2.28 ± 0.81 L and 71.3 ± 21.0%. Pirfenidone administration doses were 600 mg in 11 cases (16%), 1200 mg in 36 cases (51%), 1600 mg in 1 case (1%), and 1800 mg in 22 cases (32%). Average administration period was 355 days. Deterioration of respiratory status was defined as 10% or greater decline in percentage predicted value of FVC after 6-month treatment. We categorized three treatment response groups as following; worse group: <= -10%, inhibition group; -10%-0%, better group; 0%<. Stable pulmonary function was shown in 64% cases. Patients with autoimmune features had better prognosis than those without. In diagnostic image analysis, there were more GGO and consolidation scores and less fibrosis score in worse prognosis group with pirfenidone. As adverse effects, appetite loss (43%), diarrhea (10%), general fatigue (13%), rash (5%), headache (8%) and stupor (3%) were seen and adverse effects was main reason of pirfenidone withdrawal.

Conclusion: More than half of patients treated with pirfenidone showed stable respiratory status. Some baseline characteristics differences were seen between each treatment response group. To continue pirfenidone administration, it was important to control adverse effects.

P-I-007

SEVERE ACUTE INTERSTITIAL LUNG DISEASE IN EML4-ALK-POSITIVE NON-SMALL CELL LUNG CANCER TREATED WITH CRIZOTINIB

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Introduction: The progress of targeted therapy such as gefitinib, erlotinib or crizotinib in Non-Small Cell Lung Cancer (NSCLC), has changed the direction of NSCLC treatment. Currently, in Indonesia, with the result of EGFR mutation testing, targeted therapy (gefitinib) for NSCLC can be obtained through National Insurance Program. Interstitial pneumonia due to targeted therapy such as gefitinib or crizotinib had already been reported with different outcomes, but none was reported in Indonesia.

Case Report: Here, we reported a non-smoker Indonesian female, who was diagnosed with lung adenocarcinoma stage IV with metastasis to the pleura and brain. The analysis mutation of EGFR showed wild type for EGFR gene, and fluorescence in situ hybridization analysis from other laboratory showed presence of EML4-ALK fusion gene. She refused to have chemotherapy. She received crizotinib as first line therapy, per oral at a dose of 250 mg twice daily. After 14 days of crizotinib, she developed severe dyspnea and oxygen desaturation despite high-flow Oxygen therapy. Chest HRCT showed extensive bilateral groundglass opacities. Crizotinib then discontinued, and pulse methylprednisolone therapy was started, altogether with empirical therapy of antibiotics to reduce possible secondary infection due to high-dose steroid. She refused to have mechanical ventilation or noninvasive ventilation, instead of high-flow Venturi-mask. After more than 1 week in high-care unit, oxygen saturation increased, CRP decreased, and chest HRCT showed decreasing of groundglass opacities, with prominent post-inflammatory fibrosis. She survived, was discharged, and underwent chemotherapy after her condition became stable.

Conclusion: It is important to investigate any acute onset respiratory symptoms during targeted therapy treatment for NSCLC. Discontinuation of medication and initiation of corticosteroid treatment may reduce disease deterioration. Evaluation of inflammatory marker such as CRP might be useful to monitor disease progression, in countries where other markers of interstitial pneumonia are not available.

P-I-009

IS PULMONARY UPPER LOBE FIBROSIS ONE OF LATE-ONSET NONINFECTIOUS PULMONARY COMPLICATIONS AFTER BONE MARROW TRANSPLANTATION?

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Background and Aim of Study: Pulmonary upper lobe fibrosis (PUF) is rare and corresponds to no current classification of idiopathic interstitial pneumonias. Aetiology of PUF has been unknown. Patients after bone marrow transplantation (BMT) occasionally develop late-onset noninfectious pulmonary complications (LONIPCs). LONIPCs include bronchiolitis obliterans (BO), diffuse alveolar damage (DAD) and non-classifiable interstitial pneumonia. One report claimed that PUF manifested as one of LONIPCs. In the present study, we retrospectively examine autopsy cases after BMT in order to evaluate incidence, clinical manifestations, and pathological diagnosis of LONIPCs.

Method: We reviewed clinical, radiologic, and pathologic findings in a series of 35 autopsy cases after BMT. Autopsies were conducted at Tenri Hospital between April 1992 and June 2010.

Results: Six out of 35 patients had LONIPCs. PUF was diagnosed in 2 patients with LONIPCs. Two patients had BO and other two had DAD. One patient with PUF was a 19-year-old man at BMT who was administered immunosuppressant. The other was a 42-year-old woman who was administered steroids. Both of them developed pneumothorax. One of the patients with BO underwent lung transplant.

Conclusion: We found that PUF was recognized as one of LONIPCs. Possible relationship between BMT and PUF might give new insight to understand the aetiology of PUF.

P-I-010

CLINICAL AND PATHOLOGICAL EVALUATION OF THE 23 AUTOPSY PATIENTS WITH INTERSTITIAL PNEUMONIAS

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Background: An acute exacerbation in patients with interstitial pneumonia is associated with high mortality. However, few studies have reviewed the autopsy findings in those patients.

Methods: We retrospectively reviewed the clinical and pathological findings from the medical records in 23 consecutive patients with interstitial pneumonia, who underwent an autopsy between September 1999 and March 2014.

Results: The median age at autopsy for the patients was 75-year-old, which included 15 (65.2%) males. There were 4 patients, including 2 lung cancer patients, with chronic interstitial pneumonia complicated by bacterial bronchopneumonia without diffuse alveolar damage (DAD) in their autopsy lungs. Remaining 19 patients consisted of acute exacerbation of interstitial pneumonias (n = 15) and acute interstitial pneumonia (n = 4). Ten of the 19 patients had been treated with immunosuppressive agents (corticosteroids or anticancer drugs). Four patients developed disseminated intravascular coagulation and one patient developed acute myocardial infarction during the clinical course to death. The high-dose corticosteroid therapy was begun in 15 (84.2%) patients after admission. All of the 19 patients had DAD, concomitantly with cytomegalovirus infection in 3 patients, bacterial bronchopneumonia in 3, fungal infection in one, and incidentally found lung cancer in 2.

Conclusion: The pathological findings in critically ill patients with interstitial pneumonias, especially in those with acute exacerbation, presented DAD and a variety of additional pathological conditions. These patients resulted in death with several complications during the therapeutic process, such as high-dose corticosteroid therapy.

P-I-011

A PROSPECTIVE SURVEY BY WEB REGISTRATION ON IDIOPATHIC PULMONARY FIBROSIS IN JAPAN

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Background and Objective: There have been no prospective large-scale multicenter epidemiological studies on the clinical course from the time of diagnosis of idiopathic interstitial pneumonias (IIPs) and treatment in Japan. The purpose of this study was to reveal the current situation of the clinical practice for IIPs, and to establish an early diagnostic method and standard treatment of idiopathic pulmonary fibrosis (IPF) in Japan.

Methods: Information about clinical findings, course and treatment of patients with IIPs has been registered through the web in a collaborative effort by medical institutions across Japan that specialize in the clinical practice of interstitial pneumonia. This study was supported by a grant to the Diffuse Lung Diseases Research Group from the Ministry of Health, Labour and Welfare.

Results: There were 436 cases which were newly registered from 19 institutions during a 5-year period. IPF was the most frequent and accounted for 321 cases. Dyspnoea on exertion was the most frequent (45.2%) among the symptoms in IPF patients at the initial visit and 28.3% of the IPF cases sought medical attention because of an abnormal chest X-ray or CT without symptoms. With regard to the type of and changes in treatments for IPF, 'no treatment' was the most frequent choice until the end of the 2008 fiscal year when pirfenidone was approved for manufacture. 'No treatment' dropped from the 2009 fiscal year, during which pirfenidone therapy accounted for 32.9%. On the other hand, there were only negligible changes in steroid monotherapy, which changed from 6.2% to 7.5% of cases after 2009, and in combination therapy of steroids and immunosuppressive agents, which increased slightly from 11.2% to 13.1% in the same period. The median survival times from the onset of IPF symptoms and from the initial visit were 3,203 days and 2,090 days, respectively. The prognosis was significantly worse in the symptomatic group compared with the asymptomatic group (p = 0.0013). In 113 cases for which the cause of death was available, acute exacerbation was the most frequent in 66 cases (58.4%).

Conclusions: This study is believed to provide valuable information for understanding the current situation of clinical practice for IPF patients in Japan.

P-I-012

CLINICOPATHOLOGICAL STUDY OF INTERSTITIAL PNEUMONIA WITH ANTI-AMINOACYL tRNA SYNTHETASE (ANTI-ARS) SYNDROME

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Background: The aminoacyl-tRNA synthetases are a family of enzymes, each of which catalyzes the formation of aminoacyl-tRNA from a specific amino acid and its cognate tRNA. Autoantibodies to these synthetases have been reported and are associated with myositis, arthritis, mechanic's hand, interstitial pneumonia, and often Raynaud's phenomenon. These clinical findings constitutes a distinct syndrome named anti-aminoacyl tRNA synthetase (anti-ARS) syndrome. But there have been few reports that showed the clinical and pathological characteristics of patients with interstitial lung disease (ILD) associated with these antibodies.

Objective: The purpose of this study was to investigate the clinico-pathological findings and the response to treatments in ILD patients with anti-ARS autoantibodies.

Patients and Methods: We evaluated 7 ILD patients with anti-ARS autoantibodies who were admitted to Iwata City Hospital between 2007 to 2013. Histopathological evaluation using surgical lung biopsy was performed in all 7 patients. We retrospectively investigated their clinical, radiological, and pathological findings. Specimens were diagnosed pathologically according to histopathological patterns described in an official ATS/ERS statement in 2013.

Results: The 7 patients comprised 3 men and 4 women, and their median age was 66 years old (range, 50–76 years). Three patients had anti-Jo-1 antibody and two had anti-PL 7 antibody. The remaining two had anti-PL 12 and anti-OJ antibody, respectively. Two patients met the criteria for Sjogren's syndrome, one of them also did for dermatomyositis. All patients had a chronic clinical course. Chest computed tomography frequently showed lower lung predominant ground glass opacities (GGO) and consolidations with volume loss. Histopathologically, all but one showed nonspecific interstitial pneumonia (NSIP) pattern (cellular NSIP:4 cases, fibrosing NSIP:2), and the remaining one showed unclassifiable interstitial pneumonia. Four patients received therapy with oral prednisolone alone, two of whom had relapse in their clinical course with the reduction of prednisolone and needed the immunosuppressive agents. Two patients were treated with a combination of oral immunosuppressive agents and prednisolone, one of whom also received high-dose pulse intravenous methylprednisolone for 3 consecutive days. The remaining one had received neither of them because of the stable condition.

Conclusion: The ILD associated with anti-ARS syndrome usually have a chronic clinical course, lower lung predominant opacities with volume loss and histopathological findings of NSIP pattern. Corticosteroid therapy may show a good response in some patients, but others may have recurrences in their clinical courses and need combination of immunosuppressive agents.

P-I-013

HIGH-RESOLUTION CT FINDINGS AND INTER-OBSERVER CONCORDANCE FOR ACUTE HYPERSENSITIVITY PNEUMONITIS ASSOCIATED WITH HOME ULTRASONIC HUMIDIFIERS

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Introduction: Acute hypersensitivity pneumonitis associated with home ultrasonic humidifiers ("humidifier lung") is relatively rare. There have been few reports of the high-resolution computed tomography (HRCT) findings of this disease. We examined clinical characteristics and the HRCT findings in patients with humidifier lung and evaluated inter-observer concordance for certain radiologic features.

Patients and Methods: The study subjects were 9 patients who were diagnosed with humidifier lung at our hospital between April 2012 and May 2014. In addition to ascertaining clinical information, the CT images of each subject were evaluated independently by seven respiratory specialists and two respiratory residents for the presence of pleural effusion, mediastinal lymphadenopathy, thickening of bronchial vascular bundles, centrilobular granular shadows, and pan-lobular ground-glass opacity.

Results: Positive individual reporting of CT findings and the rates of inter-observer concordance were, respectively, pleural effusion (2/9, 88.9%), mediastinal lymphadenopathy (1/9, 88.9%), thickening of bronchial vascular bundles (0/9, 61.0%), centrilobular granular shadows (6/9, 83.0%), and pan-lobular ground-glass opacity (9/9, 94.3%). Centrilobular granular shadows were observed only in patients whose duration from beginning of inhalation to onset of symptoms is more than three months. No other correlation was found between clinical characteristics and CT findings.

Conclusions: All patients had pan-lobular ground-glass opacity on HRCT, with high rate of inter-observer concordance. This feature is therefore a useful marker for humidifier lung. The presence of centrilobular granular shadows suggest the duration from inhalation to onset exceeds three months.

P-I-014

SERUM SOLUBLE INTERLEUKIN-2 RECEPTOR LEVEL COULD DIFFERENTIATE BETWEEN PNEUMOCYSTIS JIROVECCII PNEUMONIA AND METHOTREXATE-INDUCED PNEUMONITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER METHOTREXATE THERAPY

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Objective: To clarify the differences between pneumocystis jirovecii pneumonia (PCP), methotrexate-induced pneumonitis (MTX-P), and rheumatoid arthritis (RA) associated interstitial pneumonia (RA-IP) in RA patients who remain on MTX.

Methods: Retrospective analysis of 16 PCP cases in RA treated with MTX (PCP group), 26 MTX-P cases in RA treated with MTX (MTX-P group), and 16 RA-IP in RA patients without MTX (RA-IP group) from respiratory department of Nagasaki University hospital.

Results: Compared with RA-IP group, both PCP and MTX-P group developed more rapidly. Compared with PCP and MTX-P group, PCP group showed hypersensitivity pneumonia pattern on HRCT with higher frequency than MTX-P group. Also PCP group showed higher heart rate, alveolar-arterial oxygen difference (A-aDO₂), lymphocyte cell count, serum CRP, surfactant protein-A (SP-A), soluble interleukin-2 receptor (sIL-2R), plasma β-D-glucan, and systemic inflammatory response syndrome (SIRS) items, and showed lower PaCO₂, and serum IgG level. Serum sIL-2R levels significantly correlated with A-aDO₂, lymphocyte count, serum IgG, SP-A, and SP-D, but not β-D-glucan. The cutoff level of sIL-2R that resulted in the second highest accuracy for PCP group after β-D-glucan was 1450 U/ml. This value discriminated between the PCP group and the other groups with 90.9% sensitivity and 81.0% specificity and was associated with an accuracy of 71.4%. Use of serum sIL-2R levels for diagnosis of PCP group resulted in the second largest AUC (0.931).

Conclusion: Serum sIL-2R levels could be useful for differential diagnosis between PCP and MTX-P that have similar characteristics as clinical course and HRCT findings.

P-I-015

PEMETREXED-INDUCED PNEUMONITIS IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

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Background: Pemetrexed, a new-generation multi-targeting antifolate, is being prescribed with increasing frequency in platinum-based combination regimen for advanced non-small cell lung cancer, in addition to malignant pleural mesothelioma. According to the past clinical trials in Japan, the rate of pemetrexed-induced pneumonitis was 3.6%.

Method: To determine the incidence, risk factors and the outcome of pemetrexed-induced pneumonitis, we retrospectively evaluated the clinical features of the patients with advanced non-small cell lung cancer, who had been treated with pemetrexed during the last 15 months at Fukuoka University Hospital, Japan.

Results: There were 37 consecutive patients (median age; 68-year-old, 27 males and 10 females), which included 35 patients with lung adenocarcinoma. Ten patients, including patients without any respiratory symptom, had mild interstitial pneumonia as an underlying disease. Five patients (13.5%, median age; 69-year-old, 4 males and 1 female) developed a drug-induced pneumonia possibly due to pemetrexed, during the treatment with platinum-based combination regimen in 3 patients and during the maintenance treatment with pemetrexed alone in 2 patients. All of the 5 patients were smokers and had adenocarcinoma in histology, but their pneumonitis was successfully treated with corticosteroids. Notably, 4 patients had interstitial pneumonia as an underlying disease.

Conclusion: Our results showed a higher incidence of drug-induced pneumonia during the treatment with pemetrexed-included combination regimen for advanced non-small cell lung cancer. Chest physicians and oncologists should be aware of pemetrexed-induced pneumonitis, especially in patients with existing interstitial pneumonia.

P-I-016

A NEW METHOD TO EVALUATE THE CLINICAL EFFICACY OF PIRFENIDONE FOR PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS BY USING PERSONAL FORCED VITAL CAPACITY CHANGE

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Background: Change in forced vital capacity (FVC) has been used as a primary endpoint in many clinical trials of patients with idiopathic pulmonary fibrosis (IPF). While the clinical course of IPF is recognized as heterogeneous, most of the studies did not take into account the change in FVC before initiation of treatment.

Purpose and Methods: Our main purpose was to evaluate a new method of assessing the clinical efficacy of pirfenidone in IPF. Thirty-eight IPF cases at 22 institutions belonging to the research group on diffuse pulmonary disease in Japan were enrolled. We conducted a retrospective study of IPF patients who received pirfenidone for more than 2 years. We defined a new parameter, personal FVC change (Δ FVC_{personal}), as the amount of change in FVC during the 12-month period prior to the initiation of pirfenidone. A new method of evaluating the clinical efficacy of pirfenidone was introduced by comparing personal Δ FVC with the amount of change in FVC during the 12-month period after initiation of therapy (Δ FVC_{0-12 m}) and the amount of change from 12 to 24 months after initiation of therapy (Δ FVC_{12-24 m}). We defined "A favorable response to pirfenidone" as Δ FVC_{0-12 m} or 12-24 m > Δ FVC_{personal}, and "A failure to respond to pirfenidone" as Δ FVC_{0-12 m} or 12-24 m \leq Δ FVC_{personal}.

Results: The mean Δ FVC_{personal} was -162.6 ± 23.0 ml/year. After initiation of pirfenidone therapy, Δ FVC_{0-12 m} was -30.1 ± 22.4 ml/year, and Δ FVC_{12-24 m} was -157.9 ± 25.8 ml/year. Twenty-two cases (69%) showed improvement at 12-months (Δ FVC_{0-12 m} > Δ FVC_{personal}) and 12 cases (55%) at 24 months (Δ FVC_{12-24 m} > Δ FVC_{personal}), that we classified as "A favorable response to pirfenidone". On the other hand, 10 cases (31%) failed to show improvement at 12 months (Δ FVC_{0-12 m} \leq Δ FVC_{personal}) and 10 cases (45%) at 24 months (Δ FVC_{12-24 m} \leq Δ FVC_{personal}), that we classified as "A failure to respond to pirfenidone".

Conclusion: Evaluation of the clinical efficacy of pirfenidone by using personal Δ FVC which represents the clinical course of IPF in each patient might be beneficial.

P-I-017

P-I-019

PULMONARY INVOLVEMENT IN ACUTE FEBRILE NEUTROPHILIC DERMATOSIS

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Objective: To study the clinical features, laboratory findings, radiograph, diagnosis and treatment of acute febrile neutrophilic dermatosis with respiratory system involvement and to improve physicians' understanding of it.

Methods: 17 cases of acute febrile neutrophilic dermatosis with respiratory system involvement, but microorganism cultures sterile after 1986 were retrieved from Google, Pubmed, Ovid and Wanfang and investigated retrospectively.

Results: There were 8 males and 9 females, aging 26 to 82 years (mean 53.5 ± 15.0). The airway or lung was involved earlier than skin lesion in 6 cases (35.3%), later in 9 cases (52.9%), and simultaneous in 2 cases (11.8%). The blood leukocyte counts increased in 13 cases (76.4%) with a differential of >70% neutrophils (64.7%). Similar to the skin lesion, biopsy specimen of the airway and lung lesion showed dense inflammatory infiltrates in 2 cases and interstitial inflammation, oedema, prominent interstitial and alveolar neutrophilic exudates in 5 cases, respectively. 3 cases of bronchiolitis obliterans organizing pneumonia associated with acute febrile neutrophilic dermatosis have been reported. A chest radiograph revealed bilateral reticulonodular infiltrations or ground glass opacities in 15 cases, with pleural effusion in 1 case and mediastinum lymphadenectasis in 1 case. In 13 cases underwent a bone marrow biopsy, 7 cases consistent with amyelodysplastic syndrome and 1 cases leukaemia. System corticosteroids typically induce rapid improvement, but 4 cases died of respiratory failure, multiple organ dysfunction syndrome, haemorrhage or infection due to pancytopenia.

Conclusion: Respiratory system involvement in acute febrile neutrophilic dermatosis may occur in any stage with a frequent abnormal hematopoiesis and its diagnosis should be based on the typical clinical manifestation, histology or response to corticosteroids. acute febrile neutrophilic dermatosis with respiratory system involvement should be promptly recognized in order to provide timely treatment and potentially prevent clinical deterioration.

CLINICAL FEATURES OF PATIENTS WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA (CPFE) FOCUSING ON PULMONARY HYPERTENSION: OUR EXPERIENCE

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Background: Combined pulmonary fibrosis and emphysema (CPFE) is a new concept recognized as a syndrome of concurrent emphysema and interstitial pneumonia. CPFE is characterized by high prevalence of pulmonary hypertension (PH), which is a significant predictor of survival for patients. However, very limited evidence is available regarding the management of CPFE patients complicated with PH.

Methods: Five patients with CPFE were admitted to our hospital for survey and received lung function test, echocardiography, right cardiac catheterization, treadmill test, and 6-minutes walk test. Patients with a diagnosis of complicated PH were treated with a vasodilator (bosentan) and followed up.

Results: The mean age was 73.4 years; 3 of 5 patients were male; all had smoking history; and the mean Brinkman index was as high as 1094. Lung function test revealed well preserved VC (2.376; %VC, 90.74) and FEV1.0% (76.94; FEV1.0 1.774 [103.78]) but markedly decreased %DLco (27.16). The mean MET on a treadmill was 4.175 and the mean 6-minute walk distance was 253 m. Echocardiography revealed TR in 3 patients with the mean Δ PG of 45.8 and PR in all patients with the mean Δ PG of 11.58. Right cardiac load was suspected but normal Tei index (0.3666) and TAPSE (1.812 mm) indicated preserved right ventricular function. The mean mPAP and PVR from right heart catheterization was as high as 24.4 mmHg and 383 dyne-sec-cm⁻⁵, respectively. All patients were receiving home oxygen therapy due to chronic respiratory failure. Two of 3 patients diagnosed with PH started oral bosentan and its dose was reduced in 1 patient because of hepatic impairment.

Conclusion: CPFE is associated with marked diffusion impairment and frequently complicated with PH. Complication of PH can be predicted from echocardiograms. Tracleer is expected to be effective for treatment of PH since there is no established treatment. The course of patients treated with tracleer will also be presented. We will publish details of the study results at the 19th congress of the Asian Pacific Society of Respirology (APSR).

P-I-018

INTERSTITIAL LUNG DISEASE INDUCED BY BOFU-TSUSHO-SAN: A REPORT OF 4 CASES

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Background: Bofu-tsusho-san, a herbal medicine, is widely used in Japan for losing weight and commercially available without prescription, and the herbal medicine causes interstitial lung disease (ILD). In some reports, cessation of the medicine improved ILD induced by Bofu-tsusho-san.

Objective and Methods: We retrospectively reviewed 4 cases of ILD induced by Bofu-tsusho-san to clarify clinical features and outcomes.

Results: All patients developed acute or subacute ILD. The predominant CT finding was diffuse ground-glass opacity and bronchoalveolar lavage showed a high percentage of lymphocytes. Two cases received mechanical ventilation. All cases were administered with high-dose corticosteroids, and 1 case needed combination therapy with corticosteroids and cyclosporin A. Clinical symptoms and CT findings improved rapidly in all cases after treatment.

Conclusion: In this study, a noteworthy feature is high frequency of severe respiratory failure. We clinicians should carefully review patients' medical history and diagnose accurately, treat promptly because Bofu-tsusho-san may cause severe ILD.

P-I-020

PREDICTIVE FACTORS OF DIFFERENT LUNG DISEASE ACCOMPANY DERMATOMYOSITIS: A CLINICAL CASE-CONTROL STUDY

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Background: Dermatomyositis (DM) is an inflammatory idiopathic myopathy which is characterized by proximal muscle involvement; it can affect multiple organs, especially the lung, resulting in ILD, lung fibrosis, pleurisy and lung cancer. There are many reports about DM with ILD or DM with lung cancer. But there are few reports which mentioned the predictive factors of DM with different lung diseases. Clinical features and laboratory data of patients with DM in our hospital were retrospectively reviewed and analyzed to find the predictive factors. This study was to observe 3 different groups of patients including DM with lung cancer, DM with interstitial lung disease and DM without lung damage as control retrospectively in order to understand the clinical presentation differences of lung lesion and find the predictive factors in patients with DM.

Methods: We performed a retrospective case-control study in patients with DM using the medical records of DM patients from January 2003 to March 2013 in the Third Affiliated Hospital of Sun Yat-sen University. All the clinical data were collected for 7 DM with lung cancer cases, and 14 age and sex-matched DM with ILD cases, 9 DM without lung damage. Variance analysis, Tamhane analysis and crosstab were performed among 3 groups. Chi-square test was carried out for group-group comparison. Comparisons of continuous data were made using the Student's t test or Mann-Whitney U test. were used to estimate odds ratios (Ors) and 95% confidence intervals (CIs).

Results: No arthralgia and no ILD were two independent predictive factors of patients with DM who may develop lung cancer [OR 0.478, CI = (0.312–0.733), P = 0.014; OR 7.989, CI = (0.365–0.867), P = 0.005]. Symptoms of chest tightness and breathless at onset were independent clinical predictive factors of DM patients accompanied with ILD [OR = 2.333, CI = (1.274–4.272), P = 0.000; OR = 2.8, CI = (1.387–5.654), P = 0.000]. Higher serum LDH level, RDW-CV level after therapy and presence of anti-Jo1 antibody can be served as laboratory indicators of ILD in DM patients [P = 0.046; P = 0.026; R = 1.75, CI = (1.112–2.755), P = 0.005].

Conclusions: DM patients with symptoms of chest tightness and breathless at onset were associated with significantly higher risk of developing ILD and also in these patients the higher serum LDH level, RDW-CV level after therapy and presence of anti-Jo1 antibody could be served as laboratory indicators of the presentation of ILD. On the other hand, DM patients with symptoms of no arthralgia and no ILD were associated with significantly higher risk of developing lung cancer. Our results suggest that DM patients without positive symptoms may result in a much poor prognosis.

P-I-021

ADVANCE OF PROTECTIVE EFFECT OF METALLOTHIONEIN ON PULMONARY FIBROSIS

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Pulmonary fibrosis is an interstitial lung disease characterized by progressive fibrosis of the alveolar interstitium. However, its pathogenesis is not entirely clear, and oxidative stress is thought to be important in the pathogenesis. Oxygen free radicals play an important role in the formation of pulmonary fibrosis. The role of oxidative stress in pulmonary fibrosis are mainly as follows: 1) The oxidative stress can cause alveolar epithelial necrosis; 2) Oxidative stress induced epithelial cell apoptosis; 3) Oxidative stress adjustment cytokine expression; 4) Oxidative stress in the destruction of lung tissue protease/resistant protease balance; 5) Oxidative stress can promote the transformation of epithelial mesenchymal (EMT); 6) Oxidative stress induced the NF- κ B activation. So oxidative stress is an important mechanism in the formation of pulmonary fibrosis. Metallothionein (MT) is a highly effective antioxidant, it has strong anti-oxidative stress and inhibition of apoptosis, and MT has strong ability to remove oxygen free radicals, it also can increase the content of glutathione (GSH) and glutathione reduction enzymes (GR) and inhibit proinflammatory factor (such as interleukin) expression. So metallothionein plays an important role in the prevention and mitigation of the development of pulmonary fibrosis. This article briefly describes and summarizes the protective effect of metallothionein on the development process in pulmonary fibrosis, to provide a new direction for the prevention and treatment of pulmonary fibrosis in the future.

P-I-022

CHANGES IN SERUM KL-6 AFTER INTRAVENOUS FOSFOMYCIN ADMINISTRATION IN IDIOPATHIC INTERSTITIAL PNEUMONIA

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Changes in serum KL-6 levels after intravenous fosfomycin (FOM) administration in IIPs were studied. In 17 patients, FOM was administered intravenously, at a dose of 2 g twice daily, for 14 days, and serum KL-6 was determined before and after its administration. FOM administration resulted in a reduction of serum KL-6 in all 17 patients (1273 ± 132 U/ml [mean \pm SEM] to 1023 ± 101 U/ml; $P < 0.01$).

P-I-023

SILICOSIS COMPLICATING SYSTEMIC SCLERODERMA WITH PULMONARY INTERSTITIAL FIBROSIS AND PLEURAL EFFUSIONS

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Although not usually occurring with simple silicosis, dyspnea which severely limits exertion may develop with interstitial fibrosis, secondary to either silicosis or to another disorder, such as systemic sclerosis (scleroderma). This article describes a patient with long-standing silicosis who suddenly became symptomatic and was found to have interstitial fibrosis and a pleural effusion with skin manifestations of scleroderma. After work-up, including lung lavage and biopsy, he was treated for scleroderma with prednisolone and cyclophosphamide, which partially improved his lung function and exercise capacity. The challenges in diagnosis and therapy are also discussed.

POSTER PRESENTATION – LUNG CANCER

P-J-001

WHOLE-EXOME SEQUENCE BY PERIPHERAL BLOOD DNA FROM FAMILIAL EGFR-MUTANT LUNG CANCER PATIENTS

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Rationale: NSCLC is the leading cause of cancer-related death in Japan and worldwide. The success of the tyrosine kinase inhibitor Gefitinib in the treatment of NSCLC with EGFR gene mutations dramatically changed the treatment strategy for lung cancer. EGFR gene mutations appear more frequently in Asian females. Previous studies have shown that there is a particular link in families in which the proband has an EGFR mutated tumour when compared to NSCLC with ALK rearrangements or KRAS mutation, probably due to the genetic background. However, the underlying genetic mechanisms remain to be unclear.

Methods: We found three families in which adenocarcinoma cases with EGFR gene mutations clustered, and presumed that some genetic factors lead to the carcinogenesis in these families. To gain an insight into the heritable alterations, we have performed whole exome sequencing of peripheral blood DNA from 8 patients with familial EGFR-mutant lung adenocarcinomas, 2 unaffected siblings and 2 simplex individuals by using Illumina HiSeq 2000 system. The sequence data were analyzed for mapping and pairing of reads to the NCBI human genome reference by the BWA software. Single-nucleotide variants and indels were identified using the Genome Analysis Tool Kit (GATK) v1.6 software.

Results: The average mapping of reads was 99%, and the targeted regions were sequenced with a mean fold coverage of 148-fold (range: 105–198). We found 27,985 single nucleotide variants in a patient genome on average, and the 4,319 variations were novel. Among them, 1,977 exonic variants seemed potentially pathogenic, and particularly 29 of such variations were homozygous. A total of 393 variants were common among patients in family A and not present in unaffected siblings, and 148 of those were left after excluding synonymous SNVs. Then, comparison of another exome experiment, which was previously performed with SOLiD4, yielded a total of 48 concordant non-synonymous SNPs among patients in family A and not present in unaffected siblings. We focused on the functional mutations in certain genes.

Conclusions: These results may account, in part, for the genetic background of NSCLC with EGFR gene mutations, and further studies will be needed to examine the pathogenic relevance of the mutations detected in this study.

P-J-002

SURGICAL RESECTION OF NODULAR GROUND-GLASS OPACITIES WITHOUT PERCUTANEOUS NEEDLE ASPIRATION OR BIOPSY

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Introduction: Percutaneous needle aspiration or biopsy (PCNA or PCNB) is an established diagnostic technique that has a high diagnostic yield. However, its role in the diagnosis of nodular ground-glass opacities (nGGOs) is controversial, and the necessity of preoperative histologic confirmation by PCNA or PCNB in nGGOs has not been well addressed. Thus, we here evaluated the rates of malignancy and surgery-related complications, and the cost benefits of resecting nGGOs without prior tissue diagnosis when those nGGOs were highly suspected for malignancy based on their size, radiologic characteristics, and clinical course.

Methods: Patients who underwent surgical resection of nGGOs without preoperative tissue diagnosis from January 2009 to October 2013 were retrospectively analyzed.

Results: Among 356 nGGOs of 324 patients, 330 (92.7%) nGGOs were resected without prior histologic confirmation. The rate of malignancy was 95.2% (314/330). In the multivariate analysis, larger size was found to be an independent predictor of malignancy (odds ratio, 1.086; 95% confidence interval, 1.001–1.178, $p = 0.047$). A total of 324 (98.2%) nGGOs were resected by video-assisted thoracoscopic surgery (VATS), and the rate of surgery-related complications was 6.7% (22/330). All 16 nGGOs diagnosed as benign nodules were resected by VATS, and only one patient experienced postoperative complications (prolonged air leak). Direct surgical resection without tissue diagnosis significantly reduced the total costs, hospital stay, and waiting time to surgery.

Conclusions: With careful selection of nGGOs that are highly suspicious for malignancy, surgical resection of nGGOs without tissue diagnosis is recommended as it reduces costs and hospital stay.

P-J-003

BREATH ANALYSIS USING ION MOBILITY SPECTROMETRY IN PATIENTS WITH LUNG CANCER BEFORE AND AFTER TUMOUR RESECTION

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Background: Ion Mobility Spectrometry (IMS) is a useful method for the rapid identification of analyses of volatile organic compound (VOC) peaks in respiratory diseases. Whether it can contribute to the diagnosis of non-small cell cancer (NSCLC) has not been adequately evaluated. Furthermore, there are very few reports on the assessment of lung cancer using IMS before and after tumour resection.

Method: We obtained VOCs from exhaled breath with an IMS coupled to a multi capillary column (MCC/IMS) in patients with NSCLC before and after tumour resection to analyze tumour specific VOCs.

Results: The exhaled breath of 13 patients with NSCLC (8 adenocarcinoma, 3 squamous cell carcinoma, 1 adenosquamous carcinoma, 1 lymphoepithelioma-like carcinoma), were analyzed using IMS. From the 13 patients, 57 VOC peaks were separated and analyzed. Peak-15 noted as terpinolene from the IMS database was able to separate values with a sensitivity of 61.5% and a specificity of 84.6%. Furthermore, Peak-51 noted as naphthalene was able to separate values with a sensitivity of 61.5% and a specificity of 92.3%.

Conclusion: In this study, specific VOC peaks, especially Peaks 15 and 51 were useful in identifying NSCLC before and after tumour resection.

P-J-004

OCT4 PLAYS A KEY ROLE IN THE PERSISTENCE OF GEFITINIB-RESISTANT LUNG CANCER STEM CELLS

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Accumulating evidence indicates that a small population of cancer stem cells (CSCs) is involved in resistance to cancer treatment. Oct4 is known to play an important role in reprogramming mouse or human somatic cells to undifferentiated, pluripotent stem cells. Our aim here was to elucidate the role of Oct4 in the resistance to gefitinib in non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) mutation. In this study, NSCLC cell line, PC9 which expresses the EGFR mutation, was exposed to gefitinib. After gefitinib exposure, a small fraction of viable cells were detected, and these cells were referred to as "gefitinib-resistant persisters" (GRPs). Oct4 and putative lung CSC marker CD133 were highly expressed in GRPs in PC9 cells, and PC9 GRPs exhibited sphere-forming ability in vitro and high tumorigenic potential in NOG mice, suggesting that GRPs have characteristic features of the CSCs phenotype. To investigate the role of Oct4 in the persistence of gefitinib-resistant lung CSCs, we introduced Oct4 gene into PC9 cells by lentiviral infection. Transfection of Oct4 significantly increased the number of sphere formation, reflecting the self-renewal activity, of PC9 cells under the high concentration of gefitinib in vitro. Oct4-overexpressing PC9 cells (PC9-Oct4) significantly formed tumours at 1 x 10 cells/injection in NOG mice as compared to the control cells. Furthermore, PC9-Oct4 tumours were more resistant to the gefitinib treatment as compared to the control cells in vivo. Collectively, these findings suggest that Oct4 plays a key role in the persistence of lung CSCs resistant to gefitinib in EGFR mutation-positive NSCLC. Targeting Oct4 gene may be a promising strategy for overcoming gefitinib resistance in EGFR mutation-positive NSCLC induced by lung CSCs.

P-J-005

PROTECTIVE EFFECT OF HIGH ACCUMULATIVE INHALED CORTICOSTEROID DOSE ON LUNG CANCER IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Importance: Whether the use of inhaled corticosteroid (ICS) in chronic obstructive pulmonary disease (COPD) patients can prevent the occurrence of lung cancer remains undetermined.

Objective: To assess the incidence of lung cancer in COPD patients with ICS use and without.

Design: Retrospective cohort study.

Setting: Taiwan.

Participants: From January 1966 through December 2011, from Taiwan Health Insurance database, we got 88513 COPD cases. After excluding male; associated with the diagnosis of bronchial asthma; and previously having lung cancer diagnosis before ICS use, a total of 13686 cases were enrolled.

Intervention: Users (n = 1290) and non-users (n = 12396) of inhaled corticosteroid.

Main Outcome Measurement: We used Cox Proportional hazards regression models to estimate the hazard ratios (HRS) of lung cancer incidence for ICS users vs. non-users.

Results: From 1966 to 2011 trace, per 100000 person-year lung cancer incidence rate is 235.92 in non-users and 158.67 ICS users (HR 0.70; [95% CI: 0.46–1.09]). The high-dose ICS users (ICS accumulative dose >39.4 mg) is associated with lower risk for lung cancer (HR 0.45; [95% CI: 0.21–0.96]), low-dose ICS (0 mg < ICS accumulative dose <39.48 mg) and the relevant risk for lung cancer (HR 0.95; [95% CI: 0.67–1.61]). Multivariate-adjusted including age income and underlying disease, high-dose ICS (>39.48 mg) is still associated with lower risk for lung cancer (HR 0.46; [95% CI: 0.21–0.96]).

Conclusion and Relevance: Patients with chronic obstructive pulmonary disease who had high accumulative dose of inhaled corticosteroid treatment exhibit associated with a lower risk for lung cancer.

P-J-006

BRONCHIAL BRUSHING SAMPLES ARE SUPERIOR TO BIOPSY SAMPLES FOR EGFR MUTATION TESTING IN NON-SMALL CELL LUNG CANCER

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Bronchial brushings (BB) are often used for early screening and cytological diagnosis of lung cancer. We examined the possibility of EGFR testing on cytology samples, as compared to bronchial biopsy. 150 BB samples with non-squamous histology were submitted to our department for EGFR mutation testing within one year period. Biopsy samples was concurrently submitted for histologic diagnosis. We used the PNA clamping method for EGFR test. At BB samples, 28 cases showed exon 19 deletion, 21 exon 21 mutation, 99 were wild type and 2 failed. At biopsy samples, 27 showed exon 19 deletion, 19 exon 21 mutation, 92 were wild type and 12 failed. Mutation detection cases were nearly identical in both samples (131/138, 94.9%). In two cases, exon 21 was detected in biopsy, not in BB. In five cases, exon 19 deletion (2 cases) and exon 21 mutation (3 cases) were detected in BB, not in biopsy. The median DNA content for BB compared to biopsy were 128.87 ng and 48.62 ng. The failure rate for cytology was lower than biopsy. BB samples for EGFR mutation test are superior to bronchial biopsy samples in terms of DNA quantity and rate of failure. Moreover, in inadequate biopsy sample, BB samples were a substitute material for EGFR test.

P-J-007

A PHASE II STUDY OF AMRUBICIN AND CARBOPLATIN FOR PREVIOUSLY UNTREATED PATIENTS WITH EXTENSIVE-DISEASE SMALL CELL LUNG CANCER

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Background: Amrubicin is active in the treatment of extensive-disease small cell lung cancer (ED-SCLC), and carboplatin is an analogue of cisplatin with less non-haematological toxicity.

Purpose: To determine the efficacy and toxicity of amrubicin and carboplatin combination chemotherapy for previously untreated patients with ED-SCLC.

Patients and Methods: Eligibility criteria were chemotherapy-naive ED-SCLC patients, performance status 0–1, age 75 or less, and adequate haematological, hepatic and renal function. Based on the phase I study, the patients received amrubicin 35 mg/m² i.v. infusion on days 1, 2 and 3, and carboplatin AUC 5 i.v. infusion on day 1. Four cycles of chemotherapy were repeated every 3 weeks.

Results: Thirty-five patients were enrolled and 34 patients were eligible and assessable for response, toxicity and survival. Patients' characteristics were as follows: male/female = 26/8; performance status (PS) 0/1 = 4/30; median age (range) = 64 (41–75); stage IV = 34. Evaluation of responses were 6 complete response (CR), 21 partial response (PR), and 7 stable disease (SD) (response rate 79.4%, 95%CI 63.6–88.5%). Grade 3 and 4 leukopenia, neutropenia, and thrombocytopenia occurred in 59%, 82%, and 26%, respectively. There were no treatment-related deaths or pneumonitis. Three patients experienced hypotension as an amrubicin infusion reaction. The median progression-free survival time was 6.5 months. The median overall survival time and 1-, 2- and 3-year survival rates were 15.6 months, 63%, 28% and 7%, respectively.

Conclusions: Amrubicin and carboplatin was effective and tolerable as chemotherapy for previously untreated patients with ED-SCLC. Further investigation of amrubicin and carboplatin is warranted.

P-J-008

P-J-009

OVEREXPRESSION OF ADENYLATE CYCLASE-ASSOCIATED PROTEIN 1, CAP1 MAY PREDICT BRAIN METASTASIS IN NON-SMALL CELL LUNG CANCER

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This study was designed to establish a biomarker risk model for predicting brain metastasis (BM) in non-small cell lung cancer (NSCLC). The model consists of 120 cases of NSCLC, who were treated and followed up by 4 years. The patients were divided into BM group (n = 50) and non-brain metastasis group (other visceral metastasis and those without recurrence) (n = 70). Immunohistochemical and western blot analyses were performed in metastatic tissues of NSCLC. Multivariate regression analysis was performed to correlate immunoreactive CAP1 signal with BM. Survival analyses were performed by using the Kaplan–Meier method. Both CAP1 protein content and immunoreactive were significantly higher in BM specimens compared to other-metastatic specimens. Survival analysis revealed that cyclase-associated protein 1 overexpression was significantly associated with overall survival ($P < 0.05$). ROC test suggested that the area under the curve was 73.33 % ($P < 0.001$, 95% CI 63.5% to 83.2%). When $P = 0.466$, the sensitivity was up to 79.5%, specificity 67.1%. These findings suggest that cyclase-associated protein 1 (CAP1) is involved in the BM of NSCLC, and that elevated levels of CAP1 expression may indicate a poor prognosis for patients with BM. The molecular model CAP1 may help predict the risk of BM in NSCLC.

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ASSOCIATION OF TORQUE TENO VIRUS DNA TITER WITH THE GROWTH OF PRIMARY LUNG CANCER

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Background: Several studies have reported that a viral infection is related to lung cancer. Torque teno virus (TTV) is a circular single-stranded DNA virus originally identified from a patient with post-transfusion hepatitis of unknown aetiology but its pathological significance remains unclear. We have reported involvement of TTV in patients with idiopathic pulmonary fibrosis. Although it has been shown that TTV DNA is detectable in patients with lung cancer, its role in lung cancer growth is poorly understood.

Aims and Methods: In order to elucidate the involvement of TTV in primary lung cancer, serum TTV DNA titers were measured in serum samples obtained from patients with lung cancer, by real-time PCR with primers and a probe targeting the well-conserved untranslated region of the TTV genome, capable of detecting essentially all 39 genotypes. Between November 2012 and January 2014, twenty-one patients with primary lung cancer (18 males and 3 females; average age, 66.2 years; 7 small cell carcinoma, 9 adenocarcinoma, and 5 squamous cell carcinoma) were enrolled in our institution. Serum TTV DNA titers were quantitated before and after every administration of the chemotherapy.

Results: TTV DNA was detectable in 20 patients (95%). None of them died during the observation period. The mean TTV DNA titer measured before chemotherapy was 3.6×10^4 copies. The TTV DNA titer decreased in 15 patients and increased in 3 patients in association with the response to chemotherapy. However, the TTV DNA titer increased in the remaining 2 patients despite a good response to chemotherapy. In addition, the TTV DNA titer re-elevated in 9 patients in accordance with tumour regrowth, suggesting that the change of TTV DNA titer may be correlated with tumour growth.

Conclusions: These observations constitute the first report on an association between serum TTV DNA titer and growth of lung cancer. Therefore, TTV infection might be associated with the pathogenesis of lung cancer.

P-J-010

BODY MASS INDEX (BMI), ALBUMIN AND SKELETAL MUSCLE MASS IN NON SMALL CELL LUNG CARCINOMA (NSCLC) PATIENTS BEFORE AND AFTER CHEMOTHERAPY IN PERSAHABATAN HOSPITAL JAKARTA, INDONESIA

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Background: Malnutrition is common in patients with NSCLC due to multifactorial causes. Increased risk of chemotherapy toxicity which ultimately will lead to decrease quality of life, malnutrition is considered as one of the cause. Malnutrition assessment was done using body mass index (BMI), albumin levels and percentage of skeletal muscle compare to body weight. Until now, there is no baseline data in Indonesia showing the incidence of malnutrition in NSCLC patients, before and during chemotherapy.

Purpose: We measured nutritional status of NSCLC patients based on BMI, percentage of skeletal muscle compare to body weight using BIA tool and changing trends in albumin level before and after 3 cycles of chemotherapy.

Method: Pre-post experimental study on 33 patients from 2013–2014.

Results: Thirty three patients with mean age 55.6 years old, males (90.9%), all subjects have Performance Status 2, 66.7% subjects have lung adenocarcinoma, mean BMI before first chemotherapy BMI was 19.90 and after third chemotherapy was 20.56, mean albumin level before first chemotherapy was 3.06 and mean after third chemotherapy was 2.98, mean percentage of skeletal muscle weight compare to body weight before first chemotherapy was 29.94% and after third chemotherapy was 29.58. We found significant decline in albumin level and skeletal muscle compare to body weight percentage, before and after 3 cycles of chemotherapy, while no significant decrease in BMI.

Conclusion: A decline in albumin level and skeletal muscle compare to body weight percentage after 3 cycles of chemotherapy, while no significant decrease in BMI showed us that BMI measurement is not enough as indicators of malnutrition. We should also analyze body composition to evaluate the status of nutrition in cancer patient undergoing chemotherapy.

P-J-011

OVEREXPRESSION OF TUMOUR SUPPRESSOR GENE RBM5 DOWNREGULATES EGFR EXPRESSION IN HUMAN LUNG ADENOCARCINOMA

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Background: RNA binding motif 5 (RBM5) is a tumour suppressor gene that modulates apoptosis through the regulation of alternative splicing of apoptosis-related genes. Our previous studies suggested that the RBM5 expression was negatively correlated with the expression of epidermal growth factor receptor (EGFR) in non-small cell lung cancer (NSCLC) tissues. This study aimed to determine whether RBM5 possesses the direct regulation on EGFR expression.

Method: Both in vitro and in vivo studies were carried out to determine the effect of RBM5 on the expression of EGFR. Lentivirus-mediated RBM5 overexpression was employed in lung adenocarcinoma cell line A549. Recombinant plasmid carried by attenuated Salmonella was used to induce RBM5 overexpression in subcutaneous A549 xenografts in nude mice. Real-time quantitative polymerase chain reaction and Western blotting were carried out to detect RBM5 and EGFR expression.

Results: Both in vivo and in vitro study presented that expression of RBM5 mRNA and protein was significantly reduced in RBM5 overexpression group compared to control group by real-time PCR and western blot analysis. We identified that RBM5 over-expression inhibited EGFR expression both in A549 cells and in xenografts, which indicates that RBM5 possesses the direct regulation on EGFR expression.

Conclusions: This result suggests that EGFR expression is directly regulated by RBM5 in lung adenocarcinomas cells and RBM5 might be one of the molecular targets in terms of the target therapy in lung cancer.

P-J-012

PROGNOSTIC MODEL USING CLINICAL PARAMETERS IN NON-SMALL-CELL LUNG CANCER PATIENTS

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Background/Purpose: As of now, clinical parameters have been individually studied to know their prognostic roles in non-small-cell lung cancer (NSCLC) patients. In this study, we tried to develop global prognostic model using clinical parameters in the patients.

Methods: Eight hundred NSCLC patients who were diagnosed from Jan 2001 to Dec 2009 and took pulmonary function testing at diagnosis were enrolled from prospective lung cancer cohort. The patients were treated with platinum doublets or supportive care only. Patients with stage II were 103 (12.9%), stage III of 240 (30.0%), and stage IV of 457 (57.1%). In addition to forced expiratory volume per 1 sec (% of pred.) (FEV1%), demographic data including smoking habits, and weight loss, treatment status (chemotherapy vs. palliative), histological types, stages, and laboratory estimates (C-reactive protein, haemoglobin, albumin, calcium, lactic dehydrogenase, and alkaline phosphatase) at the diagnosis were evaluated.

Results: We constructed the final model from initial full model using Cox proportional hazard analysis. With the final model, the hazard ratio (95% CI) for the effect of chemotherapy was 0.42 (0.36, 0.49), adenocarcinoma (referent squamous cell carcinoma) was 1.13 (0.95, 1.34), and other cancer was 1.29 (0.98, 1.70), stage III was 1.11 (0.86, 1.44), and stage IV was 1.56 (1.22, 1.99), log C-reactive protein was 1.13 (1.07, 1.20), weight loss was 1.29 (1.10, 1.51), FEV1% was 0.94 (0.91, 0.97), albumin was 0.78 (0.66, 0.91). Gonen and Heller's K index was 0.66 which measuring the discrimination performance of the model. We created the prognostic model on a derivation dataset and evaluate its predictions on a validation set. We split the dataset at random into equal, each of size 400 patients, and fit the Royston-Parmar model to the first half. We predicted the prognostic index for all patients, and made four prognostic groups for all patients, using cutpoints at the 15th, 50th, and 85th centiles of the prognostic index in the first half. We compute Kaplan-Meier survival curves in the four prognostic groups in the second half, and finally compare predicted and Kaplan-Meier curves in the second half graphically. We also compared survival estimates predicted on the first and second halves from the model fit on the first half. The predicted survival curves agree well with the nonparametric estimates in 15th-50th centile and 50th-85 centile groups.

Conclusions: The model using the clinical parameters appears to be validated well subjectively. Therefore, this would be helpful in classification of NSCLC patients.

P-J-013

CORTICOSTEROID THERAPY AGAINST TREATMENT-RELATED PULMONARY TOXICITIES IN PATIENTS WITH LUNG CANCER

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Background: With the recent increased use of new anti-neoplastic agents, molecular-targeted drugs and radiation in patients with lung cancer, there has been an increase in the occurrence drug- or radiation-induced pulmonary toxicities. We conducted this study to evaluate the clinical characteristics of patients with lung cancer who presented with treatment-related pulmonary toxicities and to analyze the dosage pattern of corticosteroid therapy against them.

Methods: To collect the baseline data from the patients with lung cancer who developed treatment-related pulmonary toxicities, we initially selected those who were prescribed corticosteroids between January 1, 2008 and December 31, 2012. Depending on clinical and radiological diagnoses, we classified pulmonary toxicities into drug-induced interstitial lung disease (DILD), radiation pneumonitis, acute exacerbation of chronic obstructive pulmonary disease (AE COPD) and others.

Results: We divided total patients (n = 398) into four groups, and these include 88 cases (22%) of DILD, 189 cases (47%) of radiation pneumonitis, 47 cases (12%) of AE COPD and 74 cases (19%) of others. The prescribed rate of pulse or high-dose steroid was measured as 73%, 20%, 40% and 38%, respectively (P < 0.001). In DILD radiologic findings, the 2-month mortality was significantly higher in the patients with the diffuse alveolar damage pattern (100%) as compared with those with the non-specific interstitial pneumonia (NSIP) or bronchiolitis obliterans with organizing pneumonia (BOOP) one (62% or 42%, respectively) (P = 0.032).

Conclusion: This study showed that the natural course of DILD had more unfavourable outcome requiring higher dose steroid therapy as compared with those with radiation pneumonitis or AE COPD. According to a subgroup analysis of the patients with DILD, BOOP and NSIP radiographic patterns showed more favourable outcomes.

P-J-014

P-J-016

SCHISANDRIN B INDUCES APOPTOSIS AND ARRESTS CELL CYCLE PROGRESSION IN NON-SMALL CELL LUNG CANCER CELL LINE (A549)

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Background and Objective: Lung cancer is the leading cause of cancer death in the world. Schisandrin is one of the main dibenzocyclooctadiene lignans present in the fruit of *Schisandra chinensis* (Schisandraceae). In the past several years, Schisandrin B has been revealed to possess multiple functions against cancer. The aim of this study was to determine the anticancer effects of Schisandrin B in non-small cell lung cancer cell line (A549). We also explored the mechanism of action of Schisandrin B by analyzing its influence on apoptosis and cell cycle.

Methods: Here, we show that A549 cells were cultured with Schisandrin B concentrations (0, 12.5, 25, 50 μ M) for three days. Cytotoxicity of Schisandrin B to A549 cell lines were examined using MTT cell proliferation assay. Cell cycle distribution and apoptosis was determined by flow cytometry. Expression of cell cycle and apoptosis-regulated genes was examined at both the mRNA (Real time-PCR) and protein (Western blot) levels. The phosphorylation status of cyclin-dependent kinases (CDKs), Cleaved Caspase-3, cleaved PARP protein, etc, was also examined using Western blot analysis. Invasion and migration were evaluated by transwell assays.

Results: Our findings have shown that Schisandrin B inhibits cell proliferations in A549 with an IC50 value of approximately 50 μ M at 72 h. Flowcytometry assay confirmed that Schisandrin B affected A549 cells survival by blocking cell cycle progression and inducing apoptosis. Schisandrin B inhibits the ability of invasion and metastasis. Schisandrin B treatment reduced Cyclin D1, CDK4, and CDK6 expression, which led to the blocking of G0/G1 transition. In addition, Schisandrin B increased Bax expression, caspase-3 and poly (ADP-ribose) polymerase (PARP) cleavage, and reduced Bcl-2 expression, which contributed to the apoptosis of A549 cells.

Conclusions: In vitro, Schisandrin B significantly suppresses proliferations of A549 cell, and showed a good antitumour activity. These results indicate that Schisandrin B could be an effective traditional chinese medicine preparation in human A549 cells treatment through induction apoptosis and cell cycle arrest.

MICRORNA-146A INHIBITS EPITHELIAL MESENCHYMAL TRANSITION IN NON SMALL CELL LUNG CANCER BY TARGETING INSULIN RECEPTOR SUBSTRATE 2

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During cancer progression, some tumour cells show changes in their plasticity by morphological and phenotypical conversions, as an expression of mesenchymal markers and loss of epithelial markers, collectively referred to as epithelial-mesenchymal transition (EMT). EMT has been increasingly recognized as a critical phenomenon in lung cancer progression. The goal of this study was to identify microRNAs involved in lung cancer progression. A microarray and qRT-PCR were performed to investigate the miRNA expression profiles in mesenchymal-like lung cancer cells. The role of miR-146a in lung cancer progression was measured by invasion and migration assays in vitro. Bioinformatics and luciferase report assays were used to identify the target of miR-146a. The expression of miR-146a was reduced in mesenchymal-like lung cancer cell lines. The over-expression of miR-146a induced a marked reduction of mesenchymal marker and increase epithelial marker in lung cancer cell lines. Moreover, the over-expression of miR-146a suppressed lung cancer cells migration and invasion. The expression of miR-146a was down-regulated in advanced lung cancer tissues. Insulin receptor substrate 2 (IRS2), an adaptor protein that modulates normal growth, metabolism, survival and differentiation, was identified as a target of miR-146a. miR-146a regulated the expression of IRS2 at the mRNA and protein levels. These data demonstrate for the first time that miR-146a suppresses lung cancer progression by repressing IRS2 expression. This provides a new insight into the post-transcriptional regulation of lung cancer progression by miRNAs, a potential approach for the treatment of lung cancer.

P-J-015

P-J-017

TRANSFORMING GROWTH FACTOR-BINDUCED MIR-143 EXPRESSION IN REGULATION OF NON-SMALL CELL LUNG CANCER CELL VIABILITY AND INVASION CAPACITY IN VITRO AND IN NUDE MOUSE XENOGRAFTS

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Altered expression of miRNAs contributed to development and progression of non-small cell lung cancer (NSCLC), while transforming growth factor- β (TGF- β) promoted NSCLC cell epithelial-mesenchymal transition. This study aimed to investigate the effects of TGF- β -induced miR-143 expression in the regulation of NSCLC cell viability and invasion capacity in vitro, and xenograft formation and growth in nude mice. NSCLC A549 cells were treated with TGF- β for miRNA microarray analysis. miR-143 was selected for further study of tumour cell viability, wound healing, invasion capacity in vitro and tumour growth in nude mice. The data showed that TGF- β treatment up-regulated expression of 16 miRNAs and down-regulated expression of 42 miRNAs in A549 cells. qRT-PCR and in situ hybridization data showed that miR-143 was significantly down-regulated in 24 NSCLC and lymph node metastatic tumour tissues, but up-regulated by TGF- β treatment in A549 cells. In vitro experiments showed that miR-143 expression could significantly suppress NSCLC cell viability and invasion capacity, and nude mouse experiments confirmed the in vitro data. Bioinformatic data predicted Smad3, CD44 and K-Ras as the targeting genes of miR-143. TGF- β -induced miR-143 expression was associated with suppressed expression of Smad3, CD44, and K-Ras. This study sheds light on the TGF- β up-regulation of miR-143 and the role of miR-143 in NSCLC progression, indicating that target of miR-143 expression could be further studied as a novel therapeutic strategy in future control of NSCLC.

STUDY ON THE STATIN TREATED EFFECT AND MECHANISM WITH IRRADIATION IN LUNG CANCER

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Purpose: In this study, we investigated the effect of the 3-hydroxy-3-methylglutaryl-CoA reductase inhibitor (lovastatin), as a sensitizer of lung cancer cells to ionizing radiation (IR).

Methods: Lung cancer cells (A549, HCC827, HCC95) were treated with 0 to 50 μ M lovastatin alone or in combination with 0 to 8 Gy IR and subjected to clonogenic survival and proliferation assays. To assess the mechanism of drug action, we examined the effects of lovastatin and IR on the epidermal growth factor (EGF) receptor pathways and on apoptotic markers and the cell cycle.

Results: Lovastatin inhibited clonogenic survival and proliferation of lung cancer cells and sensitized them to IR. Lovastatin attenuated IR-induced Akt phosphorylation. The drug activated IR-induced expression of p53 and caused cell cycle arrest in G1 (control cells) and cell apoptosis (radiated cells).

Conclusions: We suggest that lovastatin inhibits survival and induces radiosensitization of lung cancer cells through induction of apoptosis, which may be mediated by the inhibition of Akt phosphorylation and the activation of p53 signalling pathways.

P-J-018

A PROSPECTIVE OBSERVATIONAL STUDY EVALUATING C-MET EXPRESSION AND EGFR GENE MUTATION CORRELATION WITH ERLOTINIB RESPONSE IN 2ND LINE TREATMENT FOR ADVANCED/METASTATIC NSCLC PATIENTS – INTERIM ANALYSIS

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Background: The c-MET is associated with tumour progression and acquired resistance to epidermal growth factor tyrosine kinase inhibitors (EGFR-TKIs). The aim of this study was to evaluate the prevalence and predictive role of c-MET and EGFR mutation in non-small cell lung cancer (NSCLC).

Methods: This is a multicentre prospective observational study for patients with stage IV or recurrent NSCLC who have progressive disease after 1st line chemotherapy. The primary outcome is to measure the rates of c-MET expression/amplification and EGFR mutation in tumour tissue. MET expression was evaluated by immunohistochemistry (IHC) and gene copy number was assessed by silver in situ hybridization (SISH). EGFR mutations were analyzed by Cobas method.

Results: A total of 112 patients were enrolled and major histologic types were adenocarcinoma (65%). MET was overexpressed (MET IHC-positive) in 57.1% of the patients and the median progression-free survival (PFS) was shorter (51 vs 56 days, $p = 0.034$). MET amplification and high polysomy (MET SISH-positive) were observed in 2.7% and 10.7%, but there was no correlation with response and PFS. The detection rate of EGFR mutation was 13.5% (19 deletion: 5, L858R: 5, exon 20 insertion: 2 cases). The response rate of erlotinib was significantly higher in EGFR sensitive mutant (60.0% vs. 1.6%, $p < 0.001$) and the median PFS showed longer tendency (52 vs 116 days, $p = 0.093$).

Conclusion: In this interim analysis, we confirmed EGFR mutation is strong predictive marker and c-MET overexpression may negatively affect PFS in 2nd line erlotinib treatment.

P-J-019

Bis EXPRESSION IN SURGICALLY RESECTED LUNG CANCER AND ITS CLINICAL SIGNIFICANCE

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Background: Bis (Bcl-2 interacting cell death suppressor), also known as BAG3 or CAIR-1, has been identified as a Bcl-2 interacting protein. Several studies showed that, in human primary lymphoid, myeloblastic leukemias and other neoplastic cell types, Bis expression sustains cell survival and underlies resistance to therapy, through down-modulation of apoptosis. The purpose of this study was to investigate the Bis expression in surgically resected lung cancer and its clinical significance.

Methods: The expression of Bis protein in surgically resected lung cancer tissues was detected via immunohistochemistry. The percentage of area from individual tissue was scored according to their intensity: negative, very weak, weak and strong. The intensity of frontier area which is defined as adjacent non-tumour region was compared to that of central tumour area.

Results: A total of 121 patients (including 57 adenocarcinoma, 50 squamous cell carcinoma, 6 small cell carcinoma and others) were included in the study. Bis expression was at the highest in squamous cell carcinoma followed by adenocarcinoma and small cell carcinoma. Positive frontier activity was higher in adenocarcinoma than squamous cell carcinoma. The higher intensity of Bis expression related with increased staging of lung cancer.

Conclusions: These results suggest that Bis expression could be used as a biomarker for patients with surgically resected lung cancer.

P-J-020

MICROVESICLES DERIVED FROM HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS ATTENUATE LUNG CANCER CELL GROWTH IN VITRO AND IN VIVO

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Many studies suggest that mesenchymal stem cells (MSCs) have antitumour properties, however, the exact mechanisms remain unclear. Recently, microvesicles (MVs) are considered as a novel avenue intercellular communication, which may be a mediator in MSCs-related antitumour effect. In our study, we evaluated whether MVs derived from Human Umbilical Cord Mesenchymal Stem Cells (HUCMSCs) may inhibit lung cancer A549 cells growth using cell culture and the BALB/c nu/nu mice xenograft model. MTT assay and Ki-67 immunostaining were performed to estimate cell proliferation in vitro and in vivo. Flow cytometry and TUNEL assay were used to assess cell cycle and apoptosis. We estimated the expression of MAPK/p-MAPK, Akt/p-Akt, p-p53, p21 and Cleaved Caspase-3 by Western blot technique after exposing A549 cells to HUCMSCs-MVs for 24, 48 and 72 h to study the conceivable mechanism by which HUCMSCs-MVs attenuate lung cancer A549 cells. Our data indicated that HUCMSCs-MVs can inhibit A549 cells proliferative viability via cell cycle arrest and induce apoptosis in A549 cells in vitro and in vivo. The study showed that HUCMSCs-MVs down-regulated phosphorylation of MAPK, Akt protein kinase and up-regulated Cleaved Caspase-3 during the process of anti-proliferation and pro-apoptosis in A549 cells. These results demonstrate that HUCMSCs-MVs play a vital role in HUCMSCs-MVs-induced antitumour effect and may be a novel tool for cancer therapy as a new mechanism of cell-to-cell communication.

P-J-021

LIPOFECTAMIN 2000 MEDIATED RBM5 OVEREXPRESSION INDUCES AUTOPHAGY IN HUMAN LUNG CANCER A549 CELLS

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Background: RNA binding motif 5 (RBM5) is a tumour suppressor gene that modulates apoptosis and cell proliferation in non-small cell lung cancer (NSCLC). Overexpression of RBM5 suppresses Bcl-2 expression, which is an autophagy suppressor. This study thus investigated whether an alteration in autophagy could be induced by RBM5 overexpression in NSCLC.

Methods: GV287-RBM5 plasmid was transiently transfected into Human lung adenocarcinoma cell line A549 cells by lipofectamin 2000. Degree of autophagosome formation were evaluated by acridine orange (AO) and monodansylcadaverine (MDC) staining. LC3II expression level was examined by western blot analysis.

Results: Autophagosome formation detected by AO and MDC staining showed moderate increase in RBM5 overexpression group than control. Proteins analysis for LC3II indicated that the level of LC3II were significantly higher in RBM5 overexpression group compared to the control group.

Conclusions: Lipofectamin 2000 mediated RBM5 overexpression induces autophagy in human lung cancer A549 cells.

P-J-022

INHIBITION OF AUTOPHAGY ENHANCES APOPTOTIC POTENTIAL OF PEMETREXED AND SIMVASTATIN IN MALIGNANT MESOTHELIOMA AND LUNG CANCER CELLS

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Objectives: Pemetrexed is a multitarget antifolate for the treatment of malignant mesothelioma and non-small cell lung cancer (NSCLC) and has been shown to stimulate autophagy. In this study, we determined whether combination treatment with pemetrexed and simvastatin can induce autophagy in malignant mesothelioma and NSCLC cells. Furthermore, we determined whether inhibition of autophagy can drive malignant mesothelioma and NSCLC cells into apoptosis.

Methods: Malignant mesothelioma cells MSTO-211 and NSCLC cells A549 were treated with pemetrexed and simvastatin alone and in combination, and their effect on apoptosis was evaluated. Autophagy was assessed by transmission electron microscopy and confocal microscopy for GFP-LC3 and acridine orange. Autophagic induction by pemetrexed and simvastatin was also investigated using autophagic inhibitors or inducers, the proportion of apoptotic cells was further determined by Annexin V assay.

Results: Combination of pemetrexed and simvastatin induced more caspase dependent apoptosis and autophagy than either drug in malignant mesothelioma and NSCLC cells. 3-methyladenine (3-MA), bafilomycin A, E64d/pepstatin A, and ATG5 siRNA increased apoptotic potential of pemetrexed and simvastatin whereas rapamycin and LY294002 decreased caspase dependent apoptosis of pemetrexed and simvastatin.

Conclusion: In conclusion, combination of pemetrexed and simvastatin augments their apoptosis and autophagy in malignant mesothelioma and NSCLC cells. Inhibition of autophagy was shown to enhance apoptosis, suggesting a novel therapeutic strategy against malignant mesothelioma and lung cancer.

P-J-023

COMBINED ERLOTINIB AND TEMOZOLOMIDE WITH WHOLE BRAIN RADIATION THERAPY IN NSCLC IN ELDERLY PATIENTS WITH BRAIN METASTASIS

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Background: Non small cell lung cancer with brain metastases are usually associated with poor outcomes and survival and about 40–50% of all patients with lung cancer develop brain metastases during the course. The poor outcomes and relapses following WBRT alone indicate a need for new therapeutic options. As some patients with NSCLC have mutations in the EGFR and treating with WBRT with the anti-EGFR agent erlotinib in patients of NSCLC with brain metastases may benefit the patients in terms of disease regression and possible improvement in quality of life. Temozolomide has been already used alone or in combination with radiotherapy in the treatment of primary brain tumours and there are few studies showing its benefits in metastatic brain with WBRT. In this study we test the feasibility and efficacy of both of the drugs with WBRT.

Material and Methods: A total of 12 elderly patients of biopsy proven adenocarcinoma lung with brain metastases (on MRI) were analyzed from July 2010 to March 2012. All the patients were planned for palliative radiation of 30 Gy/10#/2 weeks to local disease with WBRT of 20 Gy/5#/1 week with concurrent Temozolomide@ 75 mg/m² followed by assessment for further therapy after 3 weeks of radiation. All the patients were evaluated 3 weekly for assessment of symptom relief and improvement or progression. After 3 weeks all the patients were started on Erlotinib@ 150 mg, daily and Temozolomide@ 150–200 mg/m², D1-5, 4 weekly.

Results: The patients' age ranged from 58 to 75 years. All the patients completed the scheduled radiation with oral steroids. Five patients progressed and died between 3 and 10 months. 1 patient defaulted during the radiation therapy and another after completion of 6 cycles of oral chemotherapy. Only 5 patients could complete the 12 cycles of oral chemotherapy with Temozolomide and Erlotinib, 4 weekly. Only 1 patient needed dose reduction of Erlotinib to 100 mg due to grade III rashes in 3rd cycle. The patients who improved after local and brain RT have shown to tolerate the further oral chemotherapy. These patients are still alive with the metastatic disease.

Conclusion: The combination of Erlotinib with temozolomide appears to be a promising therapy for treating brain metastases in NSCLC in terms of tolerability and efficacy.

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P-J-024

DIAGNOSTIC VALUE OF SURVIVIN-EXPRESSING CIRCULATING TUMOUR CELLS IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Background: The most widely used circulating tumour cell (CTC) isolation techniques rely on antibody-based capture of CTCs, which express epithelial cell surface markers that are absent from normal leucocytes. Among these, epithelial cell adhesion molecule (EpCAM) is most commonly used. Although this platform is the most standardized of any current technology, it suffers from relatively low sensitivity.

Objectives: The purpose of this prospective study was to evaluate the diagnostic value of survivin-expressing CTCs in peripheral blood of patients with non-small cell lung cancer (NSCLC).

Materials and Methods: Blood samples were collected from patients with NSCLC before treatment and healthy volunteers. The EpCAM- and survivin-expressing CTCs were detected by real-time quantitative PCR.

Results: To date, 43 patients with NSCLC stages I-IV and 15 healthy controls, all aged 52–79 years were enrolled in the study. Survivin mRNA was detected in the CTCs. Survivin-expressing CTCs were upregulated with more than 2-fold difference as compared with controls ($p = 0.004$). EpCAM was not significantly different between NSCLC patients and controls ($p = 0.409$). No correlation between the survivin-expressing CTCs levels and the stage of disease and histology can be made at this point.

Conclusion: We demonstrated the significant difference in the levels of survivin-expressing CTCs between NSCLC patients and controls. These results suggest that survivin might be useful molecular marker for CTCs.

P-J-025

PLATELET PARAMETERS IN LUNG CANCER PATIENTS

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Background: The platelet indices have been investigated in several clinical settings. Mean platelet volume (MPV) is altered in myocardial infarction, diabetes mellitus, and inflammatory diseases. Platelet distribution width (PDW) is also different in several conditions from in healthy subjects as well as MPV. These platelet parameters have not been exactly demonstrated in cancer patients. We investigated platelet indices (platelet count, MPV, PDW, and plateletcrit) in lung cancer patients and compare in between stages.

Methods: In this retrospective study, 71 lung cancer patients and 39 healthy subjects were enrolled into the study. Automated blood counter had been used to complete blood count.

Results: Platelet count and PDW were higher in lung cancer patients compared with healthy subjects while MPV was not different. Among patients with lung cancer, PDW in small cell lung cancer (SCLC) patients was higher than in non-small cell lung cancer (NSCLC) patients. Platelet indices were not different in between stage III and IV NSCLC patients and in between limited and extensive disease SCLC.

Conclusion: This study suggests that platelet might play roles in cancer biology. Ongoing research will lead to our increasing knowledge about platelets in this situation.

P-J-026

THE CONTRIBUTION OF THE CELL BLOCKS OBTAINED FROM BRONCHIAL BRUSHING SPECIMENS IN THE DIAGNOSIS OF LUNG CANCER

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Background: The cell block preparation is easier judgement of tissue organization than conventional smear preparing, and provides additional many special staining. However, it is not popular because it takes time to prepare than the conventional cytological specimen. The objective of the this study is to evaluate cell block preparation as a tool for the diagnosis of lung cancer and to correlate the findings with those from brushing cytology and histology from forceps biopsy.

Methods: We retrospectively analyzed 101 patients with primary or metastatic lung cancer who had undergone bronchoscopy in our hospital in March 2014 from January 2012. 105 cases were routinely processed and stained for cytologic and histologic examination. In addition to conventional cytology, cell blocks were prepared from each brushing sample. We prepared the cell block preparations of our original technique. Brushing smears, cell blocks and biopsy specimens were compared and evaluated for their diagnostic accuracy.

Results: In 27 cases, cytology smears and cell blocks were prepared, and lung biopsy was performed in 24 cases. The definitive diagnosis was made in 24 cell block samples of 27 cases while malignant cells identified in 23 smears. Final diagnosis was established by cell block preparation in one cases, whose smears contained no malignant cells. Pathological diagnosis was obtained in 18 samples of 24 bioptic specimens (9 adenocarcinomas, 5 squamous cell carcinomas, 2 small cell carcinomas, 1 large cell carcinoma and 1 metastatic adenocarcinoma). Immunohistochemistry stains were performed on cell blocks led to the final precise diagnosis in 2 cases and epidermal growth factor receptor (EGFR) gene mutation analysis were performed in 2 cases using cell blocks.

Conclusion: Sample processing is a very easy way of our original cell block preparation technique. Our study confirms that the cell block preparation combined with conventional smear cytology increases the diagnostic yield in lung cancer.

P-J-027

THE EFFICACY OF UFT MONOTHERAPY IN LUNG CANCER ACCORDING TO THE HISTOLOGICAL TYPES

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Background: Tegafur-uracil (UFT) is an oral 5-fluorouracil (5-FU) derivatives containing an inhibitor of dihydropyrimidine dehydrogenase (DPD) that inhibits thymidylate synthase (TS). The expression of TS is higher in squamous non-small cell lung cancer (NSCLC) than in non-squamous NSCLC. The aim of this retrospective study was to assess the efficacy of UFT monotherapy for lung cancer according to the histological subtype.

Methods: We reviewed the clinical records of patients with lung cancer treated with UFT across all treatment lines between January 2008 and July 2013. The efficacy was assessed with best overall response rate (ORR), disease control rate (DCR), progression-free survival (PFS) and overall survival (OS).

Results: A total of 149 (54 squamous NSCLC, 67 non-squamous NSCLC and 28 SCLC) patients were enrolled in this study. UFT was administered as 1st to 10th line treatment (1st line: 18.8%, 2nd to 4th line: 36.2%, more than 4th line: 45%). There were significant differences in DCR (38.9%, 31.3%, 10.7%, $p = 0.03$) and the median PFS (3.1, 4.1, 1.6 months, $p = 0.00$), but the ORR was not different (1.9%, 1.5%, 0%, $p = 0.779$). The DCR and the PFS between squamous and non-squamous NSCLC were not statistically different. The DCR was different depending on the dose of UFT (24.8% for < 600 mg/day vs. 43.2% for ≥ 600 mg/day, $p = 0.025$).

Conclusions: There was no significant difference in clinical efficacy between histologic subtypes of NSCLC.

P-J-028

DIFFERENCES EPIDEMIOLOGY AND RISK FACTORS OF LUNG CANCER BY SEX IN M DJAMIL HOSPITAL PADANG

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Background: The investigations of men and women lung cancers based on differences epidemiology and risk factors have been widely reported. These differences has not been studied in M. Djamil Hospital Padang.

Methods: A retrospective analytical study was conducted on lung cancer patients treated at the Pulmonary Department, M. Djamil Hospital Padang from January 1, 2004 until December 31, 2013 that already known cell types. Data were grouped according to gender.

Results: There were 275 lung cancer patients. Although 76.4% of whom were men, but number of men tended to decrease from year to year, while women tend to increase. Age of women were younger than men (51.02 years vs. 58.54 years, $p = 0.01$). 93.7% of men were smokers, while 95.4% of women were non-smokers ($p = 0.00$). No differences were found between the men and women in the histories of previous TB, cancers of other organs, and cancers in the family. Squamous cell was the predominant type of lung cancer in men (48.1%), while women were adeno carcinoma (46.2%); with $p = 0.036$. Advanced stage in women was more than men (90.8% vs. 78.9%, $p = 0.031$). Average survival of women were longer than men, respectively 4.90 ± 1.27 and 3.54 ± 0.44 ; $p = 0.467$.

Conclusions: Differences epidemiology and risk factors of lung cancer among men and women in M Djamil Hospital Padang were significant in trend of incidence, age, smoking factor, cell type and staging.

P-J-029

PROMOTER METHYLATION OF miR-137 AND ITS CLINICAL SIGNIFICANCE IN SURGICALLY RESECTED LUNG CANCER

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Background: Recent studies suggest that miR-137 functions as tumour suppressor in various tumours including colorectal cancer, glioblastoma multiforme, oral cancer, and squamous cell carcinoma of the head and neck. The silencing of miR-137 could be related with its abnormal promoter hypermethylation. The purpose of this study was to investigate the significance of MIR137 promoter methylation in lung cancer.

Methods: Lung cancer cell lines were treated with DNA methyltransferase inhibitor (5'-Aza) and/or HDAC inhibitor (Trichostatin A) whether miR-137 could be reactivated. From pared tumour and adjacent non-tumour lung tissues ($n = 50$), real-time RT-PCR for miR-137 expression and cyclin dependent kinase 6 (CDK6), quantitative methylation specific PCR for methylation analysis, and bisulfite modified DNA sequencing for validation were used for the study.

Results: miR-137 was reactivated by treatment with 5'-Aza and/or Trichostatin A in lung cancer cell lines. miR-137 was significantly downregulated and CDK6 was significantly upregulated in lung tumour tissues compared with adjacent non-tumour tissues. Quantitative methylation specific PCR showed increased MIR137 promoter methylation in lung tumour tissues compared with adjacent non-tumour tissues, which was further validated with bisulfite sequencing.

Conclusions: These results suggest that miR-137 has a role of tumour suppressor and its expression is regulated by promoter methylation. The decreased expression of miR-137 combined with increased expression of CDK6 could be associated with lung cancer carcinogenesis.

P-J-030

P-J-032

ACTIVITY OF PELARGONIUM QUERCETORUM AGNEW BY INDUCING APOPTOSIS-LIKE CELL DEATH ON NON-SMALL CELL LUNG CANCER CELL LINES

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Lung cancer is still a deadly disease and there is not enough success in its treatment despite new chemotherapy regimens recently introduced. Therefore, we aimed to study the anticancer activity of Pelargonium quercetorum Agnew (P. Quercetorum, PQE) extract on different lung cancer cell lines (A549, PC3, H1299). The plant was collected from Hakkari, Turkey and the methanol extract was obtained by standard methods, followed by the lyophilization. The MTT and ATP cell viability tests were used to determine in vitro cytotoxicity. M30 and M65 assays were used to determine the cell death mode (apoptosis/necrosis). Apoptosis was confirmed by Annexin-V-FITC and Hoechst 33342 staining and western blot analysis. It was found that PQE significantly inhibited the growth of the cells in a dose-dependent manner. Although there were no significant increase in M30 levels in A549, PC3 and H1299 cells, we observed 6-fold increase of M65 in PC3 and H1299 cells, approximately 4-fold increase in A549 cells when compared to the untreated control cells. Also we observed that PQE caused apoptotic cell death in all treated cell lines that was evident from pyknotic nuclei by staining with Hoechst dye 43332, as well as from the presence of Annexin-V-FITC staining. Some cells were observed to be PI positive but the nucleus of these cells did not show any enlargement that is a typical feature of primary necrosis. In addition, PARP was not cleaved in A549, PC3 and H1299 cell lines. The lack of cleavage of PARP was considered as apoptosis-like cell death, rather than typical apoptosis. In conclusion, the results warrants ingredient analysis of PQE as well as further in vivo experiments in lung cancer models.

GEFITINIB OR CHEMOTHERAPY IN PULMONARY ADENOCARCINOMA PRELIMINARY STUDY IN PERSAHABATAN HOSPITAL, JAKARTA INDONESIA

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Background: Pulmonary adenocarcinoma with sensitive mutations of the epidermal growth factor receptor (EGFR) is highly responsive to EGFR tyrosine kinase inhibitors such as gefitinib but little's known in Indonesian patients about how efficacy and safety profile compares wuth that standard chemotherapy.

Objective: To asses the profile of efficacy and safety of gefitinib for pulmonary adenocarcinoma with mutated EGFR compares standard chemotherapy for patients of pulmonary adenocarcinoma with wild type.

Methods: We randomly assigned 10 patients pulmonary adenocarcinoma with mutated EGFR to receive gefitinib and 10 patients pulmonary adenocarcinoma with wild type to receive standard chemotherapy.

Results: EGFR mutations were common in femlae (80%) and never smoker (90%), type of EGFR mutation at exon 19 deletion (50%) and L858R (50%). The efficacy of gefitinib as the first line treatment for pulmonary adenocarcinoma with mutated EGFR showed Partial Response (PR) 80% and at chemotherapy group PR 70%. The most common adverse events in gefitinib group were diarrhoea (20%) and dermatological (acne) 10% and in the chemotherapy group alopecia (70%) and nausea or vomiting (20%).

Conclusions: First line gefitinib for pulmonary adenocarcinoma with mutated EGFR had better response and acceptable toxicity as compared to standard chemotherapy in Indonesian patients.

P-J-031

P-J-034

ASSOCIATION WITH EMPHYSEMA ON COMPUTED TOMOGRAPHY AND LUNG CANCER IN SMOKERS

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Background: Lung cancer is attributable largely to tobacco consumption. Also, several studies have explored the impact of emphysema as measured by chest computed tomography (CT) on the risk of lung cancer. Despite this strong association, only a minority of smokers develop emphysema or lung cancer.

Objectives: To explore that distinguishes lung cancer with and without emphysema on CT in smokers.

Methods: We reviewed retrospectively smoking patients with pathologically proved primary lung cancer. Emphysema was graded on CT by two readers, using a standardized rubric.

Results: Six hundred and thirty-four out of 1113 lung cancer patients evaluated from January 2009 to May 2013. The mean age of the patients was 65 years and 579 (91.3%) patients were male. Three hundred and twelve (49.2%) patients had emphysema on CT chest. The most common histologies were squamous (245 (38.6%)), adenocarcinoma (206 (32.5%)), small cell carcinoma (120 (18.9%)) and others (63 (9.9%)). The non small cell lung cancer (NSCLC) patients with emphysema were more likely to have squamous histology ($p = 0.009$) and early stage (I to IIIA) ($p = 0.033$). Multivariate analysis revealed that old age, advanced stage and emphysema on CT were significant poor prognostic factors in 384 patients who were treated for lung cancer.

Conclusion: In this study, NSCLC patients with the emphysema were more likely to have squamous histology and early stage, but showed significantly poor prognosis.

INCIDENCE OF EPIDERMAL GROWTH FACTOR RECEPTORS (EGFR) MUTATIONS IN JAKARTA INDONESIA

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Background: Epidermal Growth Fcator Receptor (EGFR) mutations predict a better response to tyrosine kinase inhibitors compared to platinum-based chemotherapy in advanced non-small cell lung cancer (NSCLC). Previous studies in Asian population have reported a frequency of EGFR mutation of 50%. The aim of this study is to describe the incidence of EGFR mutations in NSCLC patients in Jakarta.

Methods: We reviewed the data of 138 NSCLC patients at Persahabatan Hospital Jakarta, who had been tested for EGFR mutation since July 2010 to December 2013 using sequencing in conjunction with Real Time PCR to detect sensitizing mutations of EGFR genes from available tumour tissue or cytologic samples.

Results: From the 138 consecutive NSCLC samples, 115 (83.3%) patients showed EGFR mutations: 82 (71.3%) exon 21 mutations (L858R) and 33 (28.7%) exon 19 deletions. In EGFR-mutated population showed the following characteristics: 88 (76.5%) male, 27 (23.5%) female; 23 (20%) age <45 years, 80 (69.5%) age 45–70 years, 12 (10.5%) age >70 years; 126 (89.5%) adenocarcinoma, 4 (3.5%) squamous cell carcinoma, 6 (7%) other NSCLC; and 63 (54.8%) smokers, 52 (45.2%) non smokers.

Conclusions: The EGFR mutation rate in NSCLC in our referral hospital is more superior than previously reported, reinforcing the importance of including EGFR mutation testing in NSCLC for the correct management of these patients.

P-J-035

CHARACTERISTICS AND SURVIVAL RATE OF SMALL CELL LUNG CANCER

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Introduction: Small cell lung cancer (SCLC) are generally more aggressive than other subtypes of lung cancer. Small cell lung cancer has a rapid doubling time, rapid growth fraction and could metastasize rapidly and widely compared to non-small cell lung cancer (NSCLC). This study aims to determine the characteristics and survival of SCLC patients.

Methods and Subjects: The study was conducted by using retrospective cohort. All subjects were SCLC patients in Persahabatan Hospital, Jakarta, Indonesia. Subjects were in and out patients between January 2008 and December 2012. Data obtained were tested by Kaplan Meier analysis of survival.

Results: Total subjects in this study were 34 SCLC patients, with majority of male 32 subjects (94.1%), mean age of 59 years old and all of the subjects (100%) were smokers. The majority of tumour have diagnosed with extensive disease (ED_SCLC) in 32 subjects (94.1%), performance status ECOG \leq 2 in 30 subjects (88.2%). Median survival time of SCLC patients were 78.75 days (2.5 months) and 1 year survival rate 11.6%. The median survival time of limited diseases (LD-SCLC) group were 365 days (12 months) but it were 60 days (2 months) in ED-SCLC group.

Conclusion: Small cell lung cancer cases were rare in Persahabatan Hospital. Patients need additional therapy after standard chemoradiotherapy to improve survival of SCLC.

P-J-036

THE CLASSIFICATION OF INTERSTITIAL PNEUMONIA BY THE OFFICIAL ATS/ERS/JRS/ALAT STATEMENT COULD PREDICT ACUTE EXACERBATION OF INTERSTITIAL LUNG DISEASE IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS WITH PRE-EXISTING INTERSTITIAL LUNG DISEASE

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Introduction: While chemotherapy is very important in the treatment of non-small cell lung cancer (NSCLC), it is generally known that NSCLC patients accompanying interstitial lung disease (ILD) should not receive chemotherapy which could result in acute-exacerbation of ILD (AE-ILD). Thus, the standard treatment of NSCLC complicating ILD is not established yet.

Purpose and Method: For the purpose of examining whether the type of ILD categorized by the official ATS/ERS/JRS/ALAT statement "idiopathic pulmonary fibrosis (IPF) by high resolution computed tomography (HRCT)" could predict chemotherapy-induced AE-ILD in NSCLC patients with ILD, we retrospectively reviewed all NSCLC patients complicating ILD who had received chemotherapy at our institute from January 2007 until December 2013. Patient's characteristics, pathology and clinical staging of lung cancer, chemotherapy, type of ILD, AE-ILD during chemotherapy and GAP index were evaluated. ILD was diagnosed by both clinical symptoms and HRCT. Radiological evaluations were performed by two of 10 years' experienced pulmonologist and radiologist. ILD was classified according to the official ATS/ERS statement published in 2013 as follows; usual interstitial pneumonia (UIP), Possible UIP and Inconsistent with UIP pattern.

Result: A total of 592 patients with NSCLC were screened and 46 patients had pre-existing ILD and received chemotherapy. The mean age was 73 years (range 46–83 years). Fifteen (35%) out of 46 patients with ILD developed chemotherapy-induced AE-ILD, which was seen more frequently in patients with UIP pattern or possible UIP pattern than in patients with pattern inconsistent with UIP (80.0 versus 9.7%, $p < 0.001$). As for the incidence of AE-ILD for chemotherapy agents, docetaxel (27%) led to AE-ILD most frequently, followed by carboplatin (17%). Multivariate analyses using four variables (age, sex, PS, and types of IP by HRCT) showed that the presence of UIP pattern or possible UIP pattern was an independent risk factor for chemotherapy-induced AE-ILD (odds ratio, 51.7; 95% confidence interval: 6.9–387.9). Comparing patients with AE-ILD and those with non-AE-ILD, there were no significant differences in patient characteristics or in the pre-chemotherapy laboratory findings in the two groups.

Conclusion: The classification of interstitial pneumonia by the official ATS/ERS/JRS/ALAT statement "IPF by HRCT", could predict AE-ILD in NSCLC patients with pre-existing ILD. ILD with UIP pattern or possible UIP pattern by the classification could be risk factors of AE-ILD.

P-J-037

EFFICACY OF FIRSTLINE DOUBLET CHEMOTHERAPY FOR END-STAGE NSCLC IN PERSAHABATAN HOSPITAL JAKARTA

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Background: Lung cancer prevalence is increasing in Indonesia as compared to previous decade. Most of the patients were come in late stage, and were treated with palliative chemotherapy. Data on 1-year survival rate of patients who received first-line doublet chemotherapy for NSCLC in Indonesia is still limited.

Purpose: To know the 1-year survival rate of patients who received firstline doublet chemotherapy NSCLC.

Method: A preliminary retrospective cohort study on 30 patients who received NSCLC first-line chemotherapy regiments (carboplatin and etoposide; carboplatin and paclitaxel; carboplatin and gemcitabine).

Results: The 1-year survival of NSCLC patients who received combination of carboplatin and etoposide was 36%, carboplatin and paclitaxel was 30% patients, carboplatin and gemcitabine was 40%.

Conclusion: NSCLC patients who received carboplatin and etoposide or carboplatin and gemcitabine have 1-year survival rate which compares favourably with carboplatin and paclitaxel.

P-J-038

P-J-039

CLINICAL PROFILE OF LUNG CARCINOMA PATIENTS WITH MUTATION OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) IN DR. WAHIDIN SUDIROHUSODO AND HASANUDDIN UNIVERSITY HOSPITAL, MAKASSAR

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Background: Worldwide, lung cancer is still the leading cause of death from all cancer. The paradigm of lung cancer therapy has now shifted towards targeted therapy. In Makassar, targeted therapeutic agents that inhibit EGFR signalling pathway, i.e. the tyrosine kinase inhibitor (TKI) such as gefitinib has been used and tends to decrease morbidity and mortality of the disease. The purpose of this study was to determine the clinical profile of lung cancer patients with EGFR mutations in Dr. Wahidin Sudirohusodo and Hasanuddin University Hospital, Makassar.

Methods: This study used a retrospective descriptive method with subjects of lung cancer patients, that has been diagnosed based on histopathological examination during period July 2013 until June 2014, at the Hospital Dr. Wahidin Sudirohusodo and RSP UNHAS Makassar, and also based on the laboratory results of EGFR mutations from Kalgen Jakarta.

Results: There were 23 subjects, aged varied between 40 to 75 years. Mean of age is 57+10 years, which means that the majority of subjects aged between 47 to 67 years. Male gender was found more than female (78.3% vs 21.7%). Smokers was found more than nonsmokers (73.9% vs 26.1%). A number of 1–2 respiratory complaints was found more than 3–4 complaints (69.6% vs 30%). Non-obese category was found more than obese (69.6% vs 30.4%). High levels (>4.7 ng/ml) of carcinoembryonic antigen (CEA) was found more than normal levels (82.6% vs 17.4%). Metastasis was found in 69.6% subjects. Classified as stage IV was found in 65.2% subjects. Histopathological diagnosis classified as non-small cell lung carcinoma (NSCLC) in 47.8%, and adenocarcinoma 52.5%. EGFR mutation results found 56.5% of wild-type type, L858R Ex19del and 21.7% respectively.

Conclusion: The findings of the clinical profile of lung cancer patients with EGFR mutations in Hospital Dr. Wahidin Sudirohusodo and RS Hasanuddin University Makassar is not much different from other findings in Indonesia.

EVALUATION OF PRE AND POST-TREATMENT POSITRON EMISSION TOMOGRAPHY FINDINGS IN SMALL CELL LUNG CANCER

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Background and Aim: Staging of small and non-small cell lung cancers, determination of response to therapy, investigation of recurrence at follow-up and restaging are major indications of Positron Emission Tomography-Computed Tomography (PET-CT) in lung cancers. In this study, we aimed to evaluate the PET-CT findings at the beginning and 3 months after treatment in small cell lung cancer (SCLC) cases.

Materials and Methods: 54 consecutive SCLC cases who were diagnosed and whose PET-CT follow-up were made in Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Department of Chest Diseases were involved in our study and data were analyzed retrospectively.

Findings: 54 SCLC patients, 2 females and 52 males with mean age 57, were involved in this study. There was no statistically significant difference between groups (only chemotherapy, CT, n = 37; chemoradiotherapy combination, CRT, n = 17) for mean of age, mass diameter, initial maximum standard uptake value (SUV_{max}). There was no statistically significant difference between CT and CRT groups for PET-CT involvements and recurrence rates in the 3, 6 and 9 months after treatment. No correlation was detected between age, mass diameter and SUV_{max} values. There was no statistically significant difference between mean of age, mass diameter and initial SUV_{max} value in the post-treatment controls of cases with and without PET-CT involvement.

Conclusion: No relationship was observed between PET-CT SUV_{max} values and treatment responses before and after treatment in SCLC cases.

P-J-040

SERUM INTERLEUKIN-17 (IL-17) AND IL-23 IN LUNG CANCER PATIENTS

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Background: Interleukin-17 (IL-17) and IL-23 play roles in several biological processes. The function of these T helper 17 (Th17) cells related cytokines has not been completely evaluated. We investigated serum IL-17 and IL-23 levels and its relationship with clinicopathological and biochemical parameters in lung cancer patients.

Methods: Forty-five lung cancer patients and 46 healthy volunteers are included to the study. Data of patients and control subjects were achieved from clinic archive and hospital computed system. IL-17 and IL-23 measurements were obtained with ELISA method. The cytokines levels were compared between patients and healthy subjects. The association of these levels with other parameters was evaluated.

Results: The ages of patients (53–84 years) and healthy subjects (42–82 years) were similar. Serum IL-23 levels were elevated in lung cancer patients than in healthy subject (491,27 ± 1263,38 ng/ml vs 240,51 ± 233,18 ng/ml; p: 0.032). IL-23 values were higher in small cell lung cancer (SCLC) patients than in non-small cell lung cancer (NSCLC) patients. Serum IL-17 levels were numerically lower in the patients, but this was not statistically significant (135,94 ± 52,36 ng/ml vs 171,33 ± 133,51 ng/ml; p: 0.124). Presence of comorbid disease (diabetes mellitus, hypertension or chronic obstructive lung disease) did not have any effect on the levels of IL-17 or IL-23. Erythrocyte sedimentation rate values were positively correlated with cytokines levels, but serum albumin levels were negatively. No significant correlation was found between serum IL-17 or IL-23 values and serum C reactive protein (CRP).

Conclusion: Serum IL-23 levels are elevated in lung cancer patients, particularly those with SCLC. IL-17 and IL-23 values are correlated inflammatory markers in the patients.

P-J-041

THE EXPERIMENT OF RNAI TARGETING HMGNS5 GENE ON PROLIFERATION OF A549 CELLS

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Objective: This is to observe the proliferation on lung cancer cell line A549 by RNAi method. It can provide a basis method to lung cancer treatment.

Methods: We use SiRNA-HMGNS5 lentivirus particles to infect A549 cells, it can make silence the expression of HMGNS5. We detected the HMGNS5 mRNA levels by Real-time PCR and Western blotting. We analyzed the proliferation and cell cycle on A549 with MTT assay.

Results: HMGNS5 gene could be down-regulated at mRNA level. SiRNA-HMGNS5-lentivirus inhibited the proliferation of A549 cells with statistically significant difference from MTT assay.

Conclusions: By silencing HMGNS5 gene, the proliferation of A549 cells can be inhibited. HMGNS5 gene may play a role in the development of lung cancer. It may be beneficial for the treatment of lung cancer.

P-J-043

PROGRESSION FREE SURVIVAL (PFS) IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) TREATED ERLOTINIB/GEFITINIB WHO FAILED PREVIOUS CHEMOTHERAPY

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Introduction: Second-line chemotherapy was given if the patient does not response (progressive) after 2 cycles of chemotherapy or progressive in the evaluation periode after completion of 4 chemotherapy cycles. Targeted therapies such as EGFR-TKI group (Erlotinib/Gefitinib) is recommended as second-line therapy for patients with lung cancer non-small cell carcinoma (NSCLC). Researcher made a study to assess progression free survival (PFS) patients with advanced NSCLC treated Erlotinib/Gefitinib who failed previous chemotherapy.

Methods: The study was a retrospective cohort study between 2009 until 2013 from the medical records advanced NSCLC patients. All patients had previously received first-line chemotherapy. Patients were treated with monotherapy EGFR-TKI such Erlotinib 1 x 150 mg/day or Gefitinib 1 x 250 mg/day. Progression free survival (PFS) calculated from the first day of therapy until the invention of progressive signs.

Results: From 31 patients NSCLC were according to inclusion and exclusion criteria's. In this study, the median overall PFS 8 months (95%CI, 6.442–9.558). Progression free survival (PFS) have significant differences in gender (p logrank = 0.044, p Breslow = 0.017, HR 0,91) and performance status (p = 0.043 HR 0,71).

Conclusion: Progression free survival (PFS) in patients with advanced NSCLC treated Erlotinib/Gefitinib who failed previous chemotherapy is long enough.

P-J-042

CLINICAL EVALUATION OF POTENTIAL USEFULNESS OF SERUM LACTATE DEHYDROGENASE (LDH) LEVEL IN FOLLOW-UP OF SMALL CELL LUNG CANCER

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Background: Lactate formation is up-regulated in tumour cells by lactate dehydrogenase (LDH). High serum LDH level is linked to many malignancies with poorer survival, but tumour LDH has not been well investigated in small cell lung cancer (SCLC). This study was to evaluate the clinical value of serum LDH level in predicting chemotherapeutic response and monitoring disease in SCLC.

Methods: Study was performed in 120 cases of SCLC confirmed by pathological examination. The evaluation of treatment response to chemotherapy was based on RECIST criteria. The serum LDH levels were determined at diagnosis and follow-up visits. The distribution and differences in LDH change and chemotherapeutic response rate was evaluated by using X2 tests. Receiver operating characteristic (ROC) curves were calculated in order to select the cut-off level of an increase in LDH indicating progress significance. The correlation of time of serum LDH normalization, time-to-progression (TTP) and overall survival (OS) were analyzed by Pearson coefficient. Influence of increasing LDH on survival was calculated using the Kaplan-Meier method.

Results: At diagnosis, significant differences in LDH levels were found in limited and extensive groups. In contrast to limited group, the extensive group showed decreased level of LDH after first-line chemotherapy. In patients who progress, LDH levels were significantly higher in the last 1-month period preceding progression compared with real-time of progression. In the follow-up, we found that prolonging of serum LDH normalization co-related to TTP and OS. An increase in LDH by at least 51.5 U/l was found to be associated to a significantly higher probability of disease progression, and patients with initial increasing LDH had a significantly reduced probability of survival.

Conclusions: Here, LDH is validated the usefulness of markers for monitoring treatment response in SCLC, and also suitable to discriminate between disease and disease-free periods.

P-J-044

FACTORS AFFECTING SURVIVAL RATE ON ADVANCED STADIUM LUNG CANCER PATIENTS IN MOEWARDI HOSPITAL

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Introduction: The incidence of lung cancer is still the highest among thoracic malignancies. Lung cancer as a malignancy is one of the biggest causes of death in both developed and growing countries. A parameter of successful cancer treatment is the survival rate. Many factors affect the survival of patients with lung cancer, especially in advanced stadium lung cancer.

Objective: To assess the relationship between survival rate of advanced stadium lung cancer, with the complications and treatment.

Method: For all advanced stadium lung cancer patients in the pulmonary ward of Moewardi Hospital since January 2012–December 2013, a cross sectional study was performed. The data was obtained through statistical test method of independent samples T-test.

Result: The 117 patients with advanced stadium lung cancer was dominated by men (62.4%). One-year survival rate of advanced stadium lung cancer patients who received chemotherapy, was 69.23% with an average life of 35 weeks. One-year survival rate of lung cancer patients who did not receive chemotherapy was 30.76% with an average life of 10 weeks. There is a relationship between the survival rate of patients with advanced stadium lung cancer complicated by pleural effusion (p = 0.000) and patients' willingness to undergo chemotherapy (p = 0.000).

Conclusion: Factors affecting the survival of patients with advanced stadium lung cancer are the presence or absence of pleural effusion as a complication, and willingness to undergo chemotherapy.

P-J-045

CHARACTERISTICS AND PREDICTIVE FACTORS OF MORTALITY IN HOSPITALIZED PRIMARY LUNG CANCER PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL JAKARTA

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Background: Lung cancer is a leading cause of death due to cancer. Many factors may predict mortality of hospitalized lung cancer patients, but data of lung cancer in Indonesia were still limited. The purpose of this study was to investigate the characteristics of lung cancer and predictive factors of mortality in hospitalized primary lung cancer patients in Cipto Mangunkusumo Hospital Jakarta.

Methods: This study used a retrospective cohort design with multivariate analysis to assess the predictive factors of mortality in hospitalized primary lung cancer patients.

Results: From total 238 cases of primary lung cancer, with an average age of 55.5 years old, 73.5% male, 229 patients (96.2%) had non small cell lung cancer and 9 patients (3.8%) had small cell lung cancer, the most were adenocarcinoma cell type in 150 patients (63%), and 221 patients (92.9%) were at advanced stage when diagnosed. Hospital mortality rate was 36.6%. Through multivariate analysis, we found that the predictive factors of hospital mortality were pneumonia, sepsis, vena cava superior syndrome, pericardial effusion, and severity of co-morbid diseases.

Conclusion: From a total 238 patients enrolled in this study, which was dominated by male, with an average age of 55.5 and mostly adenocarcinoma cells, the hospital mortality rate was 36.6%. Mortality increased with the presence of pneumonia, sepsis, vena cava superior syndrome, pericardial effusion or severity of co-morbid diseases.

P-J-047

CLINICAL CHARACTERISTICS OF ADVANCED LUNG ADENOCARCINOMA PATIENTS IN INDONESIA

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Background: Lung cancer has the highest prevalence and mortality rate worldwide in 2012. Adenocarcinoma is the most common lung cancer histology, and the only cancer with increasing incidence despite successful attempt to reduce smoking habit.

Aim: To identify the clinical characteristics of advanced lung adenocarcinoma patients in Indonesia.

Method: Study design was cross sectional. Subjects were advanced lung adenocarcinoma patients in Cipto Mangunkusumo Hospital and Dharmais National Cancer Center Hospital from January 2010 to December 2013. From medical records, subjects' data for age, gender, educational level, smoking status, occupation, and diagnosis were collected.

Results: Sixty-seven subjects participated in this study. Forty-four subjects (65.7%) were male, and 23 (34.3%) were female. Mean age at diagnosis was 58.9 years old (SD 10.9), comprised of 4 subjects (6%) were diagnosed at age younger than 40 years old, 34 (50.7%) subjects were diagnosed between age 40–60 years old, and 29 (43.3%) at age older than 60 years old. Forty-seven subjects (70.1%) had occupation history, while 20 (29.9%) never had occupation before. Six (9%) subjects had low education level, 30 (44.8%) had moderate education level, 29 (43.3%) had high education level, however 2 subjects (3%) were unknown. In subjects with known smoking status (n = 51), 30 (58.8) subjects among them had smoking history and 21 (41.2%) had never smoked before.

Conclusion: Advanced lung adenocarcinoma patients in Indonesia have mean age at diagnosis of 58.9 (SD 10.9) years old, are mostly men, have occupation history, moderate and high education level, also smoking history.

P-J-046

SECOND LINE TREATMENT FOR ADVANCED NSCLC PATIENTS WITHOUT SQUAMOUS HISTOLOGY AND EGFR MUTATION

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Background: For NSCLC (non-small cell lung cancer) patients without squamous histology and EGFR (epidermal growth factor receptor) mutation, either TKI (tyrosine kinase inhibitor) or cytotoxic chemotherapy can be used as second line treatment. We designed this study to evaluate which regimen had more favourable result.

Method: We conducted a retrospective analysis of patients with stage IIIB or IV NSCLC who had been treated with pemetrexed-cisplatin as first line treatment between February 2010 and January 2014. Patients who had EGFR mutation or were on pemetrexed maintenance therapy were excluded. We compared the median overall survival time of each second line regimen using Kaplan-Meier method and log rank test.

Result: Among 65 patients, 27 were eligible for study. 14 received TKI (erlotinib or gefitinib); 9 received docetaxel monotherapy; 4 received gemcitabine-vinorelbine combination therapy. Median age was 61, 65 and 61.5 years, respectively. All patients showed adenocarcinoma type histology except one in docetaxel group with large cell type histology. Two in TKI group were stage IIIB and others were stage IV. Response rate was 11.1% in docetaxel group and 25% in gemcitabine-vinorelbine group. TKI group only showed stable disease and progressive disease. Median overall survival time was 63 days in TKI group, 74 days in docetaxel group, and 91 days in gemcitabine-vinorelbine group. P-value was 0.589. In pairwise comparisons, p-value was 0.886 for TKI versus docetaxel group, 0.391 for TKI versus gemcitabine-vinorelbine group, and 0.248 for docetaxel versus gemcitabine-vinorelbine group.

Conclusion: Although statistical significance was absent, there was a trend that gemcitabine-vinorelbine combination therapy had more favourable response rate and survival outcome, and TKI had poor outcome. A larger study is required to confirm the efficacy of cytotoxic chemotherapy, especially gemcitabine-vinorelbine combination therapy, as second line treatment for EGFR negative NSCLC patients.

P-J-048

INFLAMMATORY MYOFIBROBLASTIC TUMOUR WITH A MALIGN APPEARANCE

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Inflammatory myofibroblastic tumour, known also as inflammatory pseudotumour, is a rare benign tumour formed with the abnormal proliferation of the inflammatory cells. Lesions are generally found in the lungs. Lesions are asymptomatic and there are no specific findings. The lesions are diagnosed with histopathological examination eventually. We want to present our case pre-diagnosed malignancy but diagnosed as benign characterized inflammatory myofibroblastic tumour after histopathological examination. A 57-year-old man was admitted to our department with mediastinal lymphadenopathies and bilateral lesions in the lungs. Thoracotomy was performed to the patient after the non-diagnostic bronchoscopy and fine needle aspiration biopsy. Because of multiple lesions and the procedure was a performed for diagnosis, wedge resection was performed for the lesion in the superior segment of the lower lobe of the right lung. The pathology of the lesion was reported as inflammatory myofibroblastic tumour. The patient was taken to the control protocol. These lesions can regress because of their inflammatory nature. But, no change and invasion of the lesion can be seen. Our case was regressed during the follow up period. Distinction of the lesions from malignant tumours in inflammatory myofibroblastic tumours is difficult as in our case. The treatment of the inflammatory myofibroblastic tumour is complete resection. Relaps after the complete resection is rare. Chemotherapy, radiation therapy, steroid treatment can be chosen for the cases where complete resection was not performed.

P-J-049

THE RELATIONSHIP BETWEEN SOME FACTORS WITH CHEMOTHERAPY RESPONSE IN NON-SMALL CELL LUNG CANCER IN DR. SOETOMO GENERAL HOSPITAL

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Background and Purpose: The majority of lung cancer patients were diagnosed at an advanced stage so that the management was given chemotherapy. Some factors thought to influence the chemotherapy response. This study aimed to evaluate the relationship between stage, performance status, age and sex with the chemotherapy response in non-small cell lung cancer (NSCLC) patients.

Patients and Methods: This is a prospective cohort study on 30 patients with NSCLC in Dr. Soetomo General Hospital that finished four cycles of chemotherapy. We studied the relationship between stage, performance status, age and sex with the chemotherapy response (semi-subjective and objective response).

Result: Data from 30 patients with NSCLC consists of: 20 male (66.7%), 10 female (33.3%); The most of their age groups is less than 54 years old (50%); 6 patients (20%) were diagnosed in stage III and 24 patients (80%) in stage IV; 21 patients (70%) with performance status ECOG 1 and 9 patients (30%) with ECOG 2. There is a significant correlation between performance status with the chemotherapy response, where the value of $p = 0,001$ ($<0,005$). There were no statistically significant correlation between stage, age and sex with the chemotherapy response ($p > 0,005$).

Conclusion: The performance status can be used as a significant factor for predicting chemotherapy response.

P-J-051

CHARACTERISTICS OF PATIENTS THAT CAME TO MOEWARDI HOSPITAL WITH CHEST PAIN IN LUNG DISEASE FROM JANUARY 2013 TO APRIL 2013

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Background: Pain is an unpleasant sensation due to complex sensory stimuli. Pain arises from the process of ischemia, inflammation, malignancy, idiopathic, mechanical disruption of the tumour, injury, surgery and structural failure. The aims of this study are to find out the common causes of chest pain and to know the average time needed to find out the cause of pain in patients with lung disease in Dr. Moewardi Hospital.

Methods: A retrospective descriptive study was conducted in 78 patients with lung disease who complained for chest pain. This study was performed in Dr. Moewardi Hospital from January 1st to April 15th 2013. The data was obtained from medical records. We use statistics analysis with Chi square, $p < 0,05$.

Results: Of the 90 patients with lung disease who complained for chest pain, 78 patients met our inclusion criteria. 46 patients were male, and 32 patients were female. This study revealed that malignancy was the most common cause of pain (53.85%), while the average time needed to find out the cause of pain was 15 days.

Conclusion: In patients with lung disease, malignancy is the most common cause of pain and to find out the cause of pain we need at least 15 days.

P-J-050

LUNG CANCER HISTOLOGICAL SUBTYPES DIAGNOSED ON ENDOSCOPIC PROCEDURES IN A TERTIARY RESPIRATORY CENTRE IN MALAYSIA

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The incidence of cancer is rising, with an estimated 14.1 million new cancer cases in 2012. Lung cancer is the most commonly diagnosed worldwide (13%) and it is also the most common cause of cancer death. In Malaysia, lung cancer is the most common cancer among males and 3rd most common (10.2%) cancer in general population. However, a large proportion (60%) is diagnosed at stage IV with only 12% diagnosed at stage I or II. In 1991–1999, a data in a university hospital in Malaysia, adenocarcinoma was the commonest lung cancer type across both gender (43.2%) as compared to 1967–1976 where squamous cell lung cancer was the commonest histological type. But since then, there is no local data of lung cancer according to histological types. This is a retrospective analysis of 203 patients diagnosed with lung cancer from a total of 1004 patients who had undergone bronchoscopy, pleuroscopy or EBUS in a tertiary respiratory centre in Malaysia. Mean age for all lung cancer cases was 61.57 ± 12.169 years old (range 18–90 years old). The peak incidence of lung cancer occur in at age of 61–70 years old (33.5%), 51–60 years old (26.6%) and 71–80 years old (22.2%). 68% were males and majority of them were Chinese (50.2%) and Malays (41.9%). A total of 51.2% had the procedure done due to findings of a lung mass radiologically. Of all lung cancer diagnosed, 73.4% were diagnosed from bronchoscopy, followed by pleuroscopy (23.6%) and EBUS (3%). Histological subtypes analysis revealed that adenocarcinoma (40.9%) and squamous cell (20.2%) accounts for the majority of lung cancer. Majority of adenocarcinomas were diagnosed by biopsies from bronchoscopy (61.4%) and pleuroscopy (34.9%). Patients diagnosed with adenocarcinoma were predominantly males (57.8%), diagnosed at age of 51–70 years old (67.4%), and of Chinese (41.9%) and Malay (57.8%) race. In the recent years, we have been sending the adenocarcinoma lung cancers for eGFR testing in order to aid targeted therapy for this lung cancer, however, we have not yield enough results to be analyzed in this study. In summary, bronchoscopy and pleuroscopy remains vital in diagnosis of all lung cancers. Adenocarcinoma remains the commonest subtypes of lung cancer and this highlights the importance of eGFR testing and further molecular studies in managing this lung cancer.

P-J-052

MORTALITY FACTORS: SUPERIOR VEIN CAVA SYNDROME PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL AND DHARMAIS CANCER HOSPITAL

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Background and Aim of Study: Superior vein cava syndrome (SVCS) is a collection of the symptoms due to superior vein cava suppression by the masses in the superior mediastinum. It is a medical emergency because it can cause a death if it isn't be treated immediately. Many factors can cause a death in Superior vein cava syndrome patients. This study aims to obtain the factors that can cause a death in Superior vein cava syndrome patients.

Methods: A cohort retrospective design was conducted in SVCS patients during January 2000 to December 2011 in Cipto Mangunkusumo Hospital and Dharmais Cancer Hospital.

Results: The study population was 151 subjects and most of the patients were male (76.2%). The outcomes of the subjects were control to polyclinic (39,1%), discharge against medical advice (11,9%), death (47%), and loss to follow up (2%). According to the death outcome, (25,2%) subjects had septic, (13,2%) septic shock, (56,3%) pneumonia, (23,8%) tuberculosis, (0,7%) acute respiratory distress syndrome, (35,8%) pleural effusion, (21,1%) respiratory failure, (11,3%) hypercoagulation.

Conclusion: Pneumonia was dominant factor that cause a death in superior vein cava syndrome patients.

P-J-053

P-J-054

INTRATUMOUR CHEMOTHERAPY OF LUNG CARCINOMA WITH NEGATIVE EGFR MUTATION

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Lung carcinoma is a common cause of cancer death globally, resulting in approximately 1–37 million deaths annually in the world. Most cases of lung cancer age between 35–75 years old. Lung carcinoma is divided into two categories, small cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). Therapy of lung carcinoma depends on the tumour stage, histological type and biological feature. Targeting therapies is the alternative therapy of lung carcinoma with EGFR mutation. Recently, intratumour chemotherapy is the alternative choice to reduce the systemic toxicity effect of systemic chemotherapy. This report is about a 75-year-old man with lung adenocarcinoma of stage IVA, with 3–4 of ECOG scale, and having negative EGFR mutation which has been given intratumour chemotherapy by transarterial route using cisplatin 30 mg. The diagnosis is based on anamnesis with chief complaints of chest pain and history of smoking about 52 years. Chest x-ray revealed right lung tumours and thoracic CT-scan with contrast revealed suspected lung tumours in the posterior segment of the right lung inferior lobe with satellite lesions and signs of tumour metastases to 5th costal and the right pleural. Histopathology of lung cancer tissue is adenocarcinoma. Intratumour chemotherapy is an alternative method of chemotherapy drug administration for lung carcinoma with poor performance status and having negative EGFR mutation.

A PRAGMATIC DILEMMA: A CASE OF LUNG ADENOCARCINOMA PRESENTING AS UPPER AND LOWER EXTREMITY VENOUS THROMBOEMBOLISM AND PROTEIN C AND S DEFICIENCY

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Introduction: Cancer continues to be one of the major causes of venous thromboembolism (VTE) worldwide, and as such, a global health burden. In the Philippines, the incidence of cancer with VTE is yet to be established, although malignancy itself is the third leading cause of morbidity and mortality. Among the malignancy types, that of the lung ranks first. And although rare, patients with lung cancer, especially the adenocarcinoma type, are at an increased risk of VTE.

Case Presentation: A 63 year-old obese female was admitted due to a 3-day history of swelling of the left leg associated with upper back pain. She is a non-smoker. Of note, however, is a history of spontaneous abortion and intake of oral contraceptive pills (OCPs). On examination, she had mid-thigh and calf asymmetry with pitting oedema and localized tenderness from the left foot to the middle 3rd of the left thigh. Venous doppler study of the left lower extremity showed totally occlusive acute to subacute deep venous thrombosis of the venous segments. In view of the upper back pain and chest xray finding of miliary-form nodules in both lungs, a computerized tomography (C.T.) of the chest with intravenous contrast confirmed left lower lobe, left paraaortic and right prevascular masses. CT scan guided biopsy of the left lower lobe mass was consistent with lung adenocarcinoma. CT venogram of the neck revealed upper extremity vein thrombosis. Subsequent hypercoagulability study showed Protein C and S deficiency. In view of the these findings, adequate anticoagulation and palliative chemotherapy were initiated.

Discussion: Venous thromboembolism has an incidence of 1–3 in 1000 per year. The patient's age, obesity, intake of OCPs and diagnosis of lung cancer were identified risk factors for VTE. Of these risk factors, cancer is the most important and well-established. J.W. Blom, et al pointed out that patients with adenocarcinoma have a higher risk of developing venous thromboembolism as compared to patients with squamous cell carcinoma. This was attributed to the interaction of circulating carcinoma mucins with leukocyte L-selectin and platelet P-selectin without requiring accompanying thrombin generation, thereby generating microthrombi. The development of another focal thrombus on the upper extremity points out to other possible risk factors other than lung malignancy. Glaring in the patient's profile is the history of spontaneous abortion; thus, a hypercoagulability workup was done and showed Protein C and S deficiency. However, the patient had a prior intake of warfarin and heparin which can give a false positive result. Repeat testing for protein C and S is recommended at least 3 to 6 weeks from the discontinuation of anticoagulant treatment (B. Lipe et al, 2011). But because of the potential risks of VTE and its life-threatening sequelae, repeat testing was forgone.

Conclusion: Venous thromboembolism arising from two or more different areas warrants a thorough investigation in order to rule in and out an inherited or acquired cause. In this case, the dilemma exists between lung malignancy or thrombophilia as a cause of thrombosis. In either case, prudent and judicious treatment of the primary lung malignancy and adequate anticoagulant therapy could prevent future occurrence of thrombosis, and thus abating its potentially life-threatening consequences.

P-J-055

SARCOMATOID CARCINOMA AND MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR IN LUNG: TWO CASE REPORTS, IMPORTANCE OF CLINICOPATHOLOGIC CORRELATION

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Primary pulmonary sarcomas account for less than 1% of all primary lung tumours. These tumours often resemble to their soft tissue components (muscle, cartilage, adipose, fibrous etc).

Case 1: A 63-year old female patient. While the aetiology of pleural effusion was investigated, a 4 cm mass was detected in the left lung. On microscopic examination, the tumour was diffusely contained in spindle cells; large pleomorphic and giant cells were in large necrosis areas. Tumour cells were immunohistochemically stained with pankeratin and vimentin. It was diagnosed as sarcomatoid carcinoma-pleomorphic carcinoma.

Case 2: A 58-year old male patient diagnosed with malignant peripheral nerve sheath tumour (MPNST) on the left thigh a year before. On routine radiological examination, a 2.5 cm dimensional subpleural mass was detected in right lung. Wedge resection was performed. Tumour tissue was comprised of spindle-shaped, large, pleomorphic mesenchymal cells. Vimentin, S100 and NSE were positive, pankeratin was negative in immunohistochemical examination. It was diagnosed as malign mesenchymal tumour metastasis-compatible with MPNST. In the diagnosis step, dialogue between clinician and pathologist is very important. For example, the two cases described above are very important tumours and their histopathological features could be mixed with each other's. Especially in the second case, if the clinician would not report to the pathologist that the patient has a primary mesenchymal tumour, the pathologist could have had much difficulty in diagnosis. At the end, this leads to performing too many different immunohistochemical staining and therefore delay in the diagnosis of patients.

P-J-057

CASE REPORT: INOPERABLE GIANT GANGLIONEUROMA

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Background: Neurogenic tumours account for 12–21% of all mediastinum neoplasms and 75–95% of all posterior mediastinum neoplasms. Ganglioneuroma arises from ganglion cell nerve. Ganglioneuroma occurs commonly in retroperitoneal mediastinum, about 40% on posterior mediastinum. The reported incidence of ganglioneuroma is one per million populations (1/1,000,000). Unfortunately, there is no data of incidence of ganglioneuroma in Indonesia.

Case Presentation: A 27-year-old man was admitted with left, episodic and non-referred chest pain since 2010. Chest x ray and computed tomography (CT) imaging showed posterior mediastinum mass, but he refused further examination and therapy. He was admitted to another hospital due to worsening pain in 2013. CT imaging showed an encapsulated semisolid to solid cystic lesion with varying density in posterior mediastinum, sized 11 x 13.9 cm and attached to the posterior chest wall, pericardium and aorta. Also, calcification and minimum pleural effusion at left chest were found, suggesting a posterior mediastinum tumour. On February 2014, he underwent thoracotomy procedure, but the mass was inoperable due to its attachment to hilus, thoracic aorta and posterior chest wall. Debulking and histopathology excision were performed. Microscopic finding showed benign mass that was suggestive of ganglioneuroma. Three months after thoracotomy, the pain decreased and there was no progressivity on chest x ray.

Discussion: The giant ganglioneuroma in our case was unusual in size with an attachment to hilus, aorta and chest wall. There was no consensus on clinical diagnostic criteria of giant mediastinum neurogenic tumour. Generally, the neurogenic tumour occupying more than half side of the chest cavity can be called a giant mediastinum neurogenic tumour. Surgical treatment for ganglioneuroma gives good prognosis, but it cannot be done in this patient. This was the first inoperable giant ganglioneuroma reported in Dr. Moewardi Hospital.

Conclusion: Ganglioneuroma is a very rare, slow growing and asymptomatic tumour. Ganglioneuroma commonly occur in children and young adult. Ganglioneuroma is classified as benign neoplasm but it can grow aggressively and invades mediastinum and spinal structure. Definitive diagnosis is made by histopathology finding. This case was unusual because of its giant size and the mass was inoperable.

P-J-056

UNUSUAL REFILLED CAVITY OF LUNG SQUAMOUS CELL CARCINOMA – A CASE REPORT AND DIFFERENTIAL DIAGNOSIS

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Most lung cancerous cavity present thick wall, and air-fluid level is less common. Generally, the cavity become bigger and bigger as the tumour grow. We present an interesting report about radiological findings in a 58-year-old male heavy smoker with a chief complaint of fever, anterior chest pain and haemoptysis, that appeared as a cavity with thin wall, sharp outline and air-fluid level directed a benign cavity lesion. What is unique about this case is that the cavity was entirely fluid refilled after antibiotics treatment, however, the mass kept the previous contour. Then the patient underwent a CT-guided percutaneous needle lung biopsy. The pathological diagnosis of the lung biopsy revealed moderately differentiated squamous cell carcinoma. The rarity of this case and its possible implications may help us to further understand the mechanism of cancerous cavity of the lung.

P-J-058

P-J-060

CASE REPORT: INTRAPULMONARY CYSTIC LYMPHANGIOMA, AGENESIS DIAFRAGMA, UNILATERAL DOLICHOSTENOMELIA, AND UNILATERAL ARACHNODACTYLY

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Background: Lymphangioma is an abnormal proliferation of lymphatic vessels. The abnormal vessels may be capillary, cavernous or cystic. Intrapulmonary lymphangioma is extremely rare, with an encounter of approximately a dozen cases only. Lymphangioma may be asymptomatic to respiratory failure. With lymphangioma it is prudent to investigate for another congenital anomalies. Chest x-ray and CT scan have proven useful in diagnosis. Lymphangioma is treated with surgical resection, whereby an incomplete surgical resection can result in recurrent lymphangioma.

Case Presentation: An 18-year-old man complained of shortness of breath for four years. Physical examination found unilateral dolichostenomelia (elongated limbs), unilateral arachnodactyly (long fingers and toes), his heart having shifted to the right and breathing sound of the left lung was decreased. A chest radiograph suspected dextrocardia and left giant bulla. CT scan of the chest revealed multiple bulla in upper lobe of left lung and scoliosis thoracalis. Echocardiography found that the heart has shifted to the right, and no dextrocardia. Bronchoscopic found intact plica vocalis and partial stenosis compression in lower lobe of left lung. Thoracotomy in 2013 found multiple bulla in upper lobe and replacement of lower lobe by multiple cystic. The cystic mass was removed by lobectomy of the upper lobe of the left lung, and there was incidental finding of agenesis diafragma. Histopathological examination of the upper lobe confirmed diagnosis of intrapulmonary cystic lymphangioma. Chest X-ray 10 days post thoracotomy found that the heart has shifted to the right, lungs were normal. Chest X-ray one year post thoracotomy found that the heart has shifted to the right, there was a giant bulla in the upper lobe of the left lung, with suspected recurrent lymphangioma.

Conclusion: Intrapulmonary cystic lymphangioma should be included in the differential diagnosis of multicystic lung lesion. Pathologic examination is very important to confirm the diagnosis. Incomplete resection was performed on this case because partial of lower lobe was normal. Chest X-ray one year post thoracotomy found suspected recurrent lymphangioma. Evaluation is needed in 3 months and 6 months post thoracotomy.

A RARE CASE WITH AN UNUSUAL PRESENTATION: ENDOBRONCHIAL METASTASIS OF PELVIC CHONDROSARCOMA

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Introduction: Chondrosarcomas are the second most frequent primary malignant bone tumours, after osteosarcomas. They are also the most common primary malignant chest wall tumours. 5–15% of chondrosarcomas are located in the thoracic wall. The most frequent site of metastasis are the lungs; other sites include the bones, brain, regional lymph nodes, and liver. Although, most pulmonary metastases present with multiple peripheral, round nodules of varying size on roentgenograms, certain metastatic sarcomas such as osteosarcomas may have unusual presentation i.e., lymphangitic carcinomatosis, endobronchial metastasis, or pneumothorax. Surgical resection remains the primary mode of therapy.

Case Presentation: A 40-year-old male patient with cough was admitted to our hospital. He had undergone hemipelvectomy for pelvic chondrosarcoma four years ago. Chest x-ray and thorax CT showed a 44 x 60 mm diameter mass in the right upper lung, and consolidation of left paracardiac location. Fiberoptic bronchoscopy showed an endobronchial metastasis in lingula which was confirmed as metastatic chondrosarcoma by histopathology. He underwent left upper lobectomy and right upper lobectomy after a month, is alive and followed-up for 8 months.

Discussion: Endobronchial metastasis is defined as documented extrathoracic malignancies metastatic to the endobronchus within a bronchoscopically visible range. Although the clinical and radiological findings of endobronchial metastasis are similar to primary lung cancer, treatment and prognosis may be different.

Conclusions: As chondrosarcoma rarely presents with endobronchial metastases, we discuss the clinical, radiological and histopathologic features of this case in the light of literature data.

P-J-059

P-J-061

PULMONARY HEMANGIOPERICYTOMA GRADE 1–2 (LOW GRADE SARCOMA)

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We report a male, 31-year-old, who was diagnosed with lung malignant hemangiopericytoma. He visited the outpatient clinic of Pulmonologi and Respiratory Medicine General Hospital Persahabatan Jakarta for follow-up. His complaints were cough with white colored sputum, symptoms that he had been experiencing for one week, along with fever. He did not complain of other respiratory symptoms. There were no abnormalities on physical examination. Computed tomography scan of thorax showed multiple nodules at left lung, subpleura and enlarged lymph nodes station 2R and 4R. Two years ago he underwent mediastinal tumour removal surgery. Before surgery, computed tomography scan showed a mass from anterior mediastinum attached to the chest wall. He underwent bronchoscopy procedure with the result of no abnormalities along the airway. Cytology examination from bronchial wash showed no malignancy cells. Mediastinum mass histopathology showed low-grade sarcoma with a tendency towards malignant hemangiopericytoma grade 1–2. After the surgery, the patient never came back for follow-ups. Hemangiopericytoma is a mesenchymal neoplasm which is derived from the pericyt. Pericyt is a type of cell which surrounds capillary blood vessels. The tumour location in the lung is very rare. Incidence of this tumour is around 3% in all of soft tissue sarcomas.

RIGHT PARATRACHEAL LYMPH NODE METASTASIS OF HURTLE CELL CARCINOMA: TRANSBRONCHIAL NEEDLE ASPIRATION CYTOLOGY

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Among the well-differentiated thyroid carcinomas, Hurtle cell carcinoma is a rare subtype. According to other well-differentiated thyroid carcinomas, it has a high tendency to be multifocal, to metastasize via lymph nodes and to distant organs. Therefore, it is considered to have more aggressive behaviour. By thyroid fine needle aspiration cytology, the diagnosis of hurtle cell neoplasia may be given preoperatively. However, histopathological examination is necessary to sign out the case as hurtle cell carcinoma according to the invasion of the vessel and/or capsule. In cases with a known Hurtle cell carcinoma, the diagnostic value of aspiration from the metastatic area is high. Herein, we presented a 74-year-old male patient who underwent subtotal thyroidectomy and was diagnosed with Hurtle cell carcinoma a month ago. The positron emission tomography revealed hypermetabolic lymph nodes in the mediastinum and hypermetabolic lesions in both lungs. Transbronchial needle aspiration cytology was performed from the right upper paratracheal lymph node with 36.6 SUVmax value and 4 x 3.8 cm in size. Microscopically, hypercellular monomorphic hurtle cell population which set monolayered sheets and overlapping groups was observed. By these findings, the patient was diagnosed as 'Hurtle cell carcinoma metastases'. In such cases, primary lung tumours are included into the differential diagnosis due to the similar cytological features. Therefore, the diagnosis is challenging. In cytology smears, distinguishing the follicle and gland formations from each other, evaluation of cellular details and specific clinical-radiological findings, are crucial during the diagnosis.

P-J-062

MULTIPLE ENDOTRACHEAL AND ENDOBRONCHIAL METASTASIS AFTER LOBECTOMY FOR PRIMARY LUNG CANCER: A CASE REPORT AND REVIEW OF THE LITERATURE

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Endotracheal and/or endobronchial metastasis from primary lung cancer is very rare. Here, we report a case of multiple endotracheal and endobronchial metastasis from squamous cell lung cancer after complete resection. A 70-year-old man underwent lobectomy of the right lower lobe for squamous cell carcinoma of the lung. Postoperative pathological staging was T1bN0M0. He was regularly followed up with chest radiography and contrast-enhanced chest CT to evaluate for recurrence. Postoperatively, chest CT and PET-CT scan were performed after 22 months again due to chronic cough. Chest CT scan revealed a small nodule in upper trachea and eccentric wall thickening in lower trachea. PET-CT scan showed a hypermetabolic nodule in upper trachea. Bronchoscopy revealed multiple polypoid lesions located in the trachea, carina and left main bronchus. Pathologic results of the biopsy revealed moderately differentiated squamous cell carcinoma, identical to the pathologic features of previously resected lung cancer. The patient underwent external beam radiotherapy. To the best of the authors' knowledge, including this case, there have been only 10 cases with metastases from pathologically proven primary lung cancer after complete surgical resection, in English literature. The pathologic types of the primary lung cancer were squamous cell carcinoma (n = 8) and adenocarcinoma (n = 2). All patients underwent lobectomy (n = 6) or bilobectomy (n = 1) or pneumonectomy (n = 3) for primary lung cancer. The median recurrence interval was 14.5 months (interquartile range, 9.5–29.8 months) after their initial operation. In conclusion, during the postoperative follow up of patients with completely resected primary lung cancer, clinicians should consider endotracheal or endobronchial metastasis when endotracheal nodules or eccentric thickening is detected at chest CT.

P-J-063

CASE REPORT AND LITERATURE REVIEW OF TRACHEOBRONCHOPATHIA OSTEOCHONDROPLASTICA WITH LUNG ADENOCARCINOMA

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Tracheobronchopathia osteochondroplastica (TO) refers to the trachea/bronchial mucosa with multiple bone or cartilage tissue nodular hyperplasia and benign lesions protruding into the lumen. Tracheobronchopathia osteochondroplastica usually manifests in adults, and affects both genders. The clinical presentation of tracheobronchopathia osteochondroplastica was nonspecific. Chest X-ray was insensitive tracheobronchopathia osteochondroplastica, but the CT scan was sensitive and specific, which played an important role in the diagnosis of tracheobronchopathia osteochondroplastica. The bronchoscopy showed that multiple whitish, hard sessile nodules projecting in tracheobronchopathia osteochondroplastica the tracheal lumen from anterior and lateral walls of the airway, with sparing of the posterior wall. Bronchial biopsies disclose the abnormal presence of cartilage and bone tissue in the bronchial submucosa. Tracheobronchopathia osteochondroplastica date there was no specific treatment for the disease and the treatment of tracheobronchopathia osteochondroplastica was usually Symptomatic treatment. Tracheobronchopathia osteochondroplastica often combined with lung cancer, especially adenocarcinoma, this article describes one case of tracheobronchopathia osteochondroplastica in patients with pulmonary adenocarcinoma, aims to raise awareness of tracheobronchopathia osteochondroplastica understanding.

P-J-064

FALSE POSITIVITY OF PET DUE TO MEDIASTINAL DISEASE IN MEDIASTINAL STAGING: CASE REPORT

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Introduction: Mediastinal staging is the most important part when deciding treatment plan and determining the prognosis of a patient with NSCLC. Mediastinal staging can be done non-invasively (CT and PET) or invasively (mediastinoscopy, EBUS and EUS). The non-invasive mediastinal staging can be false.

Case Report: A 55-year-old man was admitted with cough. A 36 mm diameter and spiculated lesion was discovered with chest computerized tomography (CT) in the right upper lobe. The bronchoscopic biopsy was non-diagnostic and he was diagnosed as epidermoid carcinoma with TIAB. The staging PET-CT was performed and the lesion (SUVmax:11.7) and left paratracheal lymph node (SUVmax:22.0) had pathologic FDG accumulation. He staged as T2N3M0 and was treated with definitive chemoradiotherapy (60 Gy Radiotherapy and Cisplatin and Etoposid). He underwent PET-CT again in order to determined the response to the treatment and left paratracheal lymph node FDG accumulation was the same with complete response of the lesion. He was referred to our clinic with this situation in order to assess for any surgical treatment. We decided on a surgical treatment plan with right upper lobectomy and excision of the left paratracheal lymph node. Because the patient was young, with no distant or ipsilateral lymph node metastasis, and complete response of the primer lesion. The lymph node was not accessible with EUS or EBUS before any surgical intervention. He underwent lymph node excision and right upper bilobectomy with staged operation. The lesion was diagnosed as parathyroid adenoma. He was discharged on 5th postoperative day without any problem.

Conclusion: Mediastinal staging of NSCLC with non-invasive methods can be misleading when a mediastinal disease accompany. Histopathologic confirmation should be done before any treatment plan.

P-J-065

A CASE SERIES OF 4 PATIENTS WITH CONCURRENT PULMONARY TUBERCULOSIS AND LUNG CANCER

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The association of pulmonary Tuberculosis (TB) and lung cancer (LC) has been noted for decades, although the exact association remains poorly understood. One theory suggests chronic scarring from TB can lead to the development of cancer, others suggest immunosuppression from cancer increases TB infection risk and some believe there is no relationship between these two. This abstract describes the case series of four patients in our respiratory unit of the Universiti Teknologi MARA, Malaysia. LC is the leading cause of cancer deaths in Malaysia and TB is a prevalent condition in Malaysia and other developing countries. In our series of 4 patients, there were no similarities from several points including gender (2 males and 1 female), age (45, 62, 82 and 83) and risk factors such family history of cancers and smoking. In addition to these patients all presenting with constitutional symptoms of cough, fever and weight loss, the imaging for all the patients showed advanced disease upon presentation with invasion to local structures including lymph nodes and mass effects like superior vena cava obstruction. Sputum stains for all 4 patients were positive for Acid Fast Bacilli (AFB), but only 2 had positive sputum cultures. All patients were commenced on local TB treatment regimes and had biopsies taken via bronchoscopies. Histology showed adenocarcinoma in 3 patients and small cell lung carcinoma in 1. The relationships between the cancer types and smoking were not seen. Radiotherapy was given for the patient with small cell, radiotherapy and chemotherapy for 1 adenocarcinoma. 1 patient refused treatment for the cancer, and another was referred for treatment but left Malaysia to return to her hometown in Indonesia and was lost to follow up. The 3 patients who continued follow up died within 3 months of diagnosis. In summary, we found that TB and LC occurred concurrently in our 4 patients where adenocarcinoma was the most common histological type seen in our case series, similar to other studies. The presentation was quite late with prognosis among the 3 patients we followed up was extremely poor with death from diagnosis within 3 months. Denise RS et. al suggested that due to similar presentations between the two diseases, there can be a delay in diagnosis hence, patients can present at a more advanced stage.

P-J-066

P-J-068

PRIMARY PLEURAL LYMPHOMA WITH RECURRENT PLEURAL EFFUSION IN A PATIENT WITH NON-HODGKIN'S LYMPHOMA

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This is a case of primary malignant lymphoma arising in the pleura. A 78 year old male presented with a 3 month history of gradually increasing shortness of breath presenting with recurrent bilateral pleural effusion. Right thoracostomy with pleural biopsy was done. A chest CT scan demonstrated nodules in the anterior segment of the right and left upper lobes. Immunohistochemical staining of the pleura with Leukocyte Common Antigen LCA (+) and B lymphocyte Antigen CD20(+) revealed a diagnosis of Non-Hodgkin's lymphoma, diffuse large B cell type. Primary pleural Non-Hodgkin's Lymphoma in an immunocompetent patient is rare. Malignant lymphoma arising in the pleura comprises 2.4% of primary chest wall tumours. Pleural tumours do not have specific imaging features, and diagnosis typically requires biopsy and immunophenotypic marker studies.

PROPHYLACTIC CRANIAL IRRADIATION MAY IMPOSE A DETRIMENTAL EFFECT ON OVERALL SURVIVAL OF PATIENTS WITH NON-SMALL CELL LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE LITERATURE

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Purpose: To determine the role of brain metastases (BM) and overall survival (OS) in patients with non-small cell lung cancer (NSCLC) by performing a meta-analysis of the RCTs (randomized controlled clinical trials) and non-RCTs (non-randomized controlled clinical trials) published in the literature.

Methods: A meta-analysis was performed using trials identified through PubMed, EMBASE and Cochrane databases. Two investigators independently assessed the quality of the trials and extracted data. The outcomes included BM, OS, median survival (MS), response rate (RR), Hazard ratios (HRs) and odds ratios (ORs), and their 95% confidence intervals (CIs) were pooled using ReMan software.

Results: Twelve trials (6 RCTs and 6 non-RCTs) involving 1,718 NSCLC patients met the inclusion criteria. They were grouped on the basis of study design for separate Meta-analyses. The results showed that prophylactic cranial irradiation (PCI) reduced the risk of BM as compared with non-PCI in NSCLC patients (OR = 0.30, 95% [CI]: 0.21–0.43, $p < 0.00001$). However, HRs for OS favoured non-PCI (HR = 1.19, 95% [CI]: 1.06–1.33 $p = 0.004$), without evidence of heterogeneity between the studies.

Conclusion: Our results suggest that although PCI decreased the risk of BM, it may impose a detrimental effect on OS of NSCLC patients. PCI is not recommended in this situation. These findings still need to be verified in larger confirmatory studies in future.

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P-J-067

A CASE REPORT OF LUNG ADENOCARCINOMA WITH PULMONARY ASCARIASIS

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Background: Lung cancer is the leading cause of cancer morbidity and mortality in the world. The main causes of pulmonary ascariasis are the migrated larvae, ectopic parasitism of mature lumbricoides and ascaris eggs deposited in the lungs. And pulmonary ascariasis accounts for the second morbidity of ectopic ascariasis. To our knowledge, lung cancer associated with pulmonary ascariasis has not been reported, so we herein firstly report a case of lung adenocarcinoma with pulmonary ascariasis.

Case: A 56-year-old man who engaged in field work was admitted in our hospital because of six months of intermittent coughing and chest pain for three months. Pulmonary CT revealed that it has a 89*72 mm oval lesions under the pleura of the upper left lung. Bronchoscopy in the upper left lobe bronchus sucked out a soft worm which was identified as an ascarid. Ultrasound-guided lung biopsy pathology result showed necrotic lung tissue. Lung CT-guided biopsy result showed poorly differentiated adenocarcinoma. The final diagnosis: (1) left lung adenocarcinoma (T3N3M1, stage IV); (2) pulmonary ascariasis. The patient was treated with albendazole and a course of chemotherapy of pemetrexed (880 mg) plus cisplatin(50 mg). Follow-up learned that the patient died in two months after discharged from our hospital.

Conclusion: Ascariasis in the lungs can cause lung abscess, pulmonary embolism, granuloma and false junction tuberculosis. So it needs to identify lung ascariasis with lung cancer on imaging. Ascarid long stay in the lungs can damage lung tissue and lead to local chronic inflammation. In recent years, as many studies have found that chronic inflammation of the lungs can cause lung cancer, so we conjectured that it might be the local chronic inflammation that caused by pulmonary ascariasis led to the lung adenocarcinoma on this patient.

POSTER PRESENTATION – OTHERS

P-K-001

GENETIC EPIDEMIOLOGY OF HEREDITARY HAEMORRHAGIC TELANGIECTASIA ASSOCIATED WITH PULMONARY ARTERIOVENOUS MALFORMATION

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Background: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant disorder characterized by aberrant vascular development such as pulmonary arteriovenous malformation (PAVM). We report here the genetic epidemiologic study and the national survey in PAVM associated with HHT in Japan.

Method And Subjects: A total of 137 pedigree members were traced of which 81 were alive and 42 were affected by HHT in a county, A (population 1.1 million) located in northern Japan. National survey for PAVMs associated with HHT was carried out among the 4,409 pulmonary specialists those who belong to Japanese Respiratory Society in 2011.

Results: Linkage analysis in two large families complicated with PAVM revealed a linkage to the HHT1 locus (encoding endoglin; ENG). Three novel mutations were found in four families, all of which led to a frame shift: a G to C transversion at the splicing donor site of intron 3 (Inv3+1 G>C) in one family, one base pair insertion (A) at nucleotide 828 (exon 7) of the endoglin cDNA in two large families (a828-29 ins A), and a four base pair deletion (AAAG) beginning with nucleotide 1120 (exon 8) of the endoglin cDNA (c.1120-1123 delAAAG) in one family. The insertion of A in exon11 (c.1470-1471 insA) mutation was found in one family. PAVMs were associated in 18 out of 42 HHT patients (42.8%) in this county. In the national epidemiologic survey in Japan, HHT was proven in 50 out of 202 PAVMs (24.7%). The percentage of female patients of PAVMs not associated with HHT was 82%, whereas that of PAVMs associated with HHT was 56%.

Summary and Conclusion: The population prevalence of HHT in the county was estimated to be 1:8,000–1:5,000, roughly comparable with those reported in European and U.S. populations, which is contradictory to the traditional view that HHT is rare among Asians. There was a gender difference in PAVMs associated with HHT and non-HHT. We recommend that families with HHT be screened for gene mutations in order that high-risk individuals complicated with PAVMs receive early diagnosis and treatment initiation that will substantially alter their clinical course and prognosis.

P-K-003

REFERENCE VALUES FOR PULMONARY FUNCTION FOR HEALTHY, NON-SMOKING ADULT FILIPINOS

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Height, age, and gender are thought to affect pulmonary function. For this reason, pulmonary function may differ among ethnic groups. The application of reference values based on another ethnic group might lead to over or under diagnosis. Therefore, establishing reference values based on Filipino data is important. Several studies in different ethnic groups have been previously conducted which revealed results dissimilar to Caucasian data. A local study was done as well but it was limited to a small sample size and constrained to a certain group of people only. This study is distinct from the previous local study in its aim to include a larger sample size and to involve a more diverse population which is more representative of the Filipino race. This is a retrospective descriptive study with a total of 2,953 participants aged 19–65 years, healthy, non-smoking Filipinos who underwent complete pulmonary function test with post bronchodilator studies in St. Luke's Medical Center in Quezon City from January 1, 2011 to December 31, 2011. Out of the 2,953, 902 patients were included in the study. Data were analyzed using ANOVA (Analysis of Variance), Pearson correlation, and multiple linear regression. Utilization of the prediction equations from the present study yielded significantly lower FEF 25-75 values compared to values from the equation of Morris. This means that the use of Caucasian reference values can lead to under diagnosis of obstructive diseases in terms of FEF 25-75. This disparity may be attributed to the height of Filipinos. Therefore, there is a significant difference in the FEF 25-75 (small airways) of the Filipino compared to Caucasians.

P-K-004

EFFECTS OF PEEP-LIKE CYCLIC STRETCHING ON THE IL-6 GENE AND PROTEIN PRODUCTION IN NORMAL HUMAN PULMONARY ARTERY ENDOTHELIAL CELLS IN VITRO

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Background and Aim: Excessive cyclic stretching is one of the main causes of ventilator-induced lung injury. To reduce lung injury, positive end-expiratory pressure (PEEP) has been used. The use of PEEP is known to prevent repeated alveolar collapse during mechanical ventilation and to reduce cytokine (IL-6) production and increase survival rates in patients treated with mechanical ventilation. However, the direct effects of mechanical stretch on the cells have not yet been determined. The aim of the present study was to examine whether the excessive mechanical stretching combined with PEEP-like stretching can suppress IL-6 gene and protein expressions in human pulmonary artery endothelial cells (HPAECs) in vitro.

Methods: The cells were stretched by a Flexcell FX-4000TTM Tension System. The cyclic stretches used were 2 elongation patterns (0% to 20% and 3% to 20% elongation) with a square waveform of 15 cycles/min, and a 1:2 ratio of stretch to relaxation time. Elongation of 0% to 20% simulates excessive stretching during mechanical ventilation and elongation of 3% to 20% simulates excessive stretching with PEEP-like stretching. The cells were stretched for various durations (0, 1, 3, 6 and 12 hours). During the experiments culture medium was sampled at 0, 3, 6 and 12 hours after the start of stretch. The IL-6 concentration of the samples was determined by an ELISA. cDNA was also synthesized from total RNA extracted from the cells before and after stretching (0, 5, 10, 30 and 60 min after the start of stretching). The IL-6 gene expression of the samples was determined by a real-time RT-PCR assay.

Results: Excessive stretching (0% to 20%) significantly increased the IL-6 production of the cells stretched for more than 3 hours compared to that of the unstretched cells (n = 5, P < 0.05), but excessive stretching with PEEP-like stretching (3% to 20%) showed no significant changes in the IL-6 protein production of the cells at any sampling points. The gene expression levels of the IL-6 peaked at an early stage (within 30 min). The peak value of the gene expression induced by excessive stretching with PEEP-like stretching was significantly lower than that induced by excessive stretching alone.

Conclusions: The levels of expressions of the IL-6 gene and protein induced by excessive stretching with PEEP-like stretching were lower than that by excessive stretching alone. PEEP-like stretching is considered to suppress the production of IL-6 from the endothelial cells during excessive mechanical ventilation.

P-K-005

P-K-006

DEVELOPING COMPETENCY IN A RESPIRATORY SYSTEM BASED PRACTICE OF FINAL YEAR MBBS STUDENTS POSTED IN PULMONARY MEDICINE THROUGH BEDSIDE TEACHING MODULES

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Introduction: Globally, respiratory diseases are a major cause of mortality and morbidity but the primary care physicians are not adequately trained to handle these cases. The clinical exposure of undergraduate medical students in Indian setting is limited to four weeks in respiratory medicine. This short duration of posting can be best utilized by developing need-based modules for bedside teaching to increase the knowledge and skills in the diagnosis and management of common pulmonary diseases.

Objectives: To improve knowledge and skills of final year MBBS students posted in Respiratory Medicine in diagnosis and management of common pulmonary diseases, by creating and implementing a bedside teaching module.

Methods: 48 undergraduate 8th semester medical students were posted in the department of respiratory medicine. Each batch consisted of 24 students which were divided into two groups, 12 students each. Two trained faculty members taught the group in rotation.

Module Preparation: The bedside teaching module was prepared by Delphi technique and the curriculum development was based on Kern's six step approach. Content covered was history taking, general examination, respiratory system examination, tuberculosis, COPD, asthma, lung cancer, chest X-rays and spirometry. A guiding document (module) and a standardized checklist for faculty was prepared. After informed consent, the students were administered pre-test questionnaire (validated by experts) to assess their knowledge, while skills were assessed by OSCE. Upon completion of these, the students evaluated the contents and quality of teaching.

Results: The knowledge and skills scores improved significantly after the introduction of teaching module, with a mean pre-test knowledge score of 12.46 (8.09) and post-test knowledge score of 43.17(10.7). The mean difference was -30.7 (7.6), $p = 0.000$ with a correlation of 0.71. Also the pre and post skills mean scores were 7.00 (4.76) and 24.79 (3.31) and the difference was a mean of -17.7 (5.3) $p < 0.000$ with correlation of 0.31, thus showing that teaching module improved the knowledge and skills significantly. Most students stated that the module enhanced their clinical skills, increased their interest in subject, helped understand difficult material and promoted enquiry and thinking.

Conclusion: A structured bedside teaching module in respiratory medicine significantly improved the knowledge and skills of final year undergraduate students. The students evaluated the contents and methods of teaching favourably.

References:

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BRIEF VERSUS INTENSIVE SMOKING CESSATION COUNSELLING: SHOULD PATIENTS BE GIVEN A CHOICE?

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Introduction: Systematic reviews call for intensive counselling with at least four weeks of follow-up support to optimize quit rates. However, some patients desire brief counselling and less active follow-up, and little information exists on whether allowing patient preference would affect the success of a smoking cessation programme. We thus investigated if a standard programme would be superior to a preference-driven programme.

Methods: Prospective before-and-after observational study of hospitalized smokers admitted from January 2012 to June 2013. In Phase I (January-December 2012), patients could choose between two smoking cessation options: brief counselling (15-minutes) without telephone support or intensive counselling (45-minutes) with four weeks of telephone support (i.e. preference-driven programme). In Phase II (January-June 2013), patients could only receive intensive counselling with telephone support (standard programme). We measured sustained abstinence rates at six months for patients, allowing for a maximum of three defaults (≤ 3 cigarettes smoked at each default), adjusting for age, gender, marital status and Fagerstrom score.

Results: 745 smokers (Phase I 384; Phase II 361) were identified, with 170 (Phase I 88/22.9%; Phase II 82/22.7%) declining smoking cessation counselling. Of the remaining 575 smokers counselled, 149 (Phase I 99/33.5%; Phase II 50/17.9%; $P < 0.001$) achieved sustained abstinence at six months. Adjusting for age, gender, marital status and Fagerstrom score, Phase II compared to Phase I was associated with decreased six-month sustained abstinence (OR 0.43, 95% CI 0.29–0.64, $P < 0.001$).

Conclusions: A standard smoking cessation programme was inferior to a patient preference-driven programme. It may be both patient-centric and resource-saving to allow patients to choose the intensity of counselling and telephone support.

P-K-007

RELATION BETWEEN SLEEP APNEOA SYNDROME AND DEPRESSION – EFFECTIVENESS OF A SELF-RELATING DEPRESSION SCALE QUESTIONNAIRE

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Objective: Sleep apnea syndrome (SAS) patients are known to have several complications such as hypertension, diabetes mellitus, gastroesophageal reflux disease (GERD) and so on. Depression is also one of complications of SAS patients. When we diagnose those complications, sometimes there exists some difficulty or miss diagnosis, especially when the doctor is not a specialist. For example, usually SAS patients have low activity because of their sleepiness. So SAS patients are possibly misdiagnosed as depression. So if we physicians can diagnose depression by a questionnaire easily, it is very useful to treat SAS patients. I examined the usefulness of a self-relating depression scale (SDS) questionnaire to diagnose depression.

Method: We did SDS questionnaire surveys and polysomnogram (PSG) examinations of outpatients who complained sleepiness. The scores of a SDS questionnaire were evaluated as follows; 23–47 were normal, 39–59 were neurosis, and 53–67 were depression. We also did surveys of prescriptions of outpatients. We regarded patients who were prescribed anti depression drugs by psychiatrists as depression and examined the relation between SDS scores and depression patients.

Result: Patients who were prescribed anti depression drugs by psychiatrists showed high scores by a SDS questionnaire, which showed the reliability of a SDS questionnaire. Almost 20% of SAS patients were diagnosed as neurosis or depression by a SDS questionnaire, which was compatible to the former report by Dr. Aoki et al (vol.111, page 994, 2009, *Psychiatria et Neurologia Japonica*). Dr. Aoki reported that 10–20% of SAS patients had a complication of depression. In our study, only 3% of SAS patients were prescribed anti depression drugs, which showed a complication of depression might be underestimated by physicians, namely by non psychiatrists.

Discussion: Our study showed the reliability of a SDS questionnaire and a complication of depression of SAS patients might be underestimated by physicians. So when we physicians are going to diagnose SAS, it is useful to use a SDS questionnaire. To do so, we physicians can consult psychiatrists more adequately and can perform treatments of SAS patients more effectively.

P-K-008

THE EFFECT OF MEDICAL EDUCATION PROJECT TO IMPROVE THE SKILLS IN READING CHEST X-RAY

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Introduction: Although Chest x-ray (CXR) is the most commonly ordered radiological study in the world, the art of reading CXR is dwindling rapidly along with the prevalence of CT scan. In Japan, Interns and residents who order a CXR must evaluate by themselves in most settings, but they seem not to be familiar with the interpretation of CXR. In this project, we gave lectures to fifth/sixth medical students and young doctors (about 5 participants/session), and evaluated the effect on knowledge, ability, and attitude in reading CXR. The goal of this project is let them (1) understand normal anatomy, technical terms and major signs on the CXRs, (2) master the routine way of reading, (3) be able to point out abnormal findings correctly, (4) be able to interpret chest x-rays with confidence.

Methods: On day 1, we gave lecture (60 min) after pre-survey (8 questions in 5 min) and pre-test (20 questions in 15 min). A few days later, post-test (same as the pre-test), review of the test (30 min), and post-survey (pre-survey plus additional questions to ask their impression about the lecture) were performed. Based on the comparison between the pre- and post-survey/test, we evaluated the effect of lecture on their knowledge, skill, and emotional aspect in reading CXR. The lecture was also evaluated by the participants with post-survey.

Results: So far, 38 medical students, interns, and residents participated in this project. Their accuracy rate of the test rose significantly from 54.7% to 75.3% ($p < 0.001$). The survey revealed that they became to be familiar with reading CXR and to be able to read CXR in an orderly manner with confidence. Most of them thought the number of questions and the length of the lecture were adequate, but 37% of the participants thought the lecture was difficult.

Discussion: Their score was increased by the lecture, but it should be checked whether they can apply their knowledge to the real clinical settings. Also, the long-term effect should be assessed. The skill to read CXR might be different among learners, so more adequate lecture and test for each level might be better for them. This project is still ongoing, so I will present the updated results with more participants at the congress.

P-K-009

EFFICACY OF AZITHROMYCIN IN THE TREATMENT OF BRONCHIECTASIS

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Background: We evaluated the efficacy of 12-week treatment with oral azithromycin in adult patients with pulmonary bronchiectasis.

Methods: A total of 78 patients with bronchiectasis confirmed by High Resolution Computed Tomography (HRCT) of the thorax were included in this study. Subjects received oral azithromycin or placebo in a randomized manner for 12 weeks, followed by placebo for another 12 weeks to evaluate the 'carry-over' effect. 24-hour sputum volume, St. George's Respiratory Questionnaire (SGRQ) score and spirometry were recorded at baseline, 12 weeks and 24 weeks, respectively. Endpoint measurements were compared from baseline to the end of each study phase.

Results: 68 subjects were included in the analysis. Mean 24-hour sputum volume significantly decreased ($p < 0.01$) during the active treatment phase, and remained decreased during the control phase ($p < 0.01$). The mean SGRQ total score with azithromycin decreased (i.e. improved health status) from baseline by more than the four-point minimum clinically important difference at the end of 12 and 24 weeks. Lung functions remained stable during oral azithromycin therapy and throughout the subsequent control phase.

Conclusion: 12-week administration of azithromycin in bronchiectasis produces significant reductions in mean sputum volume, health status and stabilization of lung function values. The beneficial effects of oral azithromycin in reducing sputum volume and improving quality of life was sustained for another 12 weeks after cessation of azithromycin.

P-K-010

P-K-012

SMOKING PATTERNS AND NICOTINE DEPENDENCE OF NORTH KOREAN MALE DEFECTORS

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Objective: Cigarette smoking in South Korea population has decreased substantially. In 1995, the smoking rate of South Korean men was 73.0%, while the number was decreased to 44.9% in 2012. However, smoking rate and patterns of North Korea population are mostly unknown. From WHO report (2009), smoking rate of North Korean men was 58%. Now in South Korea, more than 20,000 North Korean defectors settle down and we can estimate the current situation of North Korea from them. This study evaluated the smoking pattern and nicotine dependence in North Korean male defectors.

Methods: All North Korean defectors spend their first three months in South Korea in a facility learning to cope with their new home. We retrospectively analyzed the questionnaire which was done from North Korean male defectors in this facility during August 2012 to February 2014. The questionnaire consist of brief personal information, smoking history, Fagerstrom test for nicotine dependence and Kano test for social nicotine dependence.

Results: From 272 men, there were 84.2% current smokers, 12.5% ex-smokers and 3.3% ever-smokers. Mean age was 35.8±11.3 (19–65) and start age of smoking was 18.2±4.8 (7–46). Smoking amount was 0.68±0.37 pack per day with 17.0±10.7 years of smoking. Without 12 people who didn't answer, 78.08% had a family member smoking. Within 229 current smokers, 66.1% have ever tried to stop smoking and 65.1% answered to be interested in stop smoking. Fagerstrom test and Kano test for current smokers showed 3.35±2.26 (Cronbach's α : 0.62) and 13.75±4.85 (Cronbach's α : 0.68), respectively. In Kano test analysis, question 9 ("Doctors exaggerate the ill effects of smoking") and question 10 ("People can smoke at places where ashtrays are available") showed higher points than other questions.

Conclusions: Smoking rate of North Korean men was higher than our expectation and previous data. Although the interest of smoking cessation was high, the result of Kano test suggests that one-way teaching of smoking cessation by doctors can cause resistance. Further investigation needed to find diverse efficient methods of smoking cessation for North Korean smokers.

CHEST COMPUTED TOMOGRAPHIC FINDINGS IN RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

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Background: Rapidly progressive glomerulonephritis (RPGN) is a clinical syndrome manifesting with features of glomerular disease in the urine and by progressive loss of renal function over a comparatively short period of time. In patients with RPGN, coexisting pulmonary lesions are considered to be an adverse prognostic factor. However, there has been no report that examined the characteristics of coexisting pulmonary lesions and chest CT findings in patients with RPGN in detail.

Objectives: The aim of this study is to investigate the characteristics of chest CT findings in patients with RPGN.

Methods: 43 consecutive patients who were diagnosed with RPGN, had renal biopsy and undergone chest CT between January 2000 and March 2012 at our hospital, were included. Patients' background, definitive diagnosis and prognosis were evaluated using medical records. The frequency and characteristics of coexisting pulmonary lesions were evaluated using CT images, and finally, we investigated the prognostic significance of pulmonary lesion.

Results: The aetiologies of RPGN in the study were ANCA-associated glomerulonephritis (55.8%), idiopathic crescentic glomerulonephritis (9.3%), systemic lupus erythematosus (7.0%), renal amyloidosis (4.8%), Henoch-Schönlein purpura (4.7%), polyarteritis nodosa (2.3%) and Churg-Strauss syndrome (2.3%). At the time of RPGN diagnosis, coexisting pulmonary lesions were found in 15 patients (34.9%), and that was most frequent in patients with ANCA-associated glomerulonephritis. About the characteristics of CT findings, CT pattern of chronic interstitial pneumonia was the most frequent (27.9%). During the follow-up period, new pulmonary lesions were observed in seven of 15 patients (46.7%) with preceding pulmonary lesions, and seven of 28 patients (25.0%) without. Coexisting pulmonary lesions at the diagnosis of RPGN had no statistically significant prognostic impact ($P = 0.10$). However, notably after four-years of follow-up, patients with preceding pulmonary lesions seemed to have worse prognosis. The most frequent cause of death in late period of follow-up was lung cancer.

Conclusion: We considered that RPGN patients with coexisting pulmonary lesions at the diagnosis, need long-term follow-up, especially for lung cancer. A part of this study have been presented in ERS International Congress 2013.

P-K-011

ANTIBACTERIALS FOR SYSTEMIC USE IN PRIMARY HEALTH CENTRE IN PROBOLINGGO: WHERE A JUDICIOUS ANTIBIOTIC USE GOES?

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Introduction: Indonesian National Formulary was published to support rational drug use in universal coverage era. A consideration of antibiotic choices in primary health centre is limited, usually narrow spectrum and to treat susceptible bacteria.

Methods: We gathered information from six primary/community health centre in district Probolinggo. There are more than nine thousand to more than twenty three thousand people visit those health centres a year. The amount of antibiotic use was calculated in Defined Daily Dose (DDD) per 1000 patient visit day on J01 (ATC classification for antibacterials for systemic use). Data analysis with One Way ANOVA (Analysis of Variance) Microsoft excels to identify the antibiotic usage significance differences between primary health centres.

Results: Eight antibiotics (amoxicillin, ampicillin, chloramphenicol, erythromycin, ciprofloxacin, phenoxymethylpenicillin, procaine benzylpenicillin, and tetracycline) are antibiotic for primary health centre; five antibiotics (cefadroxil, cefotaxime, ceftriaxone, clindamycin, levofloxacin) are antibiotic which should only use at secondary or tertiary health centre according to Indonesian National Formulary 2013. Its DDD per 1000 patient visit day differ significantly ($p < 0.05$), i.e. 2.67; 3.27; 3.82; 4.14; 4.86; 6.22 respectively. The most three infectious diseases in those community health centres are upper respiratory tract infection, diarrhea, and influenza; which, usually, are caused by virus, not bacteria.

Conclusion: In this district broad spectrum antibiotics are used to treat some infectious disease, mostly caused by virus. Injudicious antibiotic use may increase the incidence of antibiotic resistance.

P-K-013

EX-VIVO LUNG PERFUSION FOR LUNG TRANSPLANTATION – THE AUSTRALIAN EXPERIENCE

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Introduction: Lung transplantation is limited by the availability of suitable organs. Currently, less than 25% of donated lungs are used, with poor gas exchange and the presence of infiltrates on chest radiography in particular contributing to the low utilization rate. Ex-vivo lung perfusion (EVLP) is an evolving technique whereby donor organs previously deemed unsatisfactory for transplantation are warmed, perfused and ventilated ex-vivo. This process aims to improve organ function by treatment of oedema and atelectasis whilst allowing comprehensive assessment for aspiration and infection via bronchoscopy. We report our early experience with this novel technique.

Patients: Between November 2011 and December 2013 our institution performed 61 lung transplant procedures (60 bilateral sequential, 1 single). 8 of these transplants utilized EVLP for reconditioning of donor lungs, with 2 further unsuccessful attempts at EVLP resuscitation. In contrast to other published series, we did not use donation after circulatory death (DCD) in the absence of poor gas exchange as an indication for EVLP.

Outcomes: In 7 of 8 cases, the indication for EVLP was unsatisfactory gas exchange and lung infiltrates. Mean PO₂ (FiO₂ 100; PEEP 5 mmHg) at retrieval was 174 mmHg (range 118–331 mmHg). In the final case, prolonged cold ischaemia due to remote geographic location of the donor would have made transplantation unacceptably high risk. Gas exchange improved in 8/8 cases (mean PO₂ after EVLP 435 mmHg, $p < 0.001$). No grade 3 primary graft dysfunction was present in EVLP recipients at 24 hours. At median follow-up of 1 year 10 months, 1 patient died of bronchiolitis obliterans syndrome. The remaining 7 patients are BOS grade 0 and remain well.

Conclusion: EVLP is feasible and was successful in 80% of cases in our series. This technology could lead to a significant increase in the lung utilization rate and hence the transplantation rate, without compromising safety.

P-K-014

THE USE OF THE MINI NUTRITIONAL ASSESSMENT SHORT-FORM (MNA-SF) AS A PRACTICAL TOOL FOR IDENTIFICATION OF NUTRITIONAL STATUS AMONG ELDERLY HOSPITALIZED FILIPINO PATIENTS – A PRELIMINARY STUDY

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Background and Aim of the Study: Malnutrition remains to be a major healthcare issue globally. In the elderly, malnutrition carries a low quality of life, frequent and prolonged hospitalizations and mortality. The study used the Mini Nutritional Assessment Short Form (MNA SF) as a nutrition assessment tool, which classified elderly hospitalized patients, 65 years old and above, into three nutritional status categories: normal nutritional status, at risk of malnutrition and malnourished. The Geriatric Depression Scale (GDS) was also used to assess affective status of the subjects. In our setting, a screening tool, like MNA SF, is not available to assess nutrition status on admission. Data on the use of this tool among Filipino elderly is not available.

Methodology: The study was approved by the Institutional Review Board. It used the MNA SF, the most validated and referenced nutrition screening and assessment tool for those 65 years old and above. The MNA SF was translated to Filipino. The calf circumference was used instead of Body Mass Index (BMI). The GDS, available in Filipino, was also used. A convenience sampling was done on fifty patients admitted or co-managed under Pulmonary Service. Frequency count percentage and chi square were used and analyzed using SPSS version 16.

Results: Most of the subjects were female (28/50), 65–75 years old (25/50), and admitted at the Pay Ward (20/50). The most common comorbid illnesses were: Community Acquired Pneumonia (CAP), Hypertension, Coronary Artery Disease (CAD), Acute Respiratory Failure (ARF), and Cancers other than lung. Majority were malnourished (32/50) and had suggestive features of depression (22/50).

Conclusion: The use of the MNA SF screening tool detected a high prevalence of malnutrition. These elderly hospitalized patients have suggestive features of depression. Malnourished patients need a thorough evaluation and support of a multidisciplinary team, to include geriatric health care professionals, nutrition specialists and psychiatrists. Use of this assessment form during admission is recommended, for early intervention of at risk for malnutrition and malnourished patients. Further research can be done in community setting and other centres which cater to elderly patients.

P-K-015

3 CASES OF YOUNG PATIENT WITH PULMONARY ARTERIOVENOUS FISTULA, TREATED BY VIDEO ASSISTED THORACOSCOPIC SURGERY

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Pulmonary Arteriovenous Fistula (PAVF) is the anatomical abnormal, pulmonary (PA) artery and pulmonary vein (PV) connects directly without capillary. This disease is relatively rare and incidence was reported 2 to 3 persons/100000 persons. Blood flows directly PA to PV by short-circuit, and this means PAVF has Right to Left shunt. The short-circuit flow get higher, oxygen saturation get lower. Therefore, PAVF can cause symptom of anoxemia, cardiac insufficiency and pulmonary hypertension. And the deficiency of capillary means deficiency of filtering action, so PAVF cause thromboembolic event, especially cerebral embolism and abscess. In addition, PAVF can cause hemothorax and haemoptysis. Because of these complication, PAVF requires therapy. In treatment for PAVF, patient can be performed embolic therapy and surgery. Because of its minimally invasiveness, Embolic therapy is preferable in most cases. But in the follow-up after embolic therapy, PAVF reappear in 25% patients due to recanalization and interval growth of new feeding artery. So long term following up is needed. But, it is very difficult for young patient to keep following up. And video assisted thoracic surgery (VATS) can minimize incision. We have experienced 3 cases of young patients with PAVF treated by VATS for latest 3 years. All patient were twenties without symptom, but surgery was performed for reducing risk of complications. Chest drain was removed 1–3 post-operative day. And they were discharged our hospital 2–12 post-operative day. And there was no remarkable complication on them. So, if PAVF can resect by partial resection or segmentectomy, VATS is feasible treatment, especially for young patient with single PAVF.

P-K-016

EVALUATION OF TOTAL THORACOSCOPIC EXTENDED THYMECTOMY FOR MYASTHENIA GRAVIS

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Introduction: Extended thymectomy had been performed via mid-sternal incision. Since September 2010, we have been performing total thoracoscopic extended thymectomy for myasthenia gravis (MG) that we discuss in this report. We have performed the procedure with patient in supine position and using sternum lifting method with specially designed instruments.

Case Report: A 41-year-old woman presented with MG (MGFA classification IIb). She had been found to have mild generalized myasthenia gravis 2 months earlier. On chest computed tomography and magnetic resonance imaging, a tumour 2 cm in diameter was seen in the right lobe of the thymus in the anterior mediastinum. This tumour was thought to be a Masaoka stage 1 thymoma. The patient was referred to our department, and surgery was performed. Incisions were made in 1 location on both sides of the chest, and then on the xiphoid process. Pathologically, it was B3 type and stage 2 in the Masaoka classification. The post-operative course was good. This patient left the hospital on post-operative Day 5.

Patients and Methods: After identifying contralateral phrenic nerve, we determined which approach should be selected – right thoracic approach or bilateral thoracic approach. We have mainly used bipolar tissue sealing system for thoracoscopic surgery. Between January 1989 and March 2014, we have performed 11 total thoracoscopic extended thymectomy cases among total 80 extended thymectomy cases. The myasthenia gravis case was five cases (thymoma complicated case was three cases).

Results: The total of thoracoscopy cases included 1 male and 4 female; mean age was 45.2 year; mean operative time was 362.4 minutes; mean postoperative hospital stay was 7.0 days. Compared to conventional procedure, total thoracoscopic procedure took 96.5 minutes longer in operative time. Whereas post-operative hospital stay was 7.1 days shorter. All cases of MG showed improvement of the symptoms. One of the cases could achieve the remission. No exacerbation of post-operative symptom or anti-AChR antibody increase was observed. So, the patients could be managed well in a short term control.

Conclusion: The prognosis of MG without thymoma treated by complete video-assisted thoracoscopic surgery has been almost the same as conventional extended thymectomy. We have had almost the same results in our department. In myasthenia gravis, total thoracoscopic extended thymectomy was useful in short term prognosis that we discuss in this report. Based on the results, we should continue to follow-up the mid or long term prognosis.

P-K-017

VOLATILE ORGANIC COMPOUNDS FROM TRACHEOBRONCHIAL STENT-RELATED BIOFILM FORMATION DETECTED BY ION MOBILITY SPECTROMETRY

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Background: Tracheobronchial stent-related biofilm formation is an encountered problem in interventional pulmonology that can result in pneumonia and granulations. Breath analysis such as canine scent, electronic nose and ion mobility spectrometry (IMS) has been reported to detect volatile organic compounds (VOCs).

Objective: We hypothesized that IMS can detect specific VOCs in patients with biofilm formation resulting from tracheobronchial stent placement.

Methods: From October 2011 to October 2012, we conducted a single-centre prospective study at St. Marianna University. Stent placement was performed on 21 patients with tracheobronchial stenosis. Among these patients, breath samples before and after stent removal or replacement were analyzed using IMS.

Results: Bacteriologic culture from the removed silicone stents resulted in *Pseudomonas aeruginosa* biofilm formation in 4 patients. A total of 36 peaks were used to determine Wilcoxon-Rank tests. Box-and Whisker plots were prepared and 12 peaks were identified to contribute to separation power. Five of the 12 peaks had a separation power better than 95%. From the identified peaks using the database provided, a significant difference was observed for P22: Unknown ($p < 0.05$), P23: Limonene ($p < 0.05$), P24: 2,2,4,6,6-Pentaheptylmethane ($p < 0.05$), P31: 1-Octanole ($p < 0.05$), P35: Phenylacetaldehyde ($p < 0.05$).

Conclusions: IMS was able to evaluate the degree of biofilm formation of *Pseudomonas aeruginosa* resulting from stent placement. From these results, we can consider whether to replace or removed stents in conjunction with clinical symptoms using IMS.

P-K-018

BRONCHIAL ARTERY EMBOLIZATION IN THE MANAGEMENT OF HAEMOPTYSIS IN PATIENTS WITH HAEMATOLOGIC DISEASES: FEASIBILITY AND SHORT-TERM EFFICACY

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Purpose: To evaluate the feasibility and short-term efficacy of bronchial artery embolization (BAE) in the management of haemoptysis in patients with haematologic diseases.

Materials and Methods: This is a retrospective review of 28 consecutive patients with haematologic diseases (18 men, 10 women; mean age, 54 years) who were referred for BAE for the management of haemoptysis between 2009 and 2012. Among these 28 patients, 25 patients (89%) underwent BAE, and the remaining three patients (11%) received only diagnostic angiography without embolization. The clinical, laboratory and radiographic data of 25 patients were retrospectively analyzed and we correlated clinical response with amount of haemoptysis, coagulation condition, radiographic pattern and bronchial artery hypertrophy.

Results: Of 25 patients, the amount of haemoptysis was trivial in 13 patients (52%), moderate in 10 patients (40%), and massive in 2 patients (8%). Thirteen patients (52%) had coagulopathy ($< 5 \times 10^4 \mu\text{L}$ and/or INR > 1.5). On computed tomography (CT) findings, 17 patients (68%) showed focal pulmonary haemorrhagic patterns and 8 patients (32%) showed diffuse pulmonary haemorrhagic patterns. BAE provided complete clinical response in 21 out of 25 patients (84%). Complete clinical response was not correlated with amount of haemoptysis, coagulation condition, radiographic pattern, or bronchial artery hypertrophy ($p < 0.05$). There was no significant difference in short term survival between patients with coagulopathy and those without coagulopathy ($p = 0.425$) and between patients with focal haemorrhagic pattern and those with diffuse haemorrhagic pattern ($p = 0.728$).

Conclusions: BAE in haematology patients was relatively efficient in controlling haemoptysis. The amount of haemoptysis, coagulation condition, radiographic pattern, or bronchial artery hypertrophy were not a significant factor affecting the outcome.

P-K-019

HYDROGEN GAS INHALATION AMELIORATES DIRECT LUNG INJURY AND INDIRECT CONTRALATERAL LUNG INJURY IN A MURINE ASPIRATION PNEUMONIA MODEL

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Aim: Accumulated leukocytes in the lungs produce several inflammatory cytokines and reactive oxygen and nitrogen species (ROS and RNS), which will induce ALI/ARDS. It has been reported that hydrogen (H₂) gas has the potential to eliminate highly reactive ROS and RNS. The aim of the present study was to clarify the effect of H₂ gas inhalation on direct lung injury and indirect contralateral lung injury.

Methods: Anaesthetized C57BL/6J male mice were intubated, and 5 micro-L of 0.1N HCl was administered to the left lung. Mice were randomly grouped to saline treatment instead of HCl (Sham), HCl-treatment (HCl), and 2% H₂ gas inhalation with the HCl-treatment (HCl-H₂) groups. Extra-vascular wet to dry ratio, myeloperoxidase (MPO) activity in the treated left lung and untreated right lung, serum IL-6 level and lung injury score assessed by intra-alveolar infiltrate, alveolar haemorrhage, and alveolar septal thickening from HE staining image were evaluated 4 hrs after the treatment.

Results: This aspiration pneumonia model induced direct lung injury and contralateral lung injury. The extra-vascular wet to dry ratios of the left and right lungs were significantly larger in the HCl group compared to the Sham and the HCl-H₂ group (n = 10, P < 0.01). MPO activity of the left lung was also significantly larger in the HCl group compared to those in the Sham and HCl-H₂ groups (n = 9, P < 0.05). These results suggested that H₂ gas was effective not only in the direct injured lung but also in the contralateral lung. IL-6 increased in the HCl group, but it did not statistically differ to the level in the HCl-H₂ group, suggesting H₂ gas did not interfere in the cytokine production in this model. Lung injury score for left or right lung was significantly larger in the HCl group compared to those in the Sham and HCl-H₂ groups (n = 60 (20 fields each in 3 animals), P < 0.01).

Conclusion: H₂ gas inhalation ameliorated direct lung injury and indirect contralateral lung injury in a murine aspiration pneumonia model.

P-K-020

MURINE MODEL OF POST-ARDS PULMONARY FIBROSIS

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Recent development of various treatment modalities made the mortality of acute respiratory distress syndrome (ARDS) decrease. Therefore, long term complications of survivors became very important clinical problems. One of them is persistent pulmonary fibrosis. It was reported even one year after ARDS and it can be the cause of persistent dyspnoea and inactivities. Therefore, developing the way of reducing residual pulmonary fibrosis is urgent. Intratracheal instillation of lipopolysaccharide (LPS) is common murine model of acute lung injury. However, acute lung inflammation induced with a single intratracheal instillation of LPS usually rapidly resolved. We postulated repeated lung injury by LPS can cause persistent pulmonary fibrosis and it can be similar to post-ARDS pulmonary fibrosis in human. Therefore, we evaluated whether repeated intratracheal administration of LPS is suitable methods for murine model of post-ARDS pulmonary fibrosis. Seven to eight-week-old C57BL/6 male mice were used for experiment. Under anaesthesia, phosphate buffered saline (PBS) or LPS were instilled intratracheally (PBS group, LPS 2 ug/g weekly group, LPS 1 ug/g twice weekly group, LPS 2 ug/g twice weekly group) for three weeks. In LPS 2 ug/g twice weekly group, 63% of mouse died before the end of experiment. In LPS 1 ug/g twice weekly group, 25% of mouse died, and in 2 ug/g once weekly group, only 13% of mice died before day 21. On day 21, all the mice were euthanized. We thought LPS 2 ug/g twice weekly group was not suitable for post-ARDS pulmonary fibrosis model because of high mortality. And considering the convenience of drug administration, LPS 2 ug/g once weekly group was thought to be suitable for post-ARDS pulmonary fibrosis model although the hydroxyproline level for 2 ug/g once weekly group and 1 ug/g twice weekly group was similar (79.6 ug/ml and 77.4 ug/ml respectively). We also found histologic changes were consistent with lung injury/fibrosis in both bleomycin and LPS group. Ashcroft score of PBS group was 2.7, bleomycin group was 6.0, LPS 2 ug/g weekly group was 5.0. In conclusion, repeated intratracheal instillation of LPS model (2 ug/g once weekly) can be used as murine model of post-ARDS pulmonary fibrosis.

P-K-021

RARE PLEURISY IN AETIOLOGY: HANTAVIRUS INFECTION

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Introduction: Hantavirus infection is a zoonotic disease transmitted by contact with infected rodent droppings and rarely by being bitten. We come across the disease in two types of clinical cases; Hantavirus Cardiopulmonary Syndrome (HKPS) and Haemorrhagic Fever with Renal Syndrome (HFRS). This report will introduce a case with presenting symptoms of high fever, coughs, hilar LAP, bilateral pleurisy and thrombocytopenia.

Case: 54 year-old male patient is involved with handling livestock. The patient has consulted a private healthcare centre with fever, fatigue, muscle pain and coughs complaints. Later, a mild pneumonic infiltration, hilar lymphadenomegaly and bilateral pleurisy were detected in his chest radiography together with thrombocytopenia and a high LDH, and he was transferred to our hospital. Other physical clinical findings together with a body temperature of 38,50C, conjunctivas and pharynx hyperemic, decreased breath sounds in lower regions were detected: Leucocyte 5.420/mm³, Hb 15 mg/dl, Hct %45, thrombocyte 61.000/mm³, CRP went up 20 times, LDH 265 IU/L (135–225 IU/L), and other laboratory findings normal. No pathological findings were detected in his abdominal ultrasonography. No signs related to active pulmonary tuberculosis were followed up in his thoracic computerized tomography. Due to the minimal amount of pleural effusion and other systematic problems that accompanied this, thoracocentesis wasn't done and follow-up was recommended. Systematic infections were evaluated by infectious diseases specialists. When his creatinine levels rose to 2,5 mg/dl on the sixth day of his hospitalization, nephrology specialists were consulted for vasculitis and interstitial nephritis. The repeated abdominal USG showed free fluid in bowel loops and it was thought to be a result of acute renal failure. No evidence was detected in the patient's tuberculosis analysis. An analysis of infectious agents progressing with systemic involvement, hantavirus IgM and IgG antibodies were tested positive. This was thought to have developed due to lung involvement of renal syndrome progressing with haemorrhagic fever. The renal functions of the patient whose fever reduced to normal spontaneously on the ninth day reached normal values on the third week. His repeated thoracic BT at the end of the first month, revealed that his pleurisy was completely regressed and his lung parenchyma was natural.

Conclusion: Climatic and ecological system changes that have caused a differentiation in the animal population resulted in a shift in the map of the zoonotic diseases. It must be kept in mind that these types of diseases may become more common. This case would like to draw attention to the fact that zoonotic viral diseases should be remembered in unidentified clinical conditions and that a multidisciplinary approach is vital in these diseases.

P-K-022

P-K-023

PREVALENCE AND CLINICAL CHARACTERISTICS OF OLDOSA SYNDROME IN A PHILIPPINE TERTIARY HOSPITAL SLEEP LABORATORY

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Background and Aims: Obstructive lung diseases (OLD) such as chronic obstructive pulmonary disease (COPD) and asthma, and obstructive sleep apnoea (OSA) are prevalent and may co-exist in patients. Recent literature has been suggestive of bidirectional complex interactions between OLD and OSA. The OLDOSA syndrome is the general entity to collectively describe patients with both OSA and COPD (Overlap Syndrome), or both OSA and asthma (Alternate Overlap). The aims of this study are to determine the prevalence and clinical characteristics of OLDOSA and pure OSA patients in the Sleep Laboratory of a Philippine tertiary medical centre, and to determine the correlation of OSA severity and OLD severity among patients.

Methods: A retrospective chart review of the patient database at The Medical City Sleep Laboratory from January 1, 2012 to December 31, 2013 was done which included all patients ages 18 years old and above. Diagnosed cases of OSA were cross referenced with the Pulmonary Laboratory to determine whether these patients underwent a spirometry or a pulmonary function test (PFT). Based on clinical history and spirometry or PFT results, OSA patients were categorized into OLDOSA or pure OSA groups. OLDOSA patients were further specified as Overlap Syndrome or Alternate Overlap Syndrome. Patients were also classified according to the severity of OSA and OLD. Clinical characteristics (age, gender, BMI, neck and abdominal circumference, smoking history, Epworth score), polysomnography, and spirometry results were compared between pure OSA and OLDOSA groups.

Results: Seven hundred sixteen patients ($n = 716$) underwent polysomnography, of which 587 patients were diagnosed with OSA. Among the OSA patients, 10% (59 of 587) had OLDOSA based on history and spirometry or PFT results. Among the OLDOSA patients, 63% (37 of 59) had Overlap Syndrome and 37% (22 of 59) had Alternative Overlap Syndrome. The prevalence of OLDOSA among patients referred to The Medical City Sleep Laboratory is 8.24% (59 of 716). Compared to pure OSA patients, OLDOSA patients were older (mean age 51.6 versus 46.3 years, $P = 0.007$) and had a lower apnoea-hypopnoea index (29.1 versus 38.9; $P = 0.011$). OSA and OLD severity were not correlated (Spearman's $\rho = -0.012$, $P = 0.23$).

Conclusion: Patients with OLDOSA syndrome comprise nearly 10% of the patients presenting to the sleep laboratory, are generally older, and with lower AHI scores. Prospective studies are recommended in order to determine risk factors and prognosis of OLDOSA patients.

HYDROGEN CONCENTRATION IN EXPIRATORY GAS AFTER TAKING INDIGESTIBLE SUGARS

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Aim: Hydrogen was produced in enterobacterial flora from indigestible sugars by fermentation of the sugars in the intestine. Produced hydrogen in enterobacterial flora has been reported to act as some protective agent against oxidative stress which increased several diseases like ischemia-reperfusion injury. Hydrogen produced in the intestine and contained in the blood can be detected from expiratory gas. The aim of the present study was to determine the hydrogen production in enterobacterial flora after taking indigestible sugars by evaluating expiratory gas.

Methods: Indigestible sugars used for this study was maltitol, fructooligosaccharides, and raffinose. Each indigestible sugar was dissolved in 300 mL of water. The amount of sugar contained in the water was adjusted to 0.3 g/kg-body. Ten normal healthy volunteers participated in this study. After overnight fasting, subjects drank 300 mL of water with or without indigestible sugar at 9 a.m. Expiratory gas was collected into the aluminum bag every hour from 9:00 a.m. to 9:00 p.m. Hydrogen concentration was measured by a breath gas analyzer. Hydrogen concentration was also measured in daily life without overnight fasting.

Results: Hydrogen gas concentration increased 2 hr after taking sugar-containing water and kept a high concentration for about 6 hr, but little change was observed after taking water without indigestible sugar. Time averaged hydrogen concentrations in expiratory gas after taking indigestible sugars were almost the same independent of the sugars and were significantly higher than that after taking water without sugar or in daily life ($P < 0.05$). The group of subject whose hydrogen concentration in expiratory gas was below 25 ppm during the measurements in daily life showed significantly lower hydrogen concentration after taking maltitol or fructooligosaccharides than the group whose hydrogen concentration in expiratory gas was higher in daily life. These results indicated that the hydrogen gas production may vary among different individuals depending on their enterobacterial flora.

Conclusion: Indigestible sugars can enhance hydrogen gas production, especially for the person whose hydrogen concentration in expiratory gas is higher in daily life.

P-K-024

MEDIASTINAL GIANT THYMOLIPOMA – A RARE CASE REPORT

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Introduction: Lipoma is an uncommon benign tumour accounting for 2% to 9% of mediastinal tumours. We present the case of a 56-year-old woman who sought medical attention for breathlessness of 3 months duration. Computed tomography showed a mass occupying the anterior mediastinum and extending in neck region. This mass caused compression of both lungs. Magnetic resonance imaging revealed a large fatty tumour. The tumour was resected through a thoracotomy. No postsurgical complications occurred.

Case Report: 56 years old female was referred to thoracic surgery department of the Max Superspeciality Hospital, Delhi with complaints of gradually progressive dyspnoea of 3 months duration. Clinically, the patient was hemodynamically stable. Routine blood investigations were within normal limits. A chest radiograph revealed large soft tissue opacities occupying mid and lower zones of both lung fields. The chest skiagram was not diagnostic. A computed tomography (CT) scan of the thorax revealed a large mass measuring 10.5 cm × 8.4 cm × 6.5 cm of fat attenuation (–80 to –120 HU) with minimally enhancing internal densities noted in the anterior. The mass was compressing the lungs bilaterally. There was cranial extension of mass in neck on right side and within the neck and superior mediastinum the lesion shows intensely enhancing soft tissue and admixed fat. MRI of chest was done with contrast showed large fat intensity anterior mediastinal lesion with few fibrous strands in it. The lesion was extending in bilateral hemi thorax causing compression and displacement of lungs resulting in reduction of air space. The lesion had cranial extension into neck on right side and showed intensely enhancing soft tissue admixed with fat intensity. The patient underwent median sternotomy and a large lobulated fatty mass in the anterior mediastinum that was well encapsulated and was extending to surrounding recesses was noted and it was excised en bloc. The mass weighed 15 kg. The histopathological examination of the specimen showed a lesion composed of an admixture of mature adipose tissue intercepted by fibrovascular septae. Neck mass showed lobules of colloid filled thyroid follicles separated by mature adipose tissue. The impression of histopathology was mediastinal lipoma and diffuse lipomatous infiltration of thyroid gland.

Conclusion: Lipoma is an uncommon benign neoplasm that accounts for 2% to 9% of mediastinal tumours. The weight of these tumours, according to our review of the literature, ranges from 154 g to 6000 g; in our case, the tumour weighed 15 kg. This is a very rare tumour with a big size occupying more than 70% of intrathoracic volume.

P-K-025

PROFILE AND AETIOLOGY OF SECONDARY SPONTANEOUS PNEUMOTHORAX PATIENTS IN DR CIPTO MANGUNKUSUMO NATIONAL GENERAL HOSPITAL JAKARTA, INDONESIA

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Background: In general, a pneumothorax is an emergency case and should be examined immediately. Based on the aetiology, pneumothorax is classified into spontaneous pneumothorax and traumatic pneumothorax. In the assessment of lung diseases and the factors that cause pneumothorax, it is very important to know proper guidelines in cooperation with interdisciplinary medical science and to improve the overall management of pneumothorax approach in terms of medical or surgical. Data about pneumothorax patients in Indonesia is still limited. Through this research we try to establish the profile and aetiology of the secondary spontaneous pneumothorax patients during hospitalization at the Dr. Cipto Mangunkusumo National General Hospital (RSCM).

Objective: The purpose of this study was to determine the profile and aetiology of secondary spontaneous pneumothorax patients during hospitalization in RSCM.

Methods: This study used retrospective cohort study design conducted on pneumothorax patients who were admitted in RSCM in the period January 2000 to December 2011. Data on demographics, clinical features, radiological, risk factors were collected.

Results: A total of 104 pneumothorax patients were reviewed. Their mean age was 39.7 years (SD ± 16.2 years) with a male to female ratio of 3:1. The most common symptoms of pneumothorax was shortness of breath 103 (53.3%) and abnormalities on physical examination was hyperresonant 101 (57.3%). Plain chest X-ray of pneumothorax patients showed hyperlucent avascular in only 95 (91.4%) and hyperlucent avascular with infiltrates in 79 (88.7%). Risk factors and aetiology of secondary pneumothorax obtained in this study were smoking 43 (27.2%), pneumonia 42 (26.6%), tuberculosis 37 (23.4%), chest trauma 13 (8.3%), iatrogenic 6 (3.8%), lung malignancy 6 (3.8%), COPD 5 (3.16%), asthma 5 (3.16%) and rheumatoid arthritis 1 (0.6%). The most common type of pneumothorax was secondary spontaneous pneumothorax 49 (47.1%). Most of pneumothorax patients were successfully managed by chest thoracosintesis 98 (82.3%). Outcome of pneumothorax patients were – live 69 (66.3%), died 35 (33.7%). Causes of death in pneumothorax patients was respiratory failure 16 (45.8%).

Conclusions: Profile and aetiology of secondary spontaneous pneumothorax during hospitalization were smoking, iatrogenic, chest trauma, pneumonia, COPD, bronchial asthma, tuberculosis, rheumatoid arthritis, lung malignancy. Most types of pneumothorax was secondary spontaneous pneumothorax and pneumothorax patient's management was tube thoracosintesis. Outcome of pneumothorax patients were live. Cause of death in pneumothorax patients was respiratory failure.

P-K-026

P-K-028

DIAGNOSTIC VALUE OF BRONCHOSCOPY IN PATIENTS WITH HAEMATOLOGIC MALIGNANCY AND PULMONARY INFILTRATES

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Pulmonary infections are a major cause of morbidity and mortality in patients with haematologic malignancy. Bronchoscopy is at present still the traditional first investigation in immunosuppressed patients that have developed pulmonary infiltrates. There is limited data available on the validity of fiberoptic bronchoscopy (FOB) with bronchoalveolar lavage (BAL) to determine the aetiology of pulmonary infiltrates with concurrent haematologic malignancy. We retrospectively analyzed the microbiological results of 206 bronchoscopic examinations and treatment changes used in 187 patients with haematologic malignancy and pulmonary infiltrates. Bacteria, fungi, and viruses were found in 85 (41.3%), 49 (23.8%), and 55 (28.6%) of cases, respectively, and overall yield of bronchoscopy was 65.0%. We compared the microbiological findings with respect to neutropenia, haematopoietic stem cell transplantation (HSCT) status, and the type of malignancy. There were significantly more bacterial and viral infections detected in post-HSCT patients, and more viruses were detected in patients without neutropenia. Galactomannan (GM) was measured in 149 BAL samples. With a GM index threshold of ≥ 0.5 , the sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) of the BAL GM assay were 93.94%, 86.21%, 65.96%, and 98.04%, respectively. Treatment was modified in 62 cases (30.1%). There was not a significant relationship of treatment modification with the underlying disease, HSCT, or neutropenia. Bronchoscopy with BAL is a valuable diagnostic tool to determine the aetiology and appropriate treatment in patients with haematologic malignancy and pulmonary infiltrates. A BAL GM test is recommended when invasive pulmonary aspergillosis is suspected.

NONINVASIVE MECHANICAL VENTILATION: AN 12-MONTH EXPERIENCE

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Aim: To evaluate the effectiveness of Noninvasive Mechanical Ventilation (NIMV) in hospitalized patients with the diagnosis of respiratory failure and to reveal the factors associated with treatment failure.

Methods: The patients hospitalized in our clinic with a diagnosis of respiratory failure and had an indication for NIMV were included in this study prospectively. These patients were divided into two groups. Patients that completed the treatment and were discharged from the hospital were named as Group 1 (treatment success). Group 2 (treatment failure) included patients who had the indication of intensive care unit or died after the initiation of NIMV. Demographic findings, additional diseases, hospitalization history of last year, symptoms, GCS, pulse rate, respiratory rate, chest x ray findings, beginning and first hour arterial blood gas values, duration of hospitalization were recorded. The success rate of NIMV was calculated. The data of the patients in 2 groups compared to investigate the factors effective on NIMV treatment failure.

Results: 14 (29.8%) female, 33 (70.2%) male, with a total of 47 patients who were diagnosed with respiratory failure with a mean age of 66.7 ± 11.6 , were included. Whereas 37 (78.7%) cases had the diagnosis of COPD, the rest of them had congestive heart failure, interstitial lung disease, pneumonia, OSAS, restrictive disease alone or together with COPD. Three out of 47 cases were in treatment failure group while the rest of patients were discharged. The rate of NIMV treatment success was 93.6%. The data for the patients in the 2 groups and statistical comparisons are given in Table 1. There is significant relationship between the treatment failure of NIMV in patients with respiratory failure and GCS, increased number of comorbidities, pH value at the beginning and first hour of NIMV ($p = 0.001$ and $p = 0.005$, $p = 0.011$, $p = 0.05$).

Conclusion: Low GCS, increased comorbidities, low beginning and first hour pH value are associated with failure of NPPV. In these cases, close follow-up and decision of invasive mechanical ventilation at the right time, may be lifesaving for patients.

P-K-027

EFFECTS OF RECRUITMENT MANOEUVRE IN PATIENTS UNDERGOING ROBOTIC RADICAL PROSTATECTOMY

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Introduction: An increase in the number of robotic radical prostatectomy has been seen due to better surgical outcome and lower rate of complications. To perform robotic radical prostatectomy, the patient must be placed in a steep Trendelenburg position (about 30 degree head down). This position and pneumoperitoneum can cause problems regarding intraoperative oxygenation and postoperative atelectasis. The aim of this study was to evaluate effects of recruitment manoeuvre (RM) with positive end expiratory pressure (PEEP) on intra and postoperative oxygenation.

Method: Twenty five adult patients aged between 60 and 75 years who were scheduled for elective robotic radical prostatectomy were enrolled. Patients were randomly allocated into two groups; Group P (PEEP group, $n = 12$) received 5 cm H₂O PEEP, while Group RP (RM with PEEP, $n = 13$) was given RM and 5 cm H₂O PEEP after induction and before formation of pneumoperitoneum. Measurements of oxygenation were obtained immediately after induction (T0; baseline), 30 minutes after 17 mmHg pneumoperitoneum (T1), 90 minutes after 17 mmHg pneumoperitoneum (T2), and 30 minutes after arriving at postanesthetic care unit (T3).

Results: Application of RM with PEEP resulted in significantly higher arterial oxygenation pressure (107.1 ± 40.8 vs. 85.6 ± 11.6 , $p < 0.002$), arterial/alveolar oxygen ratio (1.0 ± 0.4 vs. 0.8 ± 0.1 , $p < 0.007$), and lower alveolo-arterial pressure gradient (0.8 ± 40.4 vs. 21.8 ± 13.6 , $p < 0.006$) as well as amount of shunt (0.1 ± 5.0 vs. 2.7 ± 1.7 , $p < 0.006$) at T3. Arterial oxygenation pressure, arterial/alveolar oxygen ratio, alveolo-arterial pressure gradient, and amount of shunt were not significantly different between two groups, but the mean value of arterial oxygenation pressure and arterial/alveolar oxygen ratio was higher in Group RP. The mean value of alveolo-arterial pressure gradient and amount of shunt was lower in Group RP at T1 and T2.

Conclusion: This study showed that application of RM with PEEP improved oxygenation after robotic radical prostatectomy.

Table 1 The clinical and laboratory findings of cases and the comparison of two groups

Parameter	All cases (mean \pm SD)	Group 1 (mean \pm SD)	Group 2 (mean \pm SD)	p
Pulse rate (/min)	89.4 \pm 12.7	89.2 \pm 13.0	92.5 \pm 9.2	>0.05
Respiratory rate (/min)	20.9 \pm 3.8	20.8 \pm 3.7	21.7 \pm 4.9	>0.05
Glasgow coma scale	14.9 \pm 0.3	14.9 \pm 0.2	14.3 \pm 1.2	0.001
Comorbidities	1.61 \pm 1.32	1.45 \pm 1.17	3.67 \pm 1.52	0.005
Number of hospitalization in last year	0.34 \pm 0.79	0.36 \pm 0.81	0	>0.05
Number of ICU hospitalization in last year	0.34 \pm 0.60	0.36 \pm 0.61	0	>0.05
pH at hospitalization	7.96 \pm 0.06	7.36 \pm 0.55	7.41 \pm 0.10	0.011
pCO ₂ (mmHg) at hospitalization	66.5 \pm 8.8	66.2 \pm 8.1	70.9 \pm 18.1	>0.05
pO ₂ (mmHg) at hospitalization	61.3 \pm 22.7	58.9 \pm 19.9	95.6 \pm 38.5	0.07
pH at first hour	7.38 \pm 0.06	7.38 \pm 0.05	7.40 \pm 0.15	0.05
pCO ₂ (mmHg) at first hour	63.7 \pm 11.3	63.2 \pm 10.1	70.8 \pm 25.3	>0.05
PO ₂ (mmHg) at first hour	60.2 \pm 12.2	60.3 \pm 12.3	58.7 \pm 12.7	>0.05
C-reactive protein	52.9 \pm 70.1	52.5 \pm 71.0	60.4 \pm 70.1	>0.05

P-K-029

COMPARISON ACID FAST BACILLI EXAMINATION OF SPUTUM INDUCTION NA₂CO₃ 3% AND BRONCHOALVEOLAR LAVAGE ON SMEAR NEGATIVE PULMONARY TUBERCULOSIS

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Background: Tuberculosis (TB) remains a problem in both the developing and developed countries. Smear negative pulmonary TB patients play a role in the transmission of TB disease because nearly half of the patients had a sputum smear negative TB. Diagnosis and initial treatment in patients with smear negative pulmonary TB is essential to reduce the number of transmission and mortality. Sputum induction NaCl 3% and bronchoscopy is expected to obtain preparations for bacteriological tuberculosis examination and reinforces the value of the diagnosis pulmonary tuberculosis.

Purpose: To get a diagnostic method that has a high positivity rate value with Bronchoalveolar lavage and sputum induction NaCl 3% in the diagnosis of smear negative pulmonary tuberculosis.

Method: The study was conducted at the Department of Pulmonology and Respiratory Medicine FKUA / Dr. Soetomo Hospital, by taking 27 samples of smear negative pulmonary TB patients, aged 16–60 years old men or women who meet the inclusion and exclusion criteria.

Result: Obtained results in the induction of sputum smear examination positive in 4 samples (14.8%) and negative results for 23 samples (85.2%). The results of the BAL fluid smear examination positive in 2 samples (7.4%) and negative results as much as 25 samples (92.6%).

Conclusion: Smear examination of sputum induction gets a higher positivity value than the smear examination of Bronchoalveolar Lavage. The results smear examination in the sputum induction and Bronchoalveolar Lavage did not show significant differences.

P-K-031

GIANT SOLITARY FIBROUS TUMOUR OF THE PLEURA: A CASE REPORT

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Introduction: Solitary fibrous tumour is a rare neoplasm which most frequently occur in the pleura. Generally, they are divided into two major categories, the diffuse which are more common and localized tumours. Presently the term localized mesothelioma was replaced by solitary fibrous tumours of the pleura.

Case Presentation: A 41 year old female was admitted with a chief complaint of dyspnoea. The patient is a non smoker and was not exposed to any chemicals. She had been having chronic cough and dyspnoea upon exertion for 3 months. She sought consult where a mediastinal mass was seen on chest xray and ct scan. Invasive diagnostic work ups were done which revealed inconclusive results. She was admitted in our institution for elective excision of the mass. On examination, there was lagging of left hemithorax during inspiration, no breath sounds on the left lung field. Chest Ct scan revealed a large heterogeneously enhancing mass occupying the left superior mediastinum extending inferiorly occupying most of the left hemithorax, calcifications are seen on many aspects of the mass. During this time, a mediastinal mass was entertained considering a mature teratoma. Sternotomy with extension to anterior thoracotomy was done which revealed a huge pleural mass. Immunostaining confirmed the diagnosis of the solitary fibrous tumour of the pleura.

Discussion: Few number of Solitary fibrous tumour of the pleura (SFTP), have been reported in literature. Approximately 800 cases were reported in the literature. They may show slow growth rate over time and may reach very large sizes. In the case presented, the gigantic size of the mass was difficult to localized its anatomic origin using imaging diagnostic modalities.

Conclusion: A proposed algorithm for thoracic mass was presented by Abu Arab from European Journal Cardio-Thoracic Surgery to diagnose and to manage such diagnosis.

P-K-032

SPONTANEOUS BRONCHIAL TEAR AFTER SEVERE COUGHING BOUTS IN AN OLD FEMALE

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Introduction: Spontaneous tears of the mucosal layers are well known in esophagus after severe bouts of vomiting. But severe bouts of cough leading to a tear in the bronchial tree is not commonly seen and not reported yet. We report this rare occurrence in an immunocompromised female with respiratory infection.

Case Presentation: A 60 year old female with Chronic kidney disease secondary to Vasculitis on immunosuppressive medication and maintenance haemodialysis presented with severe cough over 2 days associated with haemoptysis of moderate quantities. She had left lower lobe consolidation with mild pleural effusion on chest radiograph and Computerized Tomogram of chest. She was in respiratory distress and required invasive ventilation. Routine investigations and coagulations parameters like PT, APTT, platelet count were normal. She was not on any anticoagulant medication. A Flexible Bronchoscopy was performed through the Endotracheal tube. It revealed a tear along the junction of left upper and lower lobe bronchi measuring about 1 cm length and 3–4 mm wide rough floor oozing fresh blood. Broncho alveolar lavage (BAL) collected from the left lower lobe was turbid but not grossly haemorrhagic. Cytological analysis of BAL revealed few Red Blood Cells and predominant Neutrophils. Subsequently BAL Culture had grown Pseudomonas which was treated with appropriate antibiotics. Her haemoptysis stopped eventually and she was extubated and discharged after, in stable condition.

Discussion: Tears in the bronchial tree are almost always trauma related and spontaneous tears are not generally heard of. On detailed review of literature there was only one odd case report of a tracheal tear in a young boy after severe bout of cough. So this is such an unusual condition not reported earlier. This patient had left lower lobe pneumonia resulting in cough but the source of bleeding was visually obvious from a tear in the mucosa at the junction of the left upper and lower lobar bronchi. The location also is too far to be injured iatrogenically by endotracheal intubation or subsequent suctioning. There was no history of any chest trauma to account for it making this a case of spontaneous bronchial tear due to severe bouts of coughing.

P-K-030

A CASE OF LEFT OPAQUE HEMITHORAX

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Opaque hemithorax on Chest X-Ray is always an interesting case for the evaluation and attracts many diagnosis. I came across a very rare and unique case of opaque left hemithorax during a routine medical check up. This young person came to me for routine medical check up and found to have decreased air entry on left chest during auscultation. The cardinal respiratory symptoms were not present and the person was actually an athlete with great stamina. Careful evaluation of the chest X ray showed central mediastinum with non-visualization of left main bronchus. CT scan of the chest showed complete absence of left main bronchus and the right main bronchus was the mere continuation of the trachea. The diagnosis of left lung complete agenesis was made. The case is unique for its rarity and simplicity in the diagnosis. The lack of knowledge may lead to more complicated diagnostic procedures like bronchoscopy.

P-K-033

P-K-035

TWO CASES OF MALIGNANT PLEURAL MESOTHELIOMA WAS DIAGNOSED BY BRONCHOSCOPY

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Purpose: Pleural biopsy is done for definitive diagnosis in many cases with malignant pleural mesothelioma. We report two cases of malignant pleural mesothelioma that exhibit infiltration and granular shadows in the lung field, was diagnosed by bronchoscopy.

Case 1: An 84-year-old man was referred in the left pneumothorax. There is no employment history of asbestos exposure. He showed a small amount of pleural effusion on both sides and granular shadow distributed in the overall lung fields in chest X-ray and chest CT. In TBLB by bronchoscopy, he was diagnosed with malignant pleural mesothelioma which has brought about pulmonary alveolar epithelial cancer like growth. Currently, it is in the observation without treatment.

Case 2: A 79-year-old woman repeated the right pneumothorax from three years ago, it was not allow the right pleural effusion in the medical examination. There is no employment history of asbestos exposure. Irregular pleural thickening around right lung infiltration in the right lower lobe, were showed in chest X-ray and the CT. In TBLB by bronchoscopy, malignant pleural mesothelioma which has brought about pulmonary alveolar epithelial cancer like growth. Currently, she was treated with Pemetrexed.

Conclusions and Discussion: In a malignant pleural mesothelioma, there are few cases that growth in the bronchiole alveolar epithelial cancer-like was diagnosed by TBLB. The number of the cases which presented such morbidity is about ten, and it is reported them this time.

ACQUIRED BRONCHESOPHAGEAL FISTULA DUE TO TUBERCULOSIS INFECTION

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Background: Bronchoesophageal fistula (BEF) is one of the lower respiratory tract defect which lies communication between bronchus and esophagus. It occurs due to congenital or acquired abnormalities. Acquired BEF is an extremely rare disorder. It reported less than 25–50% of all respiratory fistula cases. Aetiologies of acquired BEF are divided into malignancy and non-malignancy (benign BEF). The latter is usually caused by infection and trauma.

Case Report: A 40-year old female was referred by regional hospital doctor with previous diagnosis of mediastinum tumour. Four months before the referral patient had recurrent lower respiratory tract infection with symptoms of intermittent shortness of breath accompanied by chest pain and fever. Breathlessness has usually appear after eating or drinking. She expectorated thick white phlegm that sometimes turned to yellowish and odor. She ate and drank less, her body weight drastically decreased. Two months before the referral, patient have ever diagnosed as pulmonary tuberculosis and received anti-tuberculosis therapy, but it was just taken for 2 weeks, she discontinued herself. Multi-Slice Computed Tomography thorax result indicated the presence of mediastinal cystic mass accompanied by a 6.8 mm hole defect located on posterior of bronchial wall of left main bronchus. Bronchoscopy showed a fistula on the left main bronchus located 1 cm distal to the carina. Endoscopy showed a fistula on one-third upper of the esophagus. Thoracotomy surgery was performed and para-esophageal abscess was found. It followed by abscess incision and repair of esophagus and bronchial fistula. The pus acid fast bacilli smear revealed positive. Repeated bronchoscopy after surgery showed left bronchial fistula have closed. Patient received antituberculosis therapy. Two weeks after initial treatment, she returned with symptoms of nausea, vomiting and increased of liver enzymes and bilirubin. We managed her by giving Drug Induced Hepatitis treatment. She experiences improvement.

Conclusion: Benign acquired BEF is a rare case. We present acquired BEF that caused by tuberculosis infection. It coped well by thoracotomy surgery for repairing fistula and abscess incision, followed by antituberculosis management.

P-K-034

P-K-036

BRAIN METASTASES OF MALIGNANT TERATOMA

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Background: Mediastinum is the most frequent extra gonad germ cell tumours. Malignant germ cell tumours of the mediastinum account for 1–6% of mediastinum tumours. Metastases germ cell tumours to distance sites such as lungs, liver or bone are 20–50%. Incidence of brain metastases malignant teratoma is 6.2%. Here is a case of malignant mediastinum teratoma metastases to the brain with a history of craniotomy.

Case: A 18 years old male presented with shortness of breath for 2 weeks. He had performed chest X-ray and computed tomography (CT) scan which suggested mediastinum tumour. Histopathology revealed germ cell tumour. The laboratory finding showed increased of alfa feto protein (AFP) level of more than 400 IU/ml and level of beta human chorionic gondotropin (β -HCG) was 132.5 IU/ml. He had performed the first and second chemotherapy with cisplatin 35 mg and etoposide 170 mg. Shortness of breath worsened, accompanied by superior vena cava syndrome, and he was treated with neo adjuvant chemotherapy by etoposide 180 mg and carboplatin 550 mg. He had performed thoracotomy despite high level of AFP. Histopathology result from thoracotomy was mature teratoma. He defaulted from his chemotherapy. Then he visited a neurologist with bump on his head. He did not tell his history of lung disease to the neurologist. Then he performed craniotomy with malignant teratoma as a result. He had consulted a pulmonologist with diagnosis of germ cell carcinoma mediastinum metastases to the brain and planned second line chemotherapy but the patient's condition become worsened so chemotherapy was delayed.

Conclusion: Malignant teratoma metastases to the brain is rare. Patient was already diagnosed with teratoma. He had performed chemotherapy and resection. He did not come according to the schedule, and when he came back, he was found with a bump on his head. Craniotomy had been performed with unknown previous history of lung disease. He died prior to the second line chemotherapy.

INTRALOBAR SEQUESTRATION CASE DIAGNOSED INTRAOPERATIVELY

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Pulmonary sequestration is the lung tissue that has no connection to the normal tracheobronchial tree and has an abnormal aberrant vascular structure. Presentation with bronchiectasis is rare. We want to present a case that has bronchiectasis of the posterobasal segment of the left lung that was diagnosed as intralobar sequestration intraoperatively. A 21 year old man was admitted to our clinic with the complaints of cough. Thorax ct revealed saccular bronchiectasis in the posterobasal segment of the left lower lung. Frequent lower respiratory tract infection was found in the medical history of the patient. Left thoracotomy was performed to the patient with the diagnosis of bronchiectasis. There was dense adhesions in the posterobasal segment area. While dissecting the area, we saw an aberrant vascular structure originating from the thoracic aorta and finishing in the posterobasal segment. Vascular structure was dissected and secured with non absorbable suture material and cut. Wedge resection was performed to the sequestered lung parenchyma. After the operation, thorax ct was retrospectively evaluated paying special attention to the thoracic aorta adjacent to the lesion. This careful evaluation revealed that the aberrant vascular structure was overlooked. Pulmonary sequestration is a congenital malformation of the lung that has a ratio of 0.15–6.4% in all pulmonary malformations. It has a predominance of left lower lobe occurrence. Radiologically, pulmonary sequestration is generally seen as lung masses. Wei and Li have found a ratio of %1.9 patients presented with bronchiectasis in their series of 1106 cases. Surgical resection should be done for preventing the complications. Massive bleedings can occur if the aberrant vascular structure is overlooked during dissection. Sequestration of the lung must be kept in mind in especially the bronchiectasis of the posterobasal segment of the left lower lobe. In our case, careful dissecting of dense adhesions prevented the abundant bleeding.

P-K-037

RESECTABLE INTRALOBER PULMONARY SEQUESTRATION ACCOMPANIED REPEATED FEVER

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Preface: Pulmonary sequestration is a rare anomaly, which does not have a connection with the bronchial system and has blood supply from the aorta or its branches. Pulmonary sequestration should be resected for preventing infection or after having controlled infection. We experienced one case of the pulmonary sequestration in a lobe of the left lung found by a repeated pneumonia symptom.

Case: A 58 year old man had a diagnosis of left pneumonia, a pulmonary abscess and was treated with antibiotic. Because his inflammation repeated, he was referred to our hospital for further examination and treatment. Contrast CT and 3D-CT showed a cyst of greatest dimension 60 mm in the inferior lobe of left lung. Because one aberrant artery arised from descending aorta, we had a diagnosis of pulmonary sequestration. In the compartmentation lung region, the normal bronchus did not accept it. We perform a left base of lung area resection. Aberrant artery of diameter 7 mm diverged from descending aorta and was resected using stapling device. The compartmentation lungs existed in the inferior lobe of left lung. No malignant finding was found. He was discharged at 7th operative days with no remarkable event.

Summary: Because we experienced one case of the intralobar pulmonary sequestration that was caught in fever by main complaint, we report some consideration from literatures.

P-K-039

AGGRESSIVE SURGICAL STAGING FOR A PATIENT WITH MALIGNANT MELANOMA SHOULD BE DONE WHEN REQUIRED: A CASE REPORT

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Introduction: Malignant melanoma is a neoplastic disease with increasing incidence and the treatment is challenging when metastatic disease is present. The treatment option is determined according to stage of the disease.

Case Report: A 23-year-old man admitted with the resection of malign melanoma from preauricular area and staging results of primer lesion with PET-CT after resection. There were two pathologic FDG-uptake in separate body location; left axillary area and superior-anterior mediastinum. The PET-CT findings should be confirmed with histopathologically. Dynamic-CT-angiography revealed a 4.5 cm diameter lesion with heterogen density and smooth margine that had no invasion to the wall of main pulmonary artery and assending aorta. He underwent exicion of left axillary lymph node and thymic lesion. The exicion of thymic lesion started via VATS and the thymus was removed. The thymic area was explored with thoracoscope after exicion and we determined that the pericardium was intact and the lesion was under the pericardium and it was not originating from thymic tissue. The lesion was not biopsied or resected at this time. It was completely resected after ten days from his first operation by a cardiovascular surgeon. The histopathologic examination of the resected specimens revealed that non-malignant left axillary lymph node and thymus tissue and paraganglioma for intrapericardial lesion. The patient was staged as an early disease and no adjuvant therapy was planned.

Conclusion: The patient with very different SUV-Max value in the PET-CT should be confirmed with histopathologically even if it is required aggressive surgical approach.

P-K-038

SPONTANEOUS HEMOPNEUMOTHORAX DUE TO FIBROUS TISSUE EXTENDING FROM THE CHEST WALL TO THE LUNG

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Hemopneumothorax is especially associated with thoracic trauma. Apart from trauma, it is rarely associated with spontaneous pneumothorax. We here want to present our spontaneous hemopneumothorax case due to fibrous tissue extending from the chest wall to the lung. A 20 year old man was admitted to our department with complaints of dyspnoea and chest pain. The physical examination of the patient revealed diminished breath sounds in the right hemithorax and hypersonority on percussion. The thorax ct of the patient revealed hydropneumothorax and fibrous tissue extending from the chest wall to the lung. Right tube thoracostomy was performed. After the tube insertion, 500 cc hemoragic effusion and air are drained. Air leakage was finished after tube insertion and the control X- ray showed full expansion of the lung. No more drainage was seen during follow up. The whole blood count was normal at the time of the tube thoracostomy and on the control blood count. The patient was discharged after four days. Spontaneous hemopneumothorax is rarely seen when compared with spontaneous pneumothorax. Hemothorax is caused by the tearing of the adhesions between the lung and chest wall. Physicians should keep in mind that bullous lung with pleural irregularity can cause spontaneous hemopneumothorax due to the adhesions.

P-K-040

A CASE REPORT: KIKUCHI-FUJIMOTO DISEASE IN AN INDONESIAN BOY

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Kikuchi-Fujimoto Disease (KFD) is a rare disease and it is a benign and self-limited disorder. Characterized by regional cervical lymphadenopathy. Differential diagnoses should include malignant lymphoma, infectious diseases such as toxoplasmatic lymphadenitis, tuberculous lymphadenitis and cat scratch disease, and systemic lupus erythematosus (SLE). Here, we report an Indonesian boy patient who is 19 years old. A Surgion refer patient with lymphadenitis (nodes in the bilateral inguinal regional). The patient had no respiratory symptom or other systemic symptoms such as weight loss, fever or night sweats, but he had history as treated pulmonary tuberculosis 2 years ago. We evaluated serial Chest x-ray from 2010 and thorax CT, it were normal apperance. However, we also performed tests to rule out SLE, malignant, and infectious diseases, and results were negative. Diagnosis KFD have confirmed by analysis of samples from an excisional biopsy of the left inguinal lymph nodes. Regular follow-up for 6 months is done and he has a good condition without any treatment for KFD.

P-K-041

ATYPIC CARCINOID MEDIASTINAL TUMOUR WITH MYASTHENIA GRAVIS AND SUPERIOR VENA CAVA SYNDROME

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We report a case of 29 year old female with Atypic Carcinoid Mediastinal Tumour with Superior Vena Cava Syndrome (SVCS) and myasthenia Gravis (MG). She was present to our Emergency Department experiencing haemoptysis for a week, sore throat, dysphagia and dyspnoea with limited activity. Laboratory finding showed phosphat alkali 70 U/L and LDH 744 U/L. Thoracic Computed Tomography scan showed massive mass in right into dominant left hemithorax. She underwent core biopsy of mediastinum area. Histopathology of the specimen confirmed malignant cells that formed islands limited with septae of fibrotic connective tissue with small-round and uniformed nucleus. Perivascular space also found. Patient was suggested to undergo immunohistochemical smear. We've done neoadjuvant therapy. Electromyography confirmed positive Harvey Masland test.

P-K-043

BILATERAL PRIMARY SPONTANEOUS PNEUMOTHORAX IN A 16-YEAR OLD MALE

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Primary spontaneous pneumothorax (PSP) is defined as the spontaneously occurring presence of air in the pleural space in patients without clinically apparent underlying lung disease. PSP typically occurs in young, tall, lean men, especially smokers, and arguably results from the rupture of subpleural blebs or bullae. PSP is a rare, with an annual incidence of 7.4 to 18 per 100,000 in male population and 1.2 to 6.0 per 100,000 in female population. Bilateral PSP in the absence of other disease is very rare, approximately 5% of patients. We reported a case, 16-year old male presented to the hospital with a sudden onset of breathlessness at rest. There are no history of asthma or chronic cough. He was a occasionally smoker. On physical examination the patient was lean with body mass index (BMI) 17.1. The trachea was in the midline. The lung fields were bilaterally hyperresonant and breath sounds were diminished equally on both sides. His chest x-ray (CXR) revealed bilateral pneumothorax with slightly collapse of lung. After an insertion of bilateral chest tube with water shield drainage (WSD), the chief complained quickly resolved and there was an improvement on control CXR.

P-K-042

REFERENCE EQUATION FOR THE SIX-MINUTE WALK TEST IN HEALTHY FILIPINO ADULTS

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Background: The six-minute walk test (6MWT) is a practical and simple test to assess objectively a person's functional capacity. Studies on published normal reference equations for healthy Caucasians were found to be higher than other ethnic groups. There is no published reference equation for healthy Filipino adults using the 2002 American Thoracic Society Guidelines on 6MWT. **Objective:** The aim of this study were to measure total distance walked during six minutes for healthy Filipino adults aged 35–65 years old and to establish a reference equation for 6MWT in Filipino adults.

Materials and Methods: Age, gender, height, weight, baseline FEV1 and FEV6 were recorded. Level of physical activity was assessed using the Rapid Assessment of Physical Activity (RAPA) score. The 6MWT was then administered to 53 healthy volunteers (47% males) ages 35–65 years.

Results: The median distance walked was 536 m for women and 594 m for men ($p = 0.001$). The 6MWD was significantly less for shorter men and women, no matter the age. Heavier women were also found to have a shorter 6MWD. The resulting gender-specific regression equation for healthy adults are: for women, $6MWD = (-264.534) + (-1.07 * \text{Age}) + (6.31 * \text{height}) + (-2.158 * \text{weight})$ and for men, $6MWD = (1147.406) + (0.152 * \text{Age}) + (-3.049 * \text{height}) + (-0.701 * \text{weight})$.

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P-K-044

TRANSBRONCHIAL NEEDLE ASPIRATION (TBNA) IN THE EVALUATION OF AIRWAY LESIONS

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Objective: Diagnosis and staging of bronchogenic carcinoma remains by far the most common application of transbronchial needle aspiration (TBNA), but there is considerable potential for growth in other fields. We performed this study to compare the results of TBNA with forceps biopsy in the evaluation of endobronchial lesions.

Method: Patients with centrally located pulmonary lesions who were scheduled for flexible bronchoscopy, were enrolled in the study. Three TBNA specimens and three separate direct forceps biopsies (FB) were obtained from each lesion. The bleeding rate and pathologic results were compared with each other.

Results: FB was diagnostic in 89% of patients (17/19). TBNA showed malignant/atypical cells in 71.4 percent of those with malignancy on FB. In 2 cases with Unremarkable FB results, TBNA revealed malignant/atypical cells. No pneumothorax was detected. There was a mild bleeding in 12 (63.2%) cases after FB that stopped spontaneously without any intervention. No significant bleeding occurred after FNAB.

Conclusion: Obtaining additional samples from endobronchial lesions during bronchoscopy by FNAB, will increase diagnostic yield without adding any significant risk to the patient. This method could be useful particularly in haemorrhagic endobronchial lesions.

P-K-045

PARATRACHEAL CYSTS AS A POSSIBLE CAUSE OF CHRONIC COUGH

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Introduction: Paratracheal air-filled cyst, characterized by invagination of tracheal wall, is an infrequently encountered disease entity. It is usually asymptomatic, but can have nonspecific manifestations such as globus sensation in the throat, haemoptysis, swallowing difficulty, hoarseness and cough. The authors studied the patients complaining of chronic cough without other apparent causes except paratracheal cyst.

Materials and Methods: We retrospectively reviewed the charts of patients with chronic cough who underwent chest CT, gastrofibroscopy and otolaryngologic evaluation between 2011 and 2013. Cases showing asthma, lesions of pulmonary parenchyma, reflux esophagitis, sinonasal and laryngeal diseases were excluded.

Results: Among the patients included in this study, 4 have paratracheal cyst. All cysts have communicating channel with trachea and are located on the right side of trachea posterior to the thyroid gland. Mean size of cysts is 2.5 x 2 cm. One patient underwent surgery for removal of the cyst. After operation the patient's symptom had much subsided. The others were taking medication with regular follow-up.

Conclusions: Paratracheal air-filled cysts can be a cause of chronic cough in some patients. Because the cysts are usually formed by increased thoracic pressure, it is not clear whether the cysts are the cause or the consequence. In some cases surgical removal alleviating the symptom, it could be thought there is a vicious cycle between chronic cough and paratracheal cysts. To clarify the relationship, more investigations are required.

P-K-046

INFLUENCE FACTORS OF AGE AND PULMONARY FUNCTION DECREASED OXYGEN SATURATION AT ELEVATIONS ABOVE 8000 FEET IN AIRCRAFT

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Background And Objective: Changes in air pressure, temperature and atmospheric humidity on altitude will result in a decrease of oxygen partial pressure, the more dry air around, and a decrease in oxygen saturation will interact with the oxygen dissociation curve. This condition will eventually has a negative impact and disruption to the body's physiological functions due to hypoxaemia. The aim of this study is to determine the effect of the age factor to the decline of pulmonary function and oxygen saturation at elevations above 8000 feet in the air plane.

Methods: This is a quasi experimental study assessing the influence of age and lung function decline of oxygen saturation of the subjects before and during the flight. The variables in this study consist of age, pulmonary function, smoking history, respiratory complaints, chest X-ray and haemoglobin values. Before flying oxygen saturation measured by pulse oxymetry, pulmonary function with spirometry, smoking history and respiratory complaints over data charging, chest X-ray examination and haemoglobin value Hb through Sahli. Then while flying at an altitude of 8000 feet applied oxygen saturation changes re-measurement. The data were analyzed descriptively to see the distribution frequency of each variable. Chi-square statistical analysis (chi-square) was performed to examine the relationship between variables.

Results: A total of 34 samples passenger aircraft in flight two times were obtained, aged 20–40 years, described as 29 men and 5 women. The entire samples of passenger aircraft's oxygen saturation decreased by 3–5% at altitude of 8000 feet into a range between 88–93%. Based on chi-square test found that the decrease in oxygen saturation were not statistically associated with the age factor ($p = 0.441$), history of smoking ($p = 0.699$), pulmonary function status ($p = 0.301$), respiratory complaints ($p = 0.775$), chest X-ray ($p = 0.094$) and haemoglobin values ($p = 0.473$).

Conclusions: Travelling with airplane results a decreasing in oxygen saturation in accordance with the height of the flight. The decrease in oxygen saturation is not influenced by age and lung function, but based on the oxygenation state of the atmospheric air in accordance with the level of altitude in flight.

P-K-047

A CASE REPORT: PULMONARY LANGERHANS' CELL HISTIOCYTOSIS

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Introduction: Langerhans cell histiocytosis (LCH) is a rare disorder of unknown origin. The disease can regress spontaneously or with glucocorticoid therapy, or is characterized by severe manifestations, recurrent pneumothorax, progressive respiratory failure, chronic cor pulmonary and death. Over a 10-year period, only 4 cases of LCH have been identified at Pham Ngoc Thach (PNT) Hospital, Ho Chi Minh City, Vietnam.

Case Presentation: We report a case of pulmonary Langerhans' cell histiocytosis diagnosed and treated at PNT Hospital. A 16-year-old young man presented at palliative care unit (department A4) with chief symptoms of dry cough and shortness of breath during the last 2 months. He reported a history of coughing and exertional dyspnea during the last year. He is a pupil and has smoked half a packet of cigarettes daily for the last two and a half years. On physical examination, right pneumothorax was detected whereas the other organs were normal. No abnormalities were detected in blood tests. White blood cell count was 8,460/mm³ and haemoglobin level 14 g/dl. The other routine blood tests were all in normal ranges. Sputum smears for AFB and HIV testing were negative. Chest radiography showed right pneumothorax and reticulonodular shadows distributed in both lungs. Chest CT scan showed right pneumothorax together with multiple thin wall cysts with diameters of 1–1.5 cm and lesions of centrilobular nodules, predominately involving upper lobes in both lungs. Lung function test showed moderate restrictive pattern. Bronchoscopy was normal and transbronchial biopsy of the middle lobe was done but nothing specific was detected with the sample. Video-assisted thoracoscopic biopsy of the lung was performed and histological result showed hyperplasia of lung tissue including histiocytosis, langerhans cells with elongated shapes, bright and kidney-like nuclei forming clusters, and multinucleated giant cells. By immunohistochemical staining, monoclonal antibodies directed against LCA, CD68, CD1a and S.100 were observed. Clinical manifestations, chest CT scan, and pathological and immunohistochemical findings confirmed the diagnosis of Langerhans's cell histiocytosis. Drainage and pleurodesis were performed to manage pneumothorax. Smoking cessation was required. Prednisone at a starting dose of 30 mg was given daily and after 1 week of treatment, the patient got well and was transferred to palliative care clinics for follow-up.

Conclusion: Pulmonary Langerhans' cell histiocytosis should be considered in male patients with history of heavy smoking, symptoms of dry cough and dyspnea, and with specific images on chest radiography and CT scan. The disease is confirmed by biopsy of the lung with pathological characteristics.

P-K-048

P-K-049

SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF QGE031, A HIGH AFFINITY ANTI-IgE ANTIBODY IN CAUCASIAN AND JAPANESE ATOPIC SUBJECTS

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Background: QGE031 is a humanized anti-IgE antibody with approximately 50-fold higher affinity than omalizumab. We report the safety, pharmacokinetics (PK) and pharmacodynamics (PD) data from three phase I dose-escalation studies in atopic but otherwise healthy Caucasian and Japanese subjects.

Methods: All three studies were double-blind, randomized and placebo-controlled. Two of these studies enrolled Caucasian subjects aged 18–55 years. In one study, subjects received single escalating intravenous (IV) doses of 0.1–10 mg/kg QGE031 (n = 36), placebo (n = 29) or subcutaneous (SC) omalizumab (n = 8) in 7 cohorts. In the second study, subjects received multiple ascending SC doses of 0.2–4 mg/kg QGE031 (n = 70), placebo (n = 28) or open-label SC omalizumab (n = 12) in 6 cohorts. The third study enrolled Japanese subjects (20–55 years) who received single ascending SC doses of 0.6, 2 and 4 mg/kg QGE031 (n = 24) or placebo (n = 8) in 3 cohorts. Safety, tolerability, PK, free and total IgE, basophil FcεRI and surface IgE expression and, in the second study, skin prick testing (SPT) outcomes were evaluated.

Results: Adverse events (AEs) across studies [Caucasian IV: 59%, Caucasian SC: 66%; and Japanese SC: 50%] were mild to moderate in severity with no significant imbalances between cohorts. No deaths or serious AEs occurred across studies. Discontinuation rates in Caucasians were 17.8% (unrelated to AEs) in IV and 12% in SC studies, respectively, and none in the Japanese study. In the Caucasian SC study, two subjects receiving 2 mg/kg QGE031 discontinued due to AEs (unrelated to drug). Overall, nine urticarial events occurred in 8/215 subjects (Caucasian IV: 4 events [3-QGE031 highest doses and 1-placebo]; Caucasian SC: 4 events [1-QGE031 0.6 mg/kg and 3-placebo {1 subject had 2 events}]; Japanese SC: 1 event [QGE031 2 mg/kg]). Systemic exposure and half-life were dependent on the dose of QGE031 and baseline IgE across studies. QGE031 reduced free IgE below the quantification level for all doses, except for 0.6 mg/kg in Japanese study, and elicited dose- and time-dependent suppression of basophil FcεRI and surface IgE expression and SPT responses. QGE031 showed an 8.9-fold increase in PK-PD potency (95% CI: 6.1–14 fold) than omalizumab in the IV and SC studies. The extent and duration of PD effects were dependent upon QGE031 dose and baseline IgE, but robust PD responses were observed in all groups including those with high baseline IgE.

Conclusion: QGE031 was well tolerated with no serious AEs and reduced free circulating IgE, FcεRI, surface IgE, and SPT responses which were greater and for a longer duration than placebo and omalizumab.

PRESENCE OF FRAGMENTED QRS COMPLEXES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: Obstructive Sleep Apnea Syndrome (OSAS) is a disease with increasing prevalence, which is mainly characterized by increased cardiopulmonary mortality and morbidity. It is well-known that OSAS patients have increased prevalence of cardiovascular diseases including coronary heart disease, heart failure, and arrhythmias. The aim of this study was to evaluate the presence of prolonged and fragmented QRS complexes, which have previously been associated with cardiovascular mortality, in OSAS patients.

Methods: Our study included 51 patients (mean age 41.6 ± 10.1 years) who were recently diagnosed with OSAS [Apnea Hypopnea Index (AHI) ≥ 5 events/h] and never received therapy. The control group consisted of 34 volunteers (mean age 43.1 ± 11.6 years) in whom OSAS was excluded (AHI < 5 events/h). From 12-lead electrocardiogram and the QRS complexes the most prolonged QRS complex was calculated and any fragmentation in QRS complexes was sought.

Results: QRS and QTc durations were significantly longer in OSAS patients than controls (99.8 ± 13.9 ms vs. 84.7 ± 14.3 ms, p < 0.0001; 411.4 ± 26.9 ms vs. 390.1 ± 32.2 ms, p = 0.001, respectively). Fragmented QRS frequency was significantly higher in patients with OSAS [n = 31 (61%) vs. n = 12 (35%), p = 0.021]. Analysis of the patient and controls groups combined revealed a weak correlation between AHI and QRS duration (r = 0.292, p = 0.07). OSAS group had no correlation between AHI and QRS duration (r = -0.231, p = 0.203).

Conclusions: In our study fragmented QRS frequency and QRS duration were found to increase in OSAS patients. Both parameters are related with increased cardiovascular mortality in OSAS. Considering the prognostic importance of electrocardiogram parameters, it may be reasonable to recommend more detailed evaluation of OSAS patients with fragmented or prolonged QRS complexes with respect to presence of cardiovascular diseases.

P-K-050

AIRWAY STENTING IN PATIENTS WHO REQUIRE INTUBATION DUE TO MALIGNANT AIRWAY STENOSIS

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Background: Airway stenosis often causes a life-threatening condition. Critically ill patients with severe acute respiratory failure often require emergency intubation and mechanical ventilation.

Aims and Objectives: To investigate the efficacy and safety of airway stenting in patients with malignant airway stenosis who needed emergency intubation.

Methods: Patients with malignant airway stenosis who underwent emergency intubation prior to airway stent placement from April 2004 to October 2013 in a single centre were retrospectively reviewed. All stenting procedures were performed using both rigid and flexible bronchoscopes under general anaesthesia.

Results: We have performed 414 airway stenting procedures for 359 patients during the study period. Of the patients, 24 (20 male, 4 female; median age, 61 years; range, 13 to 86 years) with malignant airway stenosis (14 lung cancers, 5 esophageal cancers, 5 others) required emergency intubation prior to stenting procedures (silicone stenting in 20, metallic stenting in 4). Extubation within 48 hours after stenting could be performed in 23 of 24 patients (96%). In the 16 chemoradiotherapy naive patients, 14 patients (88%) received chemotherapy and/or radiation therapy after stenting. Retention of secretions which required stent removal and tracheostomy occurred in 1, and granulation tissue formation which required bronchoscopic resection occurred in 1. Median survival after stenting was 181 days (range 13–2255 days).

Conclusions: Airway stenting facilitates extubation in critically ill patients with malignant central airway stenosis. It is also useful for chemoradiotherapy naive patients as a bridge to additional therapies.

P-K-051

UNPLANNED EXTUBATION HAS AN IMPACT ON PATIENTS WHO USED MECHANICAL VENTILATOR IN THE INTENSIVE CARE UNIT

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Unplanned extubation (UE) which could cause airway problems, is a common event in the intensive care unit (ICU). Numerous studies on UE has shown 5–28% the morbidity rate. UE could lead to an increase in the days of mechanical ventilator use, ICU stays and hospitalization days; it was also proportional to the mortality rate and might require chronic care. Moreover, patients who suffered from UE and failed to tolerate would increase the hospital's expenditure. Factors of predicting re-intubation include higher acute physiological and chronic health evaluation (APACHE II) score, higher pre-extubation fraction of oxygenation (FIO₂) level, full ventilator support mode and pneumonia. For the above reasons, we investigated the incidence, outcome, and predictive factors in patients who suffered failed UE and the expenditure of UE failure in the adult ICU.

P-K-053

ARE PATIENTS WITH BIOPSY-PROVEN NON-ALCOHOLIC FATTY LIVER DISEASE AT INCREASED RISK OF ASTHMA? – RESULTS FROM A TURKISH CROSS-SECTIONAL STUDY

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The prevalence of both bronchial asthma and non-alcoholic fatty liver disease (NAFLD) has been steadily increasing over the last several decades. Insulin resistance represents the pathophysiological hallmark of NAFLD. Notably, it has been also recently reported that insulin resistance may play a crucial role in the pathogenesis of bronchial hyperreactivity. However, cross-sectional and longitudinal studies have shown conflicting results about the association of insulin resistance with asthma. Moreover, the question as to whether NAFLD patients have an excess risk of asthma remains open. The purpose of this study was to examine the prevalence of asthma in a hospital-based cohort of patients with biopsy-proven NAFLD. A total of 91 patients with NAFLD (43 males and 48 females; mean age, 46 ± 8 years) consecutively seen at our hospital-based specialized outpatient clinics were enrolled. Ultrasonography-guided liver biopsies were performed under conscious sedation using a 16-gauge Hepafix needle in all participants. The diagnosis of asthma was made in presence of a positive history of one of the following conditions: (1) a hospitalization for asthma (ICD-10 code: J45); or (2) an outpatient admission coded ICD-10 J45 within the last 12-month period; or (3) prescriptions for a known asthma medication within the last 12-month period. Using this definition of asthma (which is characterized by a high positive predictive value), we identified 5 NAFLD patients with a diagnosis of asthma. Therefore, the prevalence rate of asthma in our biopsy-proven NAFLD patients was 5.4%. According to the lifetime asthma prevalence percents by age collected in the United States during the National Health Interview Survey 2012, the prevalence rates of asthma in the adult population aged 35–64 years and 65 years or over are 12.4% and 10.4%, respectively. The findings from this study indicate that there is no strong relationship between biopsy-proven NAFLD and the prevalence of asthma. Against expectations, asthma prevalence was even lower in our NAFLD patients than that reported in the USA general population. However, the negative results of the present study must be interpreted with caution. Due to the small number of patients and the absence of a control group, the study may be under-powered to find some true but small differences in asthma rates between NAFLD patients and patients without overt liver disease. Another reason for the negative results of the study may be the highly selected study group (i.e., subjects referred to a specialized outpatient hepatology clinics).

P-K-052

THE SEASONAL CHANGE OF THE SELF ASSESSMENT OF ALLERGIC RHINITIS AND ASTHMA QUESTIONNAIRE (SACRA) IN JAPAN

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Background: Allergic rhinitis(AR) is commonly accompanied with asthmatics, and may impair bronchial asthma(BA) control. It is also reported that the control of AR and BA may be related with season, especially spring in Japan when cedar pollens impair AR control.

Objective And Methods: To investigate the seasonal change with symptoms of AR and BA, we used SACRA and asthma control test(ACT) for 36 asthmatics during period 1(P1 :from January to April, 2013), and period 2(P2: from August to November, 2013). We compared between AR and BA symptoms in P1 and those in P2.

Results: 20 cases(55.6%) have AR symptoms, and there are more severe cases with AR symptoms during P1. The cases with symptoms with AR both during P1 and P2 are tend to have more severe symptoms with BA. Visual analogue scale(VAS) of AR symptoms is significantly correlated with VAS of BA symptoms.

Conclusion: AR symptoms are closely related with those of BA and SACRA is the useful to evaluate both symptoms.

P-K-054

P-K-056

THE PHYSICAL FUNCTION AND MENTAL STATUS IMPAIRMENT WITH ASTHMA CONTROL IN THE ELDERLY

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Background: Poor control asthma is common in older asthmatics. We hypothesized whether physical and cognitive function impairment contributing to inhaler device uses is associated with uncontrolled asthma.

Methods: Prospective study in older asthmatics (≥ 60 years) at chest clinic. Measurement of cognitive function by using Montreal Cognitive Assessment (MOCA), handgrip power using dynamometer and peak inspiratory flow rate (PIFR) regarding different inhalers using In-CheckDial®. The presence of hand arthritis and tremor were recorded. Asthma control was assessed by using ACT®.

Result: Total 40 asthmatic participants having mean age of 71.5 years. Women were 67.5% and mean age of asthma onset was 48.8 year. Mean ACT score was 20.8 (4.1). Approximately 40 % of them experienced exacerbation in the past year. Older patients were classified uncontrolled asthma ($ACT \leq 19$) in 32.5%. Furthermore, mean MOCA was 22.2 (5.3) hence one-third was diagnosed cognitive impairment based on MOCA (≤ 26). Hand arthritis and tremor were observed in 40% and 10%. Mean handgrip strength per kg body weight ratio was 0.36 (0.1) and considered low in 57.5% of them. Regarding inhalers, accuhaler, tubuhaler and pMDI were used in 32.5, 22.5% and 40% of patients therefore mean PIFR were 89.1, 65.7 and 104.3 L/min respectively. Older asthmatics were considered having optimal PIFR (≥ 60 L/min) in 77.5%. Uncontrolled asthma was not associated with impaired cognitive function, low handgrip strength, the presence of arthritis and low PIFR for different inhalers. However, only the presence of tremor was associated with uncontrolled asthma and exacerbation history.

Conclusions: Substantial numbers of older asthmatics suffered from uncontrolled disease and exacerbation. Neither cognitive nor physical impairment was associated with uncontrolled asthma.

IMPACT OF THE AIR POLLUTION EPISODE ON PREVALENCE OF ASTHMA ON KUWAITI SCHOOL CHILDREN BORN ABOUT THE TIME OF THE WELL FIRES

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Introduction: At the end of the Gulf War in 1991, more than 700 oil wells in Kuwait were set on fire, causing significant pollution to the local environment. Our study wants to document the impact of this pollution on the population of children born around that period of time.

Objectives: To compare the prevalence of bronchial asthma in 6–7 years old school children in Kuwait between the children born during the Gulf war, who were exposed in new-born and early childhood period to the oil fires of Kuwait in 1991, and a population of 6–7 years old children born in Kuwait about 10 years later.

Methods: Parents of students at first and second years from 40 primary level schools chosen randomly across Kuwait completed written questionnaires of the International study of asthma and allergies in childhood (ISAAC).

Results: 2117 (45% females) students were surveyed in 1997 and 2079 (47.6% females) in 2007. The prevalence rates (with 95% CI) for physician diagnosis of asthma were 16.7% in 1997 and 4.2% in 2007.

Conclusion: Prevalence of bronchial asthma differs regionally and has a slightly growing tendency worldwide. Kuwait has a moderate prevalence of asthma in school children according to ISAAC criteria. Our survey documented a significant decrease in asthma prevalence in 6–7 years old children in Kuwait in the period of 10 years. We draw conclusions that the higher prevalence of asthma in the children population in 1997, compared to a similar population in 2007, may be the effect of the oil fires polluting the Kuwait environment during their neo-natal age and early childhood.

P-K-057

INFLUENCE OF MENTAL DISORDERS ON ASTHMA CONTROL

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The control of symptoms is the main idea of the treatment of patients with bronchial asthma. But there can be some psychological factors that hamper the achievement of asthma control.

Aim: To study the influence of mental disorders on asthma control.

Methods: 179 asthmatics (78% of them were women) at the age of 21–69 (on average 44 ± 1.2 years old) were examined. The mean duration of the disease was 6 ± 0.8 years. Asthma Control Test (ACT), self-questionnaire Center of Epidemiological studies of USA-Depression (CES-D) and the questionnaire Symptom Checklist-90-Revised by L.R. Derogatis (SCL-90-R) were used.

Results: The patients were divided into groups according to the severity degree and asthma control level. The 1 group included 77 patients with controlled mild and moderate asthma (1:1). The second group consisted of 102 patients with uncontrolled mild (14%), moderate (66%) and severe (20%) asthma. The groups were identical in terms of sex and age. By the tests data the majority of patients had definite disorders in the mental sphere of the pathologic level. The patients of the second group had higher than in the first group mean values of the scales of somatization (SOM) and hostility (HOS) by SCL-90-R test and of depression by CES-D test. 23 patients were found to have clinically apparent depression. The level of BA control correlated negatively with the values of the scales of SOM ($r = -0.46$) and O-C (obsessiveness – compulsiveness, $r = -0.29$) of SCL-90-R test.

Conclusion: Asthma control depends on the presence and intensity of emotional disorders (depression and hostility) and the tendency to have obsessive-compulsive symptoms. Besides, the control degree gets lower as the severity of the disease grows. To improve asthma control, it is necessary to take some preventive actions about the emotional state of asthmatics and timely identify and correct mental disorders.

P-K-055

ANALYSIS OF GROWTH FACTORS IN SERUM AND INDUCED SPUTUM FROM PATIENTS WITH ASTHMA

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Background: Epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), AA isoform of platelet-derived growth factor (PDGF-AA), BB isoform of platelet-derived growth factor (PDGF-BB) and vascular endothelial growth factor (VEGF) are involved in the pathogenesis of airway inflammation in asthma. This study investigates the relation between asthmatic phenotype and levels of these mediators in induced sputum and serum.

Method: 62 asthmatic patients were divided into eosinophilic and neutrophilic phenotype by cytological classification in induced sputum; groups of $FEV1/FVC\% > 70\%$ and $FEV1/FVC\% < 70\%$ by lung function; mild, moderate and severe asthma by asthma severity. And the concentrations of EGF, bFGF, PDGF-AA, PDGF-BB and VEGF in serum and sputum were measured using sandwich enzyme immunoassays.

Results: VEGF levels in serum and induced sputum were higher in subjects with eosinophilic phenotype than that of neutrophilic phenotype, in patients with $FEV1/FVC\% < 70\%$ than that of patients with $FEV1/FVC\% > 70\%$, in severe asthma than that of mild and moderate asthma. There were no differences of EGF, bFGF, PDGF-AA and PDGF-BB between various phenotypes.

Conclusion: Increased VEGF in serum and induced sputum were found in asthmatics with eosinophilic airway inflammation, more severe airflow limitation and asthma severity.

P-K-058

BRONCHIAL ASTHMA IN NURSING HOMES FOR ELDERLY IN JAPAN: QUESTIONNAIRE SURVEY

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Background: In Japan, about two thousands of asthmatic patients per year have been still died caused by asthma exacerbation. Of those, 1600(89.9%) were elderly patients older than 65 years. Because aging is progressing in Japan, asthma control of the elderly patients is important issue. However, little is known about the prevalence of asthma and asthma medication in nursing homes for elderly in Japan.

Objectives: To investigate the prevalence of asthma and asthma medications in nursing homes for elderly, we had demonstrated the questionnaire survey to nursing homes for elderly in Hyogo prefecture, Japan.

Methods: We had distributed the unique questionnaire survey concerned with elderly facility residents who had diagnosed asthma to 253 nursing homes for elderly in Kobe City, Hyogo prefecture, Japan from July to August 2013.

Results: We had obtained responses from 93 nursing homes for elderly. Of those, responses from 90 nursing homes for elderly were effective. The total number of residents was 6036. Of those, 233 residents (3.69%) were diagnosed with asthma. The prevalence of COPD within the asthmatic patients was 100% (in 6 nursing homes for elderly), 40–60% (in 23 nursing homes for elderly), 0% (in 43 nursing homes for elderly). In 60% of nursing homes for elderly, patients with asthma had received medication about asthma. About 53% of patients with asthma received inhaled corticosteroid (ICS) therapy. In nursing homes for elderly, 53% of patients required some assistance in inhaler technique of ICS. The use of dry powder inhaler (53%) and metered dose inhaler (42%) was more common than metered dose inhaler with spacer (10%) and nebulized dosage (3%). In 31 nursing homes for elderly, some patients experienced an asthma exacerbation. Only in 14 nursing homes for elderly, their staffs can use SABA. In 3 nursing homes for elderly, some asthmatic patients had died caused by asthma attack in the last 5 years. Staffs in nursing homes for elderly felt difficulty in the inhaler technique for elderly asthmatic patients with significant cognitive impairment.

Conclusions: We revealed that the prevalence and medications of patients with asthma in Japanese nursing homes for elderly. Many staffs of nursing homes for elderly had felt that it was difficult for elderly asthmatic patients to inhale ICS. More investigation concerned with asthma medication in nursing homes for elderly may lead to decrease the death related to asthma and the number of asthma exacerbation.

P-K-059

AVIATION PERSPECTIVE, BRONCHIAL ASTHMA: TWO CASES OF ASTHMA ENCOUNTERED IN MILITARY PILOTS

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Background: Asthma is a chronic inflammatory disorder of the airway that characterized by reversal partial obstruction. Chronic inflammation is associated with airway hyper-responsiveness that leads to wheezing, shortness of breath, chest tightness and coughing. Acute asthma exacerbations might lead to sudden incapacitation of pilot. Small airway obstruction can cause profound hypoxia, acceleration induced atelectasis and pulmonary barotrauma. Potential side effects of medication can also deteriorate pilot performance. High demanding environment of aviation needs physical and physiological fitness of pilots. Decision of continuation to flight duties in pilot who has asthma is so important.

Case 1: A 34-year-old male pilot applied in our clinic during periodic examinations. He had symptoms of wheezing, breathlessness, sneezing, excessive tearing in eyes and coughing during spring and fall seasons. These symptoms had lasted for 3 years. Exertion could trigger these symptoms. He didn't smoke before.

Results: Patient was hospitalized and screened for 1 week without medication. He had no complaints in this period. Pulmonary auscultation, chest X-Ray, and pulmonary functions test (PFT) were normal. Reversibility was negative. Complete blood count values and routine biochemistry were normal.

Case 2: A 33-year-old male patient applied in our clinic that had symptoms of wheezing, coughing without sputum and breathlessness. These complaints were seen in May and June for last 3 years. He used salbutamol inhaler when he needed. He had a smoking history of 4 packages year and quitted smoking 1 year before. **RESULTS:** Pulmonary auscultation, chest X-Ray and pulmonary function test were normal. Reversibility was negative. Complete blood count values and routine biochemistry were normal.

Discussion: Decision making in pilots who have asthma is based on type of flying duty and severity of disease. Candidate pilots and high performance aircraft pilots diagnosed with asthma are disqualified. Mild disease that is well controlled by medication may be qualified for flying duties in military transport and helicopter pilots and civil pilots. Although our two cases were diagnosed as mild intermittent asthma, they were decided to be grounded permanently and assigned to other duties.

Conclusion: Occupational requirements should be taking into account evaluation of patient diagnosed asthma as in our case. People who work in especially aviation related job should be examined and evaluated at medical centres specialized in aviation.

P-K-060

P-K-062

DEVELOPMENT OF ALLERGIC DISEASE IS ASSOCIATED WITH CONSUMPTION OF FAST FOODS

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Background: The association between the development of allergic diseases and consumption of certain foods has been reported.

Objective: To evaluate the association between food consumption and development of asthma using nationwide adolescent survey data.

Methods: This study was conducted using the eighth Korea Youth Risk Behavior Web-based Survey (KYRBWS), 2012. KYRBWS is a nationwide cross-sectional survey of health-risk behaviours among Korean middle- and high-school students aged 13–18 years. This survey included 74,186 students who were representative of the entire 3,832,799 Korean students in that age group. For balanced sampling, the survey adopted a complex sample design. The development of asthma was assessed by the question "Were you diagnosed as asthma by physician within past 12 months?" Consumption of specific foods was defined as taking the food more than 5 times a week.

Results: The estimated incidence of asthma, allergic rhinitis and atopic dermatitis were 9.3%, 33.9% and 24.3%, respectively among Korean adolescents. Consumption of fast foods was significantly associated with the development of asthma [odds ratio (OR) = 2.66, 95% confidential interval (CI): 1.99 to 3.55], rhinitis (OR = 1.22, 95% CI: 1.03 to 1.44) and atopic dermatitis (OR = 1.34, 95% CI: 1.08 to 1.65). When the variable was treated as continuous variable, the association between consumption of fast foods and the development of allergic diseases showed significant dose-effect relationship. Consumptions of vegetable, fruits and milk showed no protective effect in this population.

Conclusion: There were significant association with fast foods consumption and the development of allergic diseases in Korean adolescent survey.

P-K-061

FACTORS ASSOCIATED WITH ASTHMA CONTROL AMONG OUTPATIENTS IN BEIJING

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Background: Morbidity of asthma has increased these years and guidelines of many countries emphasize the goal of attaining and maintaining asthma control. Nowadays, level of asthma control, which is affected by multiple factors, is still insufficient. Studies on factors associated with asthma control are rarely conducted in our country. So it's necessary to investigate factors associated with asthma control to provide reference for future intervention.

Objective: To explore factors associated with asthma control among outpatients in Beijing.

Methods: 181 adult asthmatic outpatients visiting respiratory clinic in two tertiary hospitals in Beijing were selected through convenience sampling. Asthma Control Test designed by Nathan was used to measure patients' level of asthma control. Factors associated with asthma control were detected through self-designed general information questionnaire, Knowledge of Asthma/Management Plan designed by the American CDC, self-modified asthma knowledge questionnaire, self-designed avoidance of triggers questionnaire, Horne's Medication Adherence Report Scale for Asthma, inhalation technique checklist from Zhihui Shi and self-designed disease self-monitoring questionnaire. All questionnaires were filled in by patients themselves except for the inhalation technique which was graded by the researcher according to patients' demonstration.

Results: According to the Asthma Control Test, 8.3% patients were classified as completely controlled, 43.1% were well controlled and 48.6% were uncontrolled. Several factors were found to be associated with asthma control in the final logistic regression analysis, including elimination of cockroaches and rats at home (OR, 3.56; 95% CI, 1.37–9.28), smoking cessation and second-hand smoke avoidance (OR, 1.94; 95% CI, 1.03–3.68), medication adherence (OR, 2.30; 95% CI, 1.17–4.55) and recognition of opportunities to visit the doctor (OR, 2.83; 95% CI, 1.19–6.71).

Conclusions: Level of asthma control in this study has not reached the target goal. Patients' certain behaviours of avoiding triggers (such as elimination of cockroaches and rats at home, smoking cessation and second-hand smoke avoidance), medication adherence and recognition of opportunities to visit the doctor were found to be associated with asthma control.

REAL-LIFE EFFICACY OF OMALIZUMAB ADD-ON THERAPY FOR THE TREATMENT OF UNCONTROLLED ALLERGIC ASTHMA: RESULTS FROM THE TAIWANESE SUBPOPULATION OF THE EXPERIENCE REGISTRY

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Introduction: 'eXpeRience' is a post-marketing, non-interventional, observational registry that studied the real-life effectiveness, and safety of omalizumab in patients with uncontrolled persistent allergic asthma. This report presents the results from the subgroup of patients from Taiwan.

Methods: Patients with uncontrolled allergic asthma who started omalizumab within the previous 15 weeks were enrolled in the registry and received omalizumab add-on therapy for 24 months. Changes in physician's global evaluation of treatment effectiveness (GETE), asthma symptoms and control, exacerbations and safety were reported.

Results: Of the 943 patients recruited in the eXpeRience registry, 20 patients were from Taiwan with a mean asthma duration of 16.0 years. At Week 16, Month 8, Month 12, Month 18, and Month 24, the ITT population (patients receiving ≥ 1 dose of omalizumab and had ≥ 1 post-baseline efficacy assessment) included 15, 5, 5, 5 and 2 patients, respectively. While 11 patients completed the registry, 8 patients discontinued (6 lost to follow-up, one patient withdrew consent and one death occurred due to respiratory failure) and the status of one was unknown. At Week 16 (± 1 week), 5/9 patients who had a GETE assessment were observed to be responders with good/excellent physician GETE rating. 4/20 and 16/20 had partly controlled and uncontrolled asthma respectively based on investigator assessment of asthma control. At Month 24, both the patients who had continued omalizumab treatment were assessed as partly controlled. In the week prior to baseline, presence of daytime (16/20), nocturnal (14/20) asthma symptoms, limitation of activities (11/20) and rescue medication requirement (13/20) was reported for the majority of patients. At Month 24, 0/2 patients reported these outcomes in the previous week. In the year before treatment, the mean annualized rates of clinically significant and severe clinically significant exacerbations were 4.2 ($n = 17$) and 1.6 ($n = 16$) compared with 3.3 and 0.7 at Month 12 ($n = 3$), and 3.0 and 0.0 at Month 24 ($n = 2$). A total of 27 serious adverse events were reported in 6 patients, none of which were suspected to be related to omalizumab therapy.

Conclusion: This small sample describes a two year follow-up of Taiwanese patients where a large number of treatment discontinuations and registry drop-outs were observed. Larger sample size studies in Taiwan are recommended that will help better evaluate the real world effectiveness of omalizumab of in patients with uncontrolled persistent allergic asthma.

P-K-063

INVESTIGATION OF CHILDREN'S FOLLOW-UP CONSULTATIONS AFTER EMERGENCY DEPARTMENT VISITS FOR ASTHMA ATTACKS IN LARGE AND MEDIUM SIZED CITIES

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Background: Current Japanese asthma guideline recommend that every child needs follow-up after an emergency department (ED) visit. Early intervention of inhaled corticosteroids (ICS) after ED visits is associated with improved asthma control. The purpose of this study is to investigate asthmatic children's consultation after their ED visits in large and medium sized cities.

Methods: Both the pamphlet about asthma and the consultation report card were given to asthmatic children who visited the ED. The ED open at night and on holidays and have no hospitalization or operation facilities in Kobe (large city: L) and Himeji (medium-sized city: M). The patients gave the consultation report card to the doctor when they received their follow-up consultations after the ED visit. Their doctors sent the filled out consultation report cards to the committee. We analyzed the rate of the follow-up consultations after the ED visits and the prescribed follow-up medication.

Results: The total number of patients was 2785. The number of patients who visited the ED in Kobe was 2140 (0–12 month-old: 645, 2–5 year-olds: 1005, 6–15 year-olds: 482, Age unknown 8). In Himeji, the number of patients was 645 (0–12 month-old: 64, 2–5 year-olds: 334, 6–15 year-olds: 247). The number of patients who visited their ED more than two times was 325 (L: 236, M: 89). The total rate of the follow-up consultation was 49.6% (L: 48.1%, M: 54.7%). The rate of follow-up consultation in patients aged 13 to 15 in both cities were lower than 35%. Most patients received the follow-up consultations the following day after their ED visit. In the case of patients who frequently visited the ED, the total rate of zero follow-up consultation was 18.5% (L: 20.3%, M: 13.5%). Many patients were prescribed Long Acting β_2 Agonist (LABA) (60.3%), Leukotriene Antagonist (LTRA) (59.0%) and Short Acting β_2 Agonist (SABA) (32.9%). The total rate of ICS use was 25.2% (L: 23.8%, M: 29.2%), 0–12 month-olds: 14.7% (L: 14.2%, M: 18.4%), 2–5 year-olds: 19.7% (L: 19.1%, M: 21.5%), 6–15 year-olds: 45.5% (L: 46.1%, M: 44.4%).

Conclusion: The rate of the follow-up consultation was about 50% in both cities. Many patients were prescribed LABA, LTRA, and SABA. The prescription of ICS in the two cities was lower than 30%. The rate of ICS use in the patients aged 6–15 was higher than that in the patients of less than 5 years.

P-K-064

HIGHER BMI AND OBESITY IS ASSOCIATED WITH ASTHMA AND ATOPY IN KOREAN ADULTS

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Background: While many studies showed a possible relationship between obesity and asthma, the evidence for the association is not enough in Asian population, where obesity is not so common compared with western countries. In addition, the mechanisms how obesity increase the risk of asthma were poorly understood yet. We aimed to examine the relationship of obesity with asthma and atopy in Korean adult population.

Methods: We analyzed the data from Korean National Health and Nutrition Examination Survey (KNHANES) in 2010. Obesity was determined based on body mass index (BMI) and the adult subjects were classified as normal (BMI <23), overweight (23–25), obese (25–30) and very obese (≥ 30). Subjects with current asthma was assessed using self-administered questionnaire and atopy was identified by measurement of serum specific IgE to Dermatophagoides farinae, cockroach or dog.

Results: Multivariate logistic regression analysis adjusting for age, gender and smoking status found that obesity is significantly associated with asthma ($P = 0.004$). Increase risk of asthma was revealed in obese (aOR 1.63, 95% CI 1.19–2.24) and very obese group (aOR 1.96, 95% CI 1.11–3.46), while overweight was not associated with current asthma. Furthermore, higher BMI and obesity was closely related with atopy.

Conclusion: Obese and very obese subjects are at increases risk asthma. Obesity might be linked to asthma by increased sensitization to common aeroallergens.

P-K-065

ROMANIAN EXPERIENCE IN RUNNING ASTHMA AWARENESS CAMPAIGNS

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Background: For 5 years, on World Asthma Day, Romania is running asthma awareness campaigns, offering free spirometry for general public. In 2014, we conducted 2 days campaign, using case finding approach : questionnaire plus free spirometry.

Method and Materials: Questionnaire has 7 questions and addresses different issues, like possible suggestive symptoms, risk factors (smoking), previous respiratory function investigations (spirometries), existence of any therapy for respiratory problems. 1281 persons were screened, with 1246 of them fully completing the questionnaire. 56.5% (710) were women, of which 122 were smokers and 117 ex-smokers. 43.5% (536) were men, with 69 smokers and 180 ex-smokers. 93 persons were between 10–20 years and 280 between 21–40 years old.

Results: Inside the screened slot, 801 persons didn't present any respiratory symptoms. From symptomatics ones, 308 persons had dyspnea, 432 indicated cough, 284 had chest tightness, 178 had wheezing and 109 presented all the above symptoms. Regarding allergies, 104 men and 130 women were allergic to dust, 68 men and 130 women to pollen, 44 men and 71 women to animal hair, 31 men and 85 women had drugs related allergy, and 41 men and 118 women to chemicals. In the last 6 month 42 men and 54 women had a spirometry. 231 persons were known as having asthma (34 men and 31 women in 10–20 years group and 102 men and 129 women in 21–40 years group). 75 men and 104 women were under treatment for known respiratory condition. When it comes to whom is seeing patients on regular basis, 49 men and 91 women were seen by their pulmonologist, and 12 men and 33 women, by their allergologists. 282 persons (22%) were detected with lung function impairment when tested by spirometry.

Conclusion: In Romania, access to spirometry is extremely low. Treating asthma is deficient, just 77.5% (179) patients known as diagnosed with asthma being actually treated (73.5% men, 80.6% women). Pulmonologists was responsible for managing asthma in 60.6% cases (110), while allergologists were responsible for managing asthma in 19.5% cases (45). Atopies are more frequent in women, as well as tendency to be treated and seeing by physicians on regular basis, for assessing asthma control. Asthma awareness campaigns based on case findings (questionnaires plus spirometry) are usefull for detecting new cases, but also for already diagnosed cases, who were not followed up properly, regarding treatment or assessing asthma control.

P-K-068

P-K-069

A TWIN-APPROACH TO DIAGNOSING ASTHMA IN ELDERLY PATIENTS PRESENTING WITH COUGH

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Both Peak Expiratory Flow Rate (PEFR) and Inhaled Corticosteroids/Long-Acting Beta-Agonist (ICS/LABA) therapy are widely used in the management of asthma. Yet, both ICS/LABA and PEFR response have not been combined as a diagnostic test for asthma. Our retrospective study looked into the usefulness of this twin-approach, reviewing the records of 61 consecutive elderly Asian patients presenting with a persistent cough of more than three weeks (median 5 months; IQR 2 to 24 months). Only those who received ICS/LABA therapy and had PEFR measurements over at least two visits were included in our study. This study has received exempted review from the Chairman of the Parkway Independent Ethics Committee (Gleneagles Hospital). In the initial period (first to second visit), all our patients reported improvement in their symptoms. Notably, PEFR improved by a median of 45 l/min (median 4.5 days) in the 61 patients ($p < 0.001$, paired T-test). These 61 patients were further divided into two sub-groups: those who attended only two visits ($n = 30$) and those who attended more than two visits ($n = 31$). Median PEFR in the latter improved by 115 l/min ($p < 0.001$, paired T-test) in the subsequent period (first to third visit); in absolute terms, their median PEFR increased from 280 l/min to 350 l/min initially (median of 5 days), and to 395 l/min subsequently (median of 29 days). There was no significant difference in the initial number of asthma diagnoses in these two sub-groups of patients ($\chi^2(2, n = 61) = 0.5, p > 0.05$; Chi-square test, $p > 0.05$; Fisher's exact test). Further analysis of the 31 patients showed that their PEFR variability exceeded 20% in 17 (54.8%) patients initially and this rose to 22 (71.0%) patients subsequently ($r_s = 0.97$; Spearman's rank-order correlation). In conclusion, this twin-approach capitalized on the predominant bronchodilator effect of LABA to diagnose 49.2% of our patients with asthma (median of 4.5 days). Overall, the combined effect of the former and the anti-inflammatory action of ICS diagnosed 71.0% of our patients with asthma (median of 29 days). Interestingly, another group of patients with a "Repressed Bronchodilator Response" (PEFR variability between 10–20%), also benefitted in terms of cough and PEFR improvement. Ultimately, pairing ICS/LABA with PEFR response enhances the diagnostic repertoire for asthma in elderly patients presenting with persistent cough.

CHARACTERISTIC AND OUTCOME OF ADULT PATIENT WITH MECHANICAL VENTILATION IN INTENSIVE CARE UNIT PERSAHABATAN HOSPITAL

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Background: Critically ill patients require complex treatments and even require treatments in the intensive care unit (ICU). Advances in diagnosis and management in critical condition increasing the need for ICU, which often exceeds the available facilities, especially the need for mechanical ventilation. Limitations of mechanical ventilation facilities lead to medical workers must determine priorities and increasing the need for guidelines, protocols and standards in selecting patients to be treated in the ICU. APACHE II score can be used to assess outcomes of patients weaning from mechanical ventilation and mortality. Objective of this study was to assess the survival and the factors that influence it such as patient's characteristics at the beginning of the use of mechanical ventilation, mechanical ventilation settings and patient outcomes. **Method:** This research was conducted with cross-section method with sample population of adult patients admitted to the ICU and using mechanical ventilation. Sample was collected from medical record and follow up sheet. Data obtained from the research was assessed based on the demographic characteristic, cases and indication of ICU care, medical risks, the use of mechanical ventilation, and to assess the outcome of patients admitted to the ICU.

Result: From 167 subjects in the study, the majority results are most subject aged ≤ 44 70 subjects (41.9%), 101 male subjects (60.5%), using social health insurance 86 subjects (51.5%), and patients' mortality assessment results with a median APACHE II score of 46.03 (5.80 to 95.49). The study also found that patients admitted to the ICU are most not surgery cases 86 subjects (51.5%), followed by lung disease cases 68 subjects (40.7%), while the surgery cases not from lung disease 56 subjects (33.5%), installation of postoperative mechanical ventilation 81 subjects (48.5%). The most cause of death was sepsis, as many as 66 subjects (62.9%). Outcome of patients are weaning from mechanical ventilation 68 subjects (40.7%), requiring tracheostomy 8 subjects (3.8%) and discharge alive from ICU 61 subjects (36.5%).

Discussion: Patient's characteristic such as age, diagnosis and social health insurance are highly influencing patient's outcome. APACHE II score can be used to assess the mortality of patient admitted to ICU.

P-K-070

QUALITY ASSESSMENT OF CLINICAL PRACTICE GUIDELINES IN RESPIRATORY DISEASES IN CHINA: A SYSTEMATIC APPRAISAL

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Background: There are a great increase in production of clinical practice guidelines (CPGs) in respiratory diseases in China recently. However, little is known about their quality.

Objectives: To systematically evaluate the quality of CPGs for respiratory disease published in the peer-reviewed medical literature.

Methods: We performed a systematic search of scientific literature published between 1978 and 2013 to identify and select CPGs related to respiratory diseases in four Chinese databases (CBM, WANFANG, VIP, and CNKI). Four reviewers independently evaluated the quality of the eligible guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument. We calculated the overall agreement among reviewers with the intraclass correlation coefficient (ICC).

Results: A total of 109 guidelines published in 29 medical journals from 1999 to 2013 were eligible. Only 18 guidelines (16.5%) were evidence-based guidelines, four guidelines (3.7%) described the methods used to search for evidence, 16 (14.7%) appraised the quality of evidence and 15 (13.8%) graded the strength of recommendations. Only one guideline (0.9%) used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, three guidelines (2.8%) declared the involvement of methodological experts and only two declared the interest conflicts of guideline developers. 15 guidelines (13.8%) mentioned updates and the average frequency of update was 6.06 years, but the guidelines with updated versions yielded higher quality than the rest. The overall agreement among reviewers was high and the mean scores for each AGREE domain were low.

Conclusions: The quality of guidelines for respiratory diseases in China is low, although there are some increase over time. More efforts are urgently needed to ensure the high quality of CPGs using methodologically sound development frameworks so that the CPGs can be used as reliable tools for clinical decision-making in this field.

P-K-071

SINOBRONCHIAL SYNDROME (SBS) NOT TO BE MISTAKEN FOR UPPER AIRWAY COUGH SYNDROME (UACS): CLINICAL EXPERIENCE WITH LOW DOSE ERYTHROMYCIN (LDEM) THERAPY IN THAILAND

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Background: SBS is a well known and common of chronic productive cough in Japan but not widely recognized, however. Patients with unremitting cough might have been prior treated for other conditions. Accordingly, their disturbing cough that had not been considerably alleviated but responded to LDEM therapy diagnostic for SBS. Remarkably, it is not widely recognized and information regarding this disorder is limited in our country.

Aim of Study: To characterize the informative SBS characteristics and treatment outcome in our experience.

Methods: Retrospective study was conducted in Central Chest Institute of Thailand between 2010–2014. Patients were carefully evaluated and follow the Japanese Respiratory Society diagnosis criteria (1) chronic productive cough for 8 or more weeks (2) they all had any one of (2.1) clearing throat (2.2) post nasal drip (2.3) pharyngeal cobble stone and/or secretion deposition (2.4) imaging evidence of sinusitis (3) these considerably responded to LDEM, 500 mg/day.

Result: SBS was diagnosed in 81 males and 132 females [N = 213], ages 17–94 years [mean 64.5].

All had been previously or currently treated for their underlying conditions as following: bronchiectasis with or without old pulmonary TB (112), asthma (47), bronchitis (29), emphysema (10), and allergic rhinitis (13). Plain chest radiographs included: normal (56), increased reticular marking (22), bronchiectasis (102), fibrosis (20) and emphysema (13). Thorough and careful re-evaluation in this setting revealed that treatment had been usually given with prior therapy for UACS. Remarkably, it is worth to note that they still had troublesome cough with production and not responding to regimen for UACS but to LDEM therapy instead.

Conclusion: From our study, SBS could be overlooked and mistaken for UACS and clinically SBS could be indistinguishable from UACS but the former responds well to LDEM. It appeared to occur with several conditions and should be carefully considered in patients with (1) chronic productive cough with (2) associated symptoms referable to sinusitis (3) their cough alleviation not yet satisfactorily achieved (4) treatment with LDEM should be reasonably considered. It should be noted that the longer the clinical onset and the more severe the clinical and radiological features, the less favourable the result, and vice versa.

P-K-072

P-K-074

SINO BRONCHIAL SYNDROME (SBS): THE IMPORTANT BUT UNRECOGNIZED RESPIRATORY DISORDER CAUSING AIRWAY AND LUNG DAMAGE

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Background: SBS has been recognized but not widely known in Thailand for few years and the information is consistently limited however. From our experience the clinical and radiographic features varied considerably from patient to patient with unremitting annoying cough and normal chest film on one extreme to pulmonary insufficiency and chest radiologic evidence of extensive irreversible airway and lung damage on the other. Patients might have cough visits for years before the disease disclosure. From the above reasons, airway and lung damage could ultimately resulted with delayed diagnosis and treatment. However, there are no evidence to support this assumption.

Aim of Study: To find out evidence supporting that delayed diagnosis and treatment for SBS could lead to respiratory damage.

Patients and Method: A retrospective study was conducted at Central Chest Institute of Thailand between 2010–2014: ALL SBS patients who presented with radiologic evidence of airway and lung damage at the time of diagnosis and had both complete clinical and radiologic information obtained during the earlier years of onset to the last were enrolled. In order to determine the presence of SBS evolution, focus on the consecutive clinical and radiologic deterioration with ultimately respiratory destruction in a given individual was conducted.

Results: 57 SBS patients (M 12 F 45) ages 18–85 (mean 64.7) years had radiologic evidence of progressive airway and lung damage over the cough visiting period and prior diagnoses were bronchiectasis (47) old pulmonary TB (8) emphysema(1) bronchitis (1) and asthma(1). On thorough clinical exploration, patients had realized not only productive cough but also clearing throat and post nasal drip since the onset. These symptoms appeared only minimal and annoying long before deteriorating in the later years. Likewise chest radiography deterioration and evolved over years before SBS diagnosis. During which, patients had been treated for bronchial disorders year after year without considerable alleviation.

Summary: From our study it should be emphasized that both clinical and radiologic deterioration had evolved years prior to the recognition. Progressive airway and lung destruction was demonstrated from consecutive chest x-ray finding along with clinical deterioration. Ultimate irreversible damage with clinical respiratory failure was found in extreme cases. This emphasize that early recognition and treatment is warranted.

PLEURAL EFFUSION AND EMPYEMA IN CHILDREN: A PHILIPPINE EXPERIENCE

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Pleural effusion is a condition where there is excessive accumulation of fluid in the pleural cavity. It is classified as either transudate or exudate based on Light's Criteria. Empyema, on the other hand, is defined as purulent fluid collection in the pleural space. In the Philippines, an overview of the data came from both Philippine Pediatric Society (PPS) and Philippine Academy of Pediatric Pulmonologists (PAPP). PPS data of accredited hospitals were taken from January 2007 to December 2013, while PAPP experience in children aged 0 to 18 years from July 2007 to December 2013 came from 6 accredited hospitals, which are referral institutions in the Philippines. PPS data showed a total of 2001 patients with Pleural effusion, whereas 457 presented with Empyema thoracis, with the same male-to-female ratio of 1.4:1. PAPP data showed a total of 1317 patients with Pleural effusion and Empyema, with the same male-to-female ratio. According to PPS statistics, majority of patients came from Chapter 6 or National Capital Region (889), followed by Chapter 5 or Northern/Central Mindanao (199). As per PAPP data, majority of patients presented with exudative type of effusion, which can be classified into infectious and non-infectious causes. Based on pleural fluid analysis, 458 presented with infectious causes (Parapneumonic, Tuberculous), while 313 presented with non-infectious causes (Malignancy, Trauma, Others). Among culture-positive isolates, majority (28) were found to be caused by Methicillin-resistant Staphylococcus aureus. On the other hand, PPS data showed 271 cases of Empyema, non-tuberculous type, 136 cases of tuberculous with no bacterial confirmation, and 50 cases of confirmed tuberculous type. As to the management, majority of patients were treated with Medical + Thoracentesis (475), followed by Medical management alone (392) and Medical + Closed tube thoracostomy (289). Video assisted thoracoscopic surgery or VATS is an emerging surgical procedure that can also be used for treatment (41). Outcomes of disease were improved clinical parameters (609), improved diagnostic modalities like chest xray, ultrasound and CT scan (615), while complications include pleural thickening, bronchopleural fistula and others (73). Mortality was only 34 out of 1317 cases. Burden of disease shows pleural effusion and empyema in children are still significant causes of morbidity, with a total amount of >Php55,000,000 claims from January 2007 to December 2013 from the Philippine Health Insurance Corporation. Pleural effusion ranked 101 from Philhealth reimbursements, whereas it ranked 83rd according to PPS statistics.

P-K-073

P-K-075

BIRT-HOGG-DUBÉ SYNDROME COMPLICATED WITH LUNG CANCER; A POSSIBLE LINK OF THESE TWO DISEASE ENTITIES

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Birt–Hogg–Dubé syndrome (BHD) is an autosomal dominant inherited disorder characterized by pulmonary cysts, pneumothorax, skin lesions (fibrofolliculomas) and renal tumours. Repeated episodes of pneumothorax and pulmonary cystic lesions are the clinical hallmarks for discovering families affected by the syndrome. This disorder is caused by mutations in the gene coding for folliculin (FLCN) that is considered to be tumour-suppressive. Here, we present a rare case of BHD with primary lung cancer. A 65 years old Japanese woman was introduced to our hospital for further examination of multiple pulmonary cystic lesions and ground-glass attenuation in left lower lobe. She had smoking history (25 pack-years), and her younger brother was also suffered from lung cancer with multiple cysts. Surgical biopsy specimen obtained from her left lower lobe revealed adenocarcinoma, surrounded with single layer of the epithelium that was covered with collagen fibres, compatible with the pathological findings of cystic lesions in patients with BHD. A diagnosis of BHD was eventually made according to a detection of folliculin gene mutation. This is a rare case of complicating primary lung cancer in a patient with BHD, and here we discuss a possible association between carcinogenesis and BHD in the lung.

IS FOLLOW UP FOR A SOLITARY LESION ON A RIB SATISFACTORY?

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The lesion of the bony part of the thoracic cage varies from callus formation to malignant processes. Chondrosarcoma is one of the most seen malignant tumour of the ribs. We want to present a case that is thought to be fibrous dysplasia of the rib preoperatively but reported as chondrosarcoma postoperatively. 21 year old man admitted to our hospital with a mass on his front chest wall. Computed tomography of the thorax revealed a mass originating from the costochondral junction of the fifth rib. The radiological appearance of the rib was suggested as fibrous dysplasia. Whole body bone scintigraphy was done to the patient to reveal any other accumulation. The accumulation was seen only on the affected rib area. In the light of these findings, we performed a partial resection of the fifth rib with a prediagnosis of monostatic fibrous dysplasia. The defect was closed with a prolene mesh. The specimen was reported as chondrosarcoma grade I (WHO 2013). The surgical margin was tumour free but had a subcentimetric distance. Because of being a sarcoma, we performed a second operation to the patient. The fourth and the sixth ribs were also partially resected. The big defect after the resection was reconstructed with the titanium bars, clips and prolene mesh. There was no problem in the postoperative period. The patient was discharged without any complication. Extended surgical resection is the best treatment modality for chondrosarcomas. Tumour free margin of 3–4 cm is advised in all sides. Chondrosarcomas are not radiosensitive tumours, thus radiotherapy is not used routinely used for curative treatment. We do not applied radiotherapy after the first surgical resection to the surgical margins and we chose surgical treatment. Solitary or multiple lesions of the ribs must be evaluated carefully. They should be under close follow ups or the radiological assumed diagnosis should be verified by the biopsies.

P-K-076

DISTAL INTESTINAL OBSTRUCTION SYNDROME IN CYSTIC FIBROSIS – A 10 YEAR ANALYSIS

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Background: Cystic Fibrosis (CF) is the most common lethal autosomal disease in Australia, affecting ~ 1 in 2,500 live births. Meconium ileus at birth and distal intestinal obstruction syndrome (DIOS) in adulthood are commonly found in CF. This study describes the incidence, risk factors, management and outcome of DIOS in adults with CF.

Method: A retrospective audit of CF patients attending Westmead Adult CF clinic from January 2004 to January 2014 was performed to document cases of DIOS. DIOS was defined as the presence of both clinical features and radiologic evidence of small bowel obstruction with faecal loading in the caecum / terminal ileum.

Results: From January 2004 to January 2014, 192 patients (97 male and 95 female) attended the clinic for a total of 947 patient years. A total of 44 episodes of DIOS occurred in 29 patients, giving a prevalence of 4.6/100 patient years. Most patients had only one episode of DIOS during the 10 year follow-up; 8 patients had 2 episodes of DIOS and 2 patients had at least 4 episodes of DIOS. During the 10 year review period, 2 episodes of intussusception were also seen. Most episodes of DIOS were managed in-hospital with oral laxatives and enemas. The 2 cases of intussusception required laparotomy and bowel resection. One patient presented to another hospital with severe abdominal pain which was misdiagnosed as appendicitis, treated with appendicectomy. There were no deaths related to these bowel complications.

Conclusion: DIOS is relatively common in the CF clinic. Treatment with oral laxatives and enemas was quickly effective in most patients. All doctors should be aware of DIOS as a common complication of CF, but should be vigilant for other rare complications such as intussusception.

P-K-078

PREDICTION OF THE CLINICAL COURSE OF PNEUMOTHORAX USING CHEST X-RAY

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Rationale: To our knowledge, expiratory X-rays are not thought to confer additional benefit in the routine assessment of pneumothorax. However, there have been no reports concerning the usefulness of the comparison of inspiratory and expiratory X-rays for the assessment of pneumothorax.

Methods: We retrospectively reviewed the patients with pneumothorax who underwent both inspiratory and expiratory chest X-rays at our hospital between April 2011 and August 2013. The area of lung, hemithorax, and pneumothorax were calculated using DICOM image processing software (ImageJ version 1.45 s; National Institutes of Health, Bethesda, MD, USA). We examined the correlation between these measurements and the clinical course of pneumothorax.

Results: 111 episodes of pneumothoraces occurred in 95 patients were included (89 male and 22 female, the mean age was 41.7 year-old). The number primary spontaneous pneumothorax, secondary spontaneous pneumothorax, and iatrogenic pneumothorax were 74, 34, and 3, respectively. 79 pneumothoraces improved within the first three days, and univariate analysis revealed that "the degree of pneumothorax on inspiratory X-ray" ($p < 0.01$), "the degree of pneumothorax on expiratory X-ray" ($p = 0.03$), and "the inspiratory-to-expiratory area ratio of the pneumothorax" ($p = 0.01$) were significantly different between the improved group and unimproved group. Among these three measurements, "the inspiratory-to-expiratory area ratio of the pneumothorax" had the highest area under the ROC curve value (0.792).

Conclusion: The inspiratory-to-expiratory area ratio of the pneumothorax on chest X-rays may be useful for the prediction of clinical course of pneumothorax.

P-K-077

A RARE PRESENTATION OF POLAND SYNDROME: LUNG HERNIATION

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Poland syndrome is characterized by anterior chest wall and upper extremity anomalies. It has a variety of components. They are generally presented with the agenesis of the pectoral muscle. Here we want to present a case that presented with lung herniation due to the agenesis of the chondral bundle (chondral rib and intercostal muscles) on the anterior chest wall. A 21 year old man was admitted to our clinic with a swelling on anterior chest wall during cough. Nothing considerable on physical examination was found except the softness of the swelling area. No component of the thoracic cage was palpated. Chest X ray of the patient showed normal bone ribs. Thorax ct which is taken while the patient was performing valsalva manoeuvre revealed agenesis of the first two chondral bundles. No respiratory impairment was observed such as flail chest. Because of having normal and functional pectoral muscles, no bad cosmetic appearance was observed. The patient was informed about the deformity and he did not want a surgical correction. Typical appearance of the syndrome is generally caused by the agenesis of the pectoral muscles that makes the diagnosis easy. In our patient these muscles were in their anatomical position but intercostal muscles and chondral ribs were missing. This syndrome is seen 1 in 7,000 to 1 in 100,000 live births in the population. It is generally seen on the right side. Lung herniation has a ratio of % 8. Surgery is performed to this patient for cosmetic reasons or for the disability of the upper extremity movements. We have not performed surgery for our patient as a result of not having a bad appearance and disability.

P-K-079

SOLITARY BULLAE DETECTED IN A JET PILOT AND ITS TREATMENT

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Background: Bullae of the lung generally do not give symptoms unless they are very big in size. In the studies, 90% of apical sub-pleural blebs or bullae were identified in patients with spontaneous pneumothorax cases. Due to pilots' exposure to sudden changes in altitude and G-force during executing their job, pilot who has bullae are more at risk of pneumothorax compared to other occupational groups. Therefore we presented this case that requires unusual treatment.

Case: 42 years old male pilot applied in our clinic during periodic examinations. He had no symptoms or complaints. Pulmonary auscultation and pulmonary functions test (PFT) were normal. Complete blood count values and routine biochemistry were normal. Chest X-Ray showed reticular pattern in right upper zone. Sub-pleural solitary bullae on the apical segment of right lungs were observed in the thorax HRCT.

Conclusion: Ascending to high altitude causes air expansions in volume and pilots executing sudden manoeuvres in the air subject to G-forces up to 9 times of gravity. These physical changes affect the lungs, as a result of; there is a significant increase in the risk of pneumothorax in jet pilots. For these reasons, regulation does not allow jet pilots with bullae to flying duties. In normal circumstances, this kind of medical condition does not require any further intervention. In our case, bullectomy via right thoracotomy performed. 2 months after resting, jet pilot was allowed to flying duties.

P-K-080

P-K-082

PPLICATION OF THE DIAPHRAGM FROM MINI INCISION (CASE REPORT)

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Plication of the diaphragm is a surgery done for the fixation and pulling downward of the paralyzed diaphragm to prevent the paradoxical movement of the diaphragm during respiration. We want to express our results of thoracoscopic diaphragm plication in an obese female patient. A sixty nine year old female admitted to our department with a complaint of dyspnea. Physical examination of the patient revealed decreased breath sounds in the left lower hemithorax. Left hemidiaphragmatic eventration was found on the chest X-ray of the patient. Respiratory function test revealed restrictive respiratory failure. When we examined the patient's history, we have found that the patient had undergone a bypass operation one year ago. We suggested diaphragmatic plication to the patient after the fluoroscopy that showed paralysis of the left hemidiaphragm. Procedures of the surgery was declared to the patient and minimally invasive approach was planned for the patient because of obesity and advanced age. Plication of the diaphragm was performed with a 4 cm. utility access in the 7 th intercostal space and a camera port in the 4 th intercostal space. Pain complaint was minimal in postoperative period and dyspnea was disappeared. The FVC value was improved from %57 to %96. Recent advanced minimally invasive interventions are used in nearly every part of the thoracic surgery practice. In this patient by using a 3 cm incision, we minimized the negative effect of the thoracotomy on respiratory functions. Diaphragmatic plication via VATS is a safe procedure with acceptable results.

P-K-081

A CASE THYMOMA WITH MYASTHENIC CRISIS

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Background: Thymoma is an anterior mediastinal tumour that has correlation with Myasthenia gravis (MG). Approximately 35–50% patient with thymoma have MG. If MG not terated completely it can develop to myasthenic crisis. This case disscuss about patient with undiagnosed myasthenia gravis that develop to myasthenic crisis with an incidental finding of a thymoma that need prolonged mechanical ventilation.

Case Report: A 56 years old Man, was admitted with complain of dysphagia. The patient underwent esophagogastroduodenoskopi examination and the result was spasme/dysfunction upper esophageal sphincter. Two days after admission, patient develop shortness of breath. CT of the thoracs revealed a larged anterior mediastinal mass, measuring 4.2 x 6.2 x 9.1 cm suggestive of thymoma. Seven days after admission, he develop Myasthenic crisis and transferred to ICU for mecanical ventilation. Therapy for MG was started, mestinon 3 x 60 mg, prostigmin 2 x 1 ampoule, methylprednisolon 3 x125 mg. After two week being treated in ICU, the patient undergo extended thymectomy. Intraoperatively there was a well encapsulated mass, measuring 6 x 9 x 2 cm. Pathological examination result was haemorrhagic cystic thymoma type A. Ventilator weaning was done 3 days after surgery and he was extubated 9 days after. After mobilization, the patient discharged well with therapy mestinon and prednison tablet.

Discussion: Thymoma is a tumour that origin from the thymic gland. Approximately 35–60% patient with thymoma have MG. Myasthenia crisis is defined as severe weakness of respiratory and upper airway muscle leading to respiratory failure requiring ventilatory support. Post operatif myasthenic patient who are unable to be weaned of ventilator beyond 24 hour also considered have crisis. Poor control of MG, drug (steroid, muscle relaxant, anticholinesterase), systemic infection, and emotional stress are common precipitant of a crisis. For this case, ventilatory support is the mainstay of treatment. Studies revealed that both plasma exchange and IVIG are effective in treating myasthenic crisis. The use anticholinesterase (piridostigmin) remain controversial in view of cardiac complication. High dose prednisolone also administrated during the crisis. About 15% patient with MG have a thymoma and thymectomy is always recomended. Aproximately 67% patient showed improvement of MG simptom after the operation.

Conclusion: Myasthenic crisis is a life threatening condition. Ventilatory support is the mainstay of treatment. Patient tend to respond to high dose prednisolone combined with IVIG or plasma exchange. Thymectomy is always recomended in patients with thymoma.

A FATAL CASE OF MILIARY TUBERCULOSIS COMPLICATING WITH PULMONARY ALVEOLAR PROTEINOSIS

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Introduction: Miliary tuberculosis (TB) is the widespread dissemination of mycobacterium tuberculosis via hematogenous spread. Complicating of this uncommon form of TB with pulmonary alveolar proteinosis (PAP), a rare disorder of surfactant homeostasis, is very rare event. we describe herein a fatal case of a 36-year-old women with miliary TB complicating with PAP.

Case Report: A 36-year-old women was admitted to our hospital due to fever, cough and progressive dyspnea from 1 month ago. Two weeks befor admission she went to the emergency department at another hospital. Chest radiography was normal and patient received azythromycin. Her symptoms progressed to include night sweats, headache, vomiting and weight loss. On presentation the patient was in moderate respiratory distress. A new chest radiography showed innumerable tiny indistinct nodules. High resolution computed tomography (HRCT) scan of chest showed a combination of diffuse ground-glass opacity and micronodular pattern. Treatment was started with broad spectrum antibiotics and on suspicion of acute interstitial pneumonitis or other acute interstitial involvement, systemic glucocorticoid was initiated. Bronchoscopy was performed. The bronchoalveolar lavage fluid (BALF) was turbid with some debris. Staining and culture of BALF was negative for bacterial, fungal (including *P. jirovecii*) organisms and viral antigens. Acid-fast staining was negative. Cellular analysis showed 86% macrophage, 8% lymphocyte and 6% polymorphonuclear cells. Cytologic examination of the fluid was negative for malignancy. Papanicolaous-stained specimen of BALF revealed acellular eosinophilic lipoproteinaceous material and periodic acid-Schiff positive foamy-appearing macrophages, in favour of PAP. Because of severe headache and nuchal rigidity lumbar puncture was done. Cerebrospinal fluid analysis showed lymphocytosis with high protein and low glucose; gram stain and culture and acid-fast staining were negative. A polymerase chain reaction (PCR)-based assay of BALF reported positive for mycobacterium tuberculosis and molecular analysis did not rise the suspicion of an antibiotic resistance. A quadruple anti-TB therapy was started. During next days her condition deteriorated and pancytopenia developed. Because of severe refractory hypoxaemia the patient intubated. Her condition did not improve despite maximal medical therapy and she died 18 days after admission.

Discussion: We described the case of a young women with refractory respiratory failure caused by disseminated TB and PAP, which was unresponsive to conventional treatments. Addition of PAP had been changed typical radiologic presentation and BALF cellular analysis of miliary TB. It was very well possible that PAP had a grave impact on prognosis of the patient.

P-K-083

THE SERUM LEVELS AND SIGNIFICANCE OF TRANSFORMING GROWTH FACTOR BETA 1 AND ANGIOTENSIN II IN PATIENTS WITH ASTHMA

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Determine the expression of transforming growth factor $\beta 1$ (TGF- $\beta 1$) and angiotensin II (Ang II) in serum of 38 cases of bronchial asthma. Carry out the correlation analysis with total serum immunoglobulin E (IgE) levels and lung function. Explore the relationship between TGF- $\beta 1$ and Ang II and study their role and significance in bronchial asthma.

Method: Determine total IgE in serum of 38 cases of patients with bronchial asthma with enzyme-linked immunosorbent assay (ELISA), which elevated total serum IgE of patients 25 cases, 13 cases of patients with normal serum total IgE, 20 healthy people in normal control group. Determine expression of TGF- $\beta 1$ in serum. Radioimmunoassay was used to determine TGF- $\beta 1$ expression in serum. Forced expiratory volume in one second (FEV₁)% FEV₁ predicted, FEV₁/forced vital capacity (FVC) and peak expiratory flow (PEF) of asthma group were measured.

Result: 1. The expression of TGF- $\beta 1$ in both IgE elevated asthma group and IgE normal group [(264.04 ± 128.07) pg / ml, (498.11 ± 478.24) pg / ml] were lower than the control group [(736.46 ± 686.07) pg / ml], the difference was statistically significant, P all < 0.01. 2. Asthma group with IgE elevated, group with IgE normal and normal control group, the expression of Ang II in serum [(427.48 ± 230.63) pg / ml, (419.36 ± 217.11) pg / ml, (525.00 ± 152.52) pg / ml] were pairwise comparison no significant difference, (P all > 0.5). 3. TGF- $\beta 1$ in serum has no significant correlation with FEV₁% pre, FEV₁/FVC and PEF ($r = 0.02$, $P = 0.91$, $r = 0.06$, $P = 0.70$, $r = -0.05$, $P = 0.78$). 4. Ang II in serum has no significant correlation with FEV₁% pre, FEV₁/FVC and PEF ($r = 0.00$, $P = 1.00$, $r = -0.27$, $P = 0.10$, $r = 0.02$, $P = 0.89$). 5. FEV₁% pre, FEV₁/FVC and PEF of IgE elevated asthma group [64.46 ± 25.77, 60.66 ± 13.30, 4.87 ± 2.26] and IgE normal group [56.80 ± 23.89, 52.67 ± 18.56, 3.38 ± 2.33] showed no significant difference, (P all > 0.5). 6. The expression of TGF- $\beta 1$ and Ang II in serum had no correlation ($r = -0.004$, $p = 0.980$).

Conclusion: 1. Compared with the healthy control group, TGF- $\beta 1$ expressed lower in the presence blood of patients with asthma. 2. Ang II in peripheral blood has no significant correlation with lung function and expression of TGF- $\beta 1$ in peripheral blood. There was no difference of Ang II expression in peripheral serum between asthma patients and healthy people, which could be explained that Ang II may play a major role in local tissue rather than in peripheral blood. 3. The concentration of TGF- $\beta 1$ in peripheral blood can be used as monitoring indicators of the severity of asthma.

P-K-084

CORRELATION BETWEEN TOBACCO SMOKE EXPOSURE AT HOME WITH RESPIRATORY SYMPTOMS, HOSPITALIZATION AND SCHOOL ABSENTEEISM DUE TO RESPIRATORY ILLNESS IN CHILDREN

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Introduction: Family member's smoking behaviour at home influence exposure to tobacco smoke in children. In Indonesia, more than 43 million children who are exposed to tobacco smoke are at a greater risk of health hazard and morbidity for children. This study investigates the impact of environmental tobacco smoke (ETS) exposure on respiratory symptoms, hospitalization and school absenteeism related respiratory illness in children.

Methods: We conducted a cross sectional study of 128 school children age 6–12 years from elementary schools in Jakarta. Parental reports of household smoking ascertain ETS exposure. Respiratory outcomes were based on parental report of wheezing, cough, upper respiratory infection in the past 12 months and physician diagnosed asthma at any time. Morbidity caused by ETS exposure was based on the frequency of hospitalization and respiratory illness-related school absenteeism collected from questionnaire. We analyzed relationship between ETS exposure with respiratory symptoms, hospitalization and school absenteeism due to respiratory illness.

Results: A total 128 nonsmokers children age 6–12 years (mean 9.8 ± 1.6 years old) were enrolled in the study. Subjects were divided into 64 children exposed to ETS and 64 children unexposed to ETS. Current household ETS exposure was significantly associated with cough, upper respiratory infection in previous 12 month, and not associated with wheeze and asthma in children. Cough episode ≥ 3 x per year was found 26.6% in exposed group and 6% in unexposed group. Upper respiratory infection ≥ 3 episode per year was 32.8% in exposed group and only 4.7% in unexposed group. Household ETS exposure was associated with hospitalization ≥ 1 time per year due to respiratory illness in children and not associated with school absenteeism in children. In exposed group, children living with ≥ 1 adult who smoked at home had 8.4 greater risk ≥ 5 days absent from school per year than children living with one smoker at home. Cough symptoms ≥ 3 episode per year was found in 50% children exposed to >10 cigarettes per day and 14.3% in children exposed to 1–10 cigarettes per day. There was no significant association between duration of ETS exposure per day with respiratory symptoms, hospitalization and school absenteeism in children exposed to ETS.

Conclusions: Tobacco smoke exposure at home in children has significant association with frequent cough episode, upper respiratory infection and hospitalization due to respiratory illness in one year.

P-K-085

P-K-086

THE IMPACT OF PARTICULATE MATTER WITH THEIR DIAMETERS LESS THAN 2.5MM (PM2.5) LEVELS ON EMERGENCY DEPARTMENT VISITS WITH RESPIRATORY COMPLICATIONS IN OSAKA

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Backgrounds: Particulate matters (PM) are small particle either in solid or liquid forms suspended in the atmosphere. PM with their diameters less than 2.5 µm are referred to as PM2.5. It has received greater attention recently because of its adverse effect on human health, including asthma attacks and increased mortality of cardiac diseases. Little has been revealed on the impact of PM2.5 exposure and its relation to the emergency department (ED) visits in Japan. We hypothesized that greater PM2.5 levels were associated with increased ED visits with respiratory complications.

Patients and Methods: Retrospective analysis was performed to study the association of PM2.5 levels and ED visits with respiratory complications. All medical records at Osaka Emergency Room foundation from April 2012 to March 2013 were reviewed. To minimize the bias by day of the week, we selected the ER visits on weekend and holidays. PM2.5 levels were referred from Atmospheric Environmental Regional Observation System (AEROS), as well as the meteorological conditions including the weather, temperature, wind speed and precipitations from the database of Japan Meteorological Agency.

Results: PM2.5 levels in Osaka increased during summer and decreased in winter. Seasonal projections of PM2.5 were observed in spring and autumn due to westerly wind. Two thousands and five hundreds sixty nine ED visits were eligible for our analysis, whose diagnoses included asthma attack, asthmatic bronchitis, bronchitis, pneumonia and COPD exacerbations. Significant negative correlation was observed between ED visits with respiratory complications and temperature by simple linear regression analysis. Contrary to our hypothesis, significant negative correlation was revealed between ED visits and PM2.5 levels. Multiple regression analysis demonstrated both the lower temperature and decreased levels of PM2.5 were the contributing factors to the increased ED visits.

Conclusion: Decreased levels of PM2.5 might reflect other meteorological conditions contributing to the increased ED visits in Osaka. We will add bibliographical review to discuss our findings.

A CASE OF MEDIASTINAL CHONDROSARCOMA: A CASE REPORT

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Background: Chondrosarcoma in any part of the mediastinum is rare. It is particularly unusual in the posterior mediastinum and is a unique tumour in the dumbbell variety. Previously published chondrosarcomas of the anterior mediastinum were found to originate from osteocartilaginous structures, either tracheobronchial or parietal. No patient with mediastinal sarcomas other than malignant peripheral nerve tumours survived more than two years. Furthermore, the median survival after diagnosis of recurrent disease was only three months.

Case illustration: A 28-year-old man was referred to our institute with chief complaint of progressive dyspnoe 1 month prior to admission. Dyspnoe was accompanied with cough, low grade fever, with fluid, air and tumour at the middle of the lung. He was then referred to Cipto Mangunkusumo hospital for further evaluation. Chest X-ray and CT-scan revealed a mediastinal mass and pneumothorax. EBUS TBNA, bronchoscopy, esophagoscopy, and biopsy were done, specimen taken by EBUS TBNA showing suspicious as Thymoma, and still need confirmation with bigger specimen for additional immunohistochemistry test. Approaching the mass through EUS, help us got bigger specimen. Secondary assessment for finding bigger tissue decided to approach through esophagus using endoscopic ultrasound. Luckily we got bigger specimen and histopathologically and find concluded as chondrosarcoma. Patient underwent five session of radiotherapy but failed to thoracotomy because he could not intubate. Patient was discharged with future plan of chemotherapy.

Conclusion: Due to an exceedingly rare incidence of mediastinal chondrosarcoma presented as mediastinal tumours, the diagnosis of this tumour may be difficult with small biopsy or needle biopsy specimens that demonstrate only one of the two tissue elements and may be mistaken for other tumours such as type A thymoma, solitary fibrous tumour, and synovial sarcoma. Immunohistochemistry may play an important role in the differential diagnosis of these tumours.

P-K-087

THE "MONTHLY" PNEUMOTHORAX

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Introduction: Catamenial Pneumothorax (CP) refers to a pneumothorax occurring in association with menses due to thoracic endometriosis. Among the four presentations of Thoracic Endometriosis Syndrome, CP has a relative frequency of 70%. The right hemithorax is more frequently affected (85%). Patients are often in their reproductive age and present with chest pain and recurrent pneumothoraces within 24–48 hours of their menstrual cycle. We present a case of recurrent pneumothoraces in a young female with intra-operative finding consistent with thoracic endometriosis.

Case Presentation: J.V. is a 39, female, non-smoker, who first presented with a spontaneous right pneumothorax during a routine medical clearance for work permit renewal. Right lung fully re-expanded after 6 days of chest tube drainage. She re-presented a month later with palpitations and dyspnea. CXR showed a recurrence of the right pneumothorax. She was referred to our cardiothoracic surgeon and underwent right VATS plication of diaphragm, pleural biopsy, wedge resection of right upper lobe and talc pleurodesis. Intraoperatively, endometrial like haemorrhagic lesions found on parietal pleural surface of the posterior chest wall and diaphragmatic surface.

Discussion: A high index of suspicion for thoracic endometriosis should exist for women of reproductive age who presents with recurrent chest pain, pneumothorax or haemoptysis around the time of menses. Diagnosis is often delayed due to the lack of correlation of symptoms with the timing of the menstrual period. Chest CT scans may show small cavities or scarring and bullae formation. Thoracoscopy is increasingly used in the diagnosis of Thoracic Endometriosis. The typical findings include implants on the diaphragmatic surface and pleura and diaphragmatic perforations. The yield is higher when the operation is done during menses. First line of therapy after stabilizing the patient's initial presentation is still hormonal suppression, but recurrence rate is high. Patients with recurrent pneumothorax should generally undergo VATS with excision of endometrial implants and repair of diaphragmatic perforations, followed by pleurodesis. In our case, thoracic endometriosis was an incidental finding during VATS. In retrospect, our case is typical of catamenial pneumothorax- female in her reproductive age, presenting with recurrent spontaneous pneumothorax, 1 month apart, which may have coincided with her menstrual cycle.

P-K-088

MANAGEMENT OF HOSPITALIZED 472 PATIENTS WITH THORACIC TRAUMA DURING 20-YEAR PERIOD

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Thoracic trauma is any form of physical injury to the chest. Thoracic traumas account for 25% of all deaths from traumatic injury. The initial management in the golden hour after injury relates directly to chances of survival in thoracic trauma. In this study we reviewed the consequences of various types of thoracic injuries and treatment modalities. We hospitalized a total of 472 patients with major thoracic trauma, consisting of 252 cases with blunt trauma and 220 cases with penetrating trauma (caused by 133 gunshot wounds and 87 stab wounds) between January 1993 and December 2012. Four hundred twenty-one males and 51 females (mean age: 33.81) were enrolled into our study. In the blunt trauma group, 17 hemopneumothoraces, 38 hemothoraces, 38 pneumothoraces, 35 major lung injuries, 6 flail chest, 2 contusion of the heart and 161 ribs, 15 sternal and 9 clavicular fractures were observed. One patient was quadriparalyzed and polytrauma was seen in 33 patients. Among patients with gunshot wounds, there were 57 hemopneumothoraces, 42 hemothoraces, 15 pneumothoraces, and 35 lung injuries. Among patients with stab wounds, there were 22 hemopneumothoraces, 24 hemothoraces and 29 pneumothoraces. In the patients with thoracic trauma, tube thoracostomy was performed in 211, thoracotomy in 25, video-assisted thoracic surgery in 8, laparotomy in 28, median sternotomy in 1 and other non-thoracic operations in 20. Mean hospitalization was 7.6 days. There were five mortality in patients with blunt trauma and two mortality in patients with penetrating trauma. Tube thoracostomy is very valuable in the management of patients with pneumothorax and/or hemothorax except for some thoracic trauma cases with uncontrolled intrathoracic bleeding or visceral organ injury.

P-K-089

SURVEY OF COGNITIVE SITUATION IN PARENTS' KNOWLEDGE OF ALLERGIC DISEASE

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Objective: To investigate the awareness of childhood allergic disease by parents in Guangzhou, the result of this survey can help parents improve their life management measures and treatment for children with allergic disease.

Methods: Questionnaires were carried out on the parents of kindergarten in different areas in Guangzhou city, the results were analyzed by SPSS17.0. Spearman correlation and descriptive statistical analysis was used to analyze the results.

Results: Among the 2540 parents that were handed out, 44.7% of parents think they don't understand types of allergic disease and its symptoms, only 3.6% parents were fully aware of it. 64.8% of parents would not take children with mild allergy symptoms to consultation and treatment. 8.7% of the parents do not know how to prevent the occurrence of allergic diseases. The majority of parents (65.7%) consider keeping away from allergens as the primary way to prevention; only 26.1% of parents are aware of desensitization therapy. Through the Spearman analyses, there are a correlation of the parents cognitive level of allergic diseases and prevention for children with allergy, and the association is statistically significant ($P < 0.001$).

Conclusion: Parents' awareness of allergic disease among children is generally low, medical workers should pay more attention to publicity and education of allergic disease, help parents improve their children's life management measures and treatment for children with allergic disease.

P-K-090

DIAGNOSTIC YIELD IN TB DETECTION USING TWO SPOT SAMPLES ON SAME DAY

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Introduction: In Revised National TB Control Programme, a sputum positive case means 2 positive slides out of 3 sample in two days. But in India, high-grade positive results are very high indicating late reporting (advanced disease) to the microscopic centre. Majority also reports with chest X-ray taken at the periphery with suggestive lesions of TB.

Aim of the Study: To evaluate efficacy of TB detection by doing two spot sample on same day.

Material and Method: Among the District TB Centre attendance very high clinical TB suspects / chest X-ray suspects were subjected for two spot sample smear AFB, one hour apart on same day of reporting the District TB Centre. They were also instructed to come on the next day for usual morning & spot examination.

Result: Of the 20 case evaluated in 3 months span 12 were found positive for all the two spots (60%). 4 cases were 2+ and 8 cases were 3+. The entire patient was 40–60 age group and 8 were male and 4 were female among positives.

Conclusion: Two spot sample on the same day of highly TB suspect will yield a high TB detection qualifying the definition of RNTCP. This strategy will help early detection, lesser patient expenditure and prevent spread by early instruction of treatment.

P-K-091

P-K-093

THE CORRELATION BETWEEN CD4 LEVEL AND TNF ALFA WITH RADIOLOGIC APPEARANCE IN HIV-TB PATIENTS

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Objective: The research aimed to investigate the correlation between the CD4 level and TNF- α with radiologic appearance in HIV-TB Patients.

Method: The research was an observational study with the Cross Sectional design conducted in Wahidin Sudirohusodo Hospital, Makassar from November 2012 to Januari 2013 consisting of 32 respondents. The populations were all the HIV/AIDS with TB patients who fulfilled inclusive and exclusive criteria. The respondents were taken using the Consecutive Sampling. We examined the CD4 level, TNF- α , CXR and data analysis using Chi Square test dan Fisher Exact test.

Results: Mean CD4 level in this study is 42,13 sel/mm³. The study results show no significant correlation between CD 4 level with radiologic appearance (CXR lesion). This could be due to severity of HIV/AIDS. In late stage of HIV, radiologic appearance could be atypical lesion. In this study, 93,8% patients have CD4 level less than 200. Some study showed that CD4 level less than 200 will found atypical lesion on chest X-Ray. Mean level of TNF- α is 18,63 pg/ml. Statistical analysis based on Chi-Square test TNF- α to radiologic appearance shows no significant correlation between them. Cytokine not only produced by macrophage activation but also by other immune system include: lymphocytes, natural killer cells, mast cell and endothelial cells, fibroblasts, microglial cells. Our result is similar with study by Cunha C et al that found decrease of T cell presentation that expressed TNF- α , especially in CD8 T Lymphocyte on HIV-TB patients. Mean level of TNF- α in HIV-TB less than other group (HIV patients and TB patients). Study by Myong et al in di Seoul, 2005, found that decrease level of TNF- α in patients with HIV-TB coinfection due to decrease of alveolar macrophage apoptosis.

The Limitation of Our Study: We did not exclude other opportunistic infection that could affected the level of CD4, TNF- α and severity of chest X-Ray lesion.

Conclusion: The results of the research indicate that there is no significant correlation between the CD4 level, TNF- α with Radiologic appearance of TB-HIV patients.

STRIDOR IN WARFARIN TOXICITY: A CASE REPORT

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Background: Laryngeal haematoma is extremely rare complication of Coumadin toxicity and it can present as a life-threatening upper airway obstruction. To date, this is the first reported case in Philippine Heart Center.

Case Presentation: This is a case of 66 y/o woman, with five day history of non-productive cough, throat itchiness, hoarseness, and difficulty of swallowing. She was a diagnosed case of Rheumatic Heart Disease and underwent Mitral Valve Repair last 2003. Patient had cardioembolic stroke last 2002, a chronic atrial fibrillation and had been on long term Coumadin therapy with a well-controlled International Normalised Ratio (INR). Patient was not in cardiorespiratory distress but with stridor, enlarged palpable cervical lymph nodes, hyperemic pharyngeal mucosae, rhonchi on both lung fields, and irregularly irregular cardiac rate and rhythm. Baseline Prothrombin Time INR on admission was high at 9.190. Arterial Blood Gas showed acute respiratory alkalosis with adequate oxygenation at room air. Computed Tomography Scan of the neck showed thickening of the retropharyngeal soft tissue space at the level C1-C4 with small air pockets relating to an inflammatory process with possible abscess formation. Direct rigid laryngoscopy showed erythematous, soft tissue haematoma at the laryngeal area. No vocal cord paresis, nor mass was seen. The pharyngeal area was relatively normal. Patient was managed conservatively as a case of Upper airway obstruction secondary to warfarin toxicity. Patient was given with intravenous Vitamin K. Repeat Protime INR was already achieved at 1.30 hence Coumadin was resumed. There was also complete resolution of stridor on the 3rd hospital stay. A repeat laryngoscopy and showed significant regression of haematoma and swelling.

Discussion: Haematoma located at the upper airway is frequently secondary to blunt and penetrating trauma, and surgical complication. However, as a complication of Coumadin therapy, it is extremely rare. Early stages show with vague symptoms, such as a sore throat, but later presenting symptoms include dyspnoea, stridor, dysphagia or neck swelling/ecchymosis. Data in the Philippines are lacking, however in the Philippine Heart Center this is the first reported case to date. Upper airway obstruction warrants prompt diagnosis and treatment. It can be managed conservatively once detected early. Intubation and open tracheostomy are options if airway needs to be secured.

Conclusion: In a patient who has been on oral anticoagulant and presented with a stridor, haematoma of the upper airway should strongly be considered. Early detection can save life with conservative management.

P-K-092

A RARE CAUSE OF MULTIPLE HYDATID CYST: BLUNT TRAUMA

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Multiple hydatid cyst as a result of rupture of the hydatid cyst after a blunt trauma is a rare entity. We here want to present our multiple hydatid cyst case occurred after a blunt trauma. A 21 year old man was admitted to our department with a complaint of chest pain. The Chest Ct of the patient revealed multiple cystic lesions and a cavitory lesion in the right hemithorax. The cystic lesions were in the lung parenchyma and in the chest wall. In the physical examination of the patient we saw a thoracotomy scar. When we examined the patient history, we found a fall history from a tree. He was then taken to a hospital where right pneumothorax was diagnosed. Tube thoracostomy was applied to the patient and afterwards he had been operated. After the operation he was said to have hydatid cyst. As we have seen multiple cystic lesion and a cavitory lesion after the patients history, we thought that cavitory lesion is secondary to surgery and the cystic lesions are the dissemination of the hydatid cyst. We have prescribed antihelminthic drugs. Patient will be evaluated for surgery after the medical treatment. After the surgery of a ruptured hydatid cyst, medical treatment must be prescribed to prevent dissemination. Medical treatment should be prescribed for cases that are disseminated before performing surgery. Pneumothorax and dissemination of the cyst are rare complications of hydatid cyst. Physicians should be aware of these rare complications when managing this disease.

P-K-094

INSPIRATORY FLOW RATES USING IN-CHECK ORAL IN PATIENTS OF OBSTRUCTIVE AIRWAY DISEASES IN INDIAN POPULATION

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No organizations provided

Introduction: During the inspiratory effort, the asthma or COPD patient generates a pressure drop with a consequent activation of the dry powder inhaler (DPI) or breath-actuated inhaler (BAI) device. This inspiratory flow has to be high enough to guarantee an optimal deposition of the medication in the lungs. Such peak inspiratory flows (PIFs) are dependent on the patient's inhalation effort. It has been shown that optimal inspiratory flow rates may not be achieved in few patients, especially in children or elderly patients with COPD, especially during acute exacerbations. PIFs >60 L.min⁻¹ are generally accepted to be the optimal flows for most of the devices, while PIFs <30 L.min⁻¹ are believed to be insufficient for generating any effect.

Methods: The present study compared PIF rates in patients (n = 178) with asthma including children and in COPD patients including elderly. PIF was measured using the in-check dial (Clement Clarke International Ltd, Harlow, UK). The highest value of the three attempts was recorded. An arbitrary cut-off at a PIF of 45 L.min⁻¹ was made in order to distinguish therapeutic flows from sub-therapeutic levels.

Results: The mean (\pm SD) PIF was 201.89 (\pm 82.74) L.min⁻¹ and 134.78 (\pm 61.85) L.min⁻¹ in patients with asthma (n = 132; mean age = 35.88 years) and COPD (n = 46; mean age = 64.54 years), respectively. The paediatric (\leq 12 years) asthma patients (n = 22, mean age = 7.98) and severe COPD patients (n = 34, mean age = 64.41); demonstrated a mean (\pm SD) PIF of 124.54 (\pm 50.68) L.min⁻¹ and 124.70 (\pm 60.46) L.min⁻¹, respectively; these two subgroups representing the two ends of the spectrum with generally the lowest PIF values. The lowest PIF value recorded was 40 L.min⁻¹ in 3 patients (2 elderly severe COPD patients and 1 paediatric asthma patient). PIF measured by the in-check method correlated positively with the percent predicted forced expiratory volume in one second (FEV₁%) (r = 0.53). PIF showed a strong positive correlation with age till 12 years (r = 0.60) while for 13 to 84 years it showed a moderate negative correlation (r = -0.50). PIF correlated positively with height (r = 0.51) and negatively with severity of disease for both asthma and COPD.

Conclusion: In conclusion, the present study demonstrates the ability across all age groups, including children and elderly patients, to generate sufficient inspiratory flow to activate the available DPIs and BAIs, irrespective of the age or severity of asthma or chronic obstructive pulmonary disease.

P-L-002

DERIVATION OF THE PREDICTED EQUATION FOR PEAK INSPIRATORY FLOW RATE (PIFR) FOR CHILDREN AGED 4–15 YEARS IN AN INDIAN POPULATION

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The PIFR represents the strength of the diaphragm contraction and can be used as a marker of lung and thoracic cage growth. We aimed to study the PIFR values and derive its predicted equation for school children.

Methods: 2254 boys and girls between the ages of 4–15 yrs were invited to participate. Parents of 1855 children who consented filled in a health questionnaire. After measuring height and weight, highest of the 3 PIFR values measured using the Clement Clarke Peak Inspiratory Flow Meter® (UK), were used for analysis. Stepwise multiple regression analyses were then used to determine which combination of variables best fitted the model. 80% of the data was used for deriving the predicted equation and 20% was used for validation.

Results: Out of 1855 eligible children, 427 boys and 401 girls were found suitable (no asthma, no respiratory symptoms for 12 months). Height was the only significant factor that affected variance (r = 0.80 for boys; 0.75 for girls). The predicted PIFR equations were – for boys: PIFR = 2.859 × Ht-218.36; for girls: PIFR = 2.324 × Ht-159.64. The predicted values matched the actual values in the remaining 20% children.

Conclusion: This is the first predicted equation for PIFR for school children aged 4–15 years for an Indian population.

P-L-003

BRONCHO DILATOR RESPONSE TO SALBUTAMOL DELIVERED BY METERED DOSE INHALER WITH SPACER VERSUS DRY POWDER INHALER IN ACUTE ASTHMA IN CHILDREN

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Background: Asthma is a chronic inflammatory disorder and salbutamol inhalation is the mainstay of treatment for acute exacerbation of asthma. A number of delivery systems for asthma medication have been developed for children, each having its own advantages and disadvantages. In adults, a good number of studies conducted to compare the clinical efficacy of different inhalation systems for asthma management but in case of children, very limited number of studies exist and so far knowledge none in our country.

Objective: To compare the broncho dilator effect of salbutamol inhalation delivered through metered dose inhaler (MDI) with spacer and dry powder inhaler (DPI) in children presenting with mild and moderate acute asthma.

Method: Children of 6 to 15 years of age (N = 206) with mild or moderate acute exacerbation of asthma were assessed primarily and randomly distributed into two groups having equal number of patients and received 400 micro-gram of salbutamol delivered by either MDI with spacer or DPI device. The primary outcome variable was peak expiratory flow rate (PEFR) and secondary outcome variables were percent predicted PEFR, heart rate, respiratory rate, oxygen saturation, wheezing and accessory muscle scores. Changes in primary and secondary outcome variables, before and after drug intervention were recorded and subjected to statistical tests for significance. Separate analyses were done for mild and moderate asthma patients.

Results: The changes in primary outcome variable (PEFR) in both groups before and after intervention was 179.19 \pm 33.27 vs. 197.52 \pm 57.01 liters/min and 184.81 \pm 59.65 vs. 202.83 \pm 64.76 liters/min respectively, which was statistically highly significant (P = 0.001). Similar significant changes were also observed in case of secondary outcome variables.

Conclusion: Broncho dilator response to salbutamol in mild or moderate acute asthma in children is similar when equal amount of drug is delivered either through an MDI with spacer or a DPI.

POSTER PRESENTATION – PAEDIATRICS

P-L-001

A RARE CAUSE OF CONGENITAL STRIDOR IN A TWO-MONTH-OLD INFANT

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Congenital saccular cysts are rare. They present with stridor and oftentimes mimic a benign condition such as laryngomalacia. The management differs, thus a careful investigation is warranted. A 2-month-old female infant was admitted due to persistent inspiratory stridor which started at day 3 of life. Patient has had previous consultations and was told to have laryngomalacia. On computed tomography of the upper airway, a partially demonstrated cyst along the levolateral aspect of the left aryepiglottic fold was noted. Direct laryngoscopy showed a smooth walled cyst arising from the left aryepiglottic fold. Unroofing and marsupialization of the cyst was done. Symptoms of saccular cysts are non specific. A thorough history, imaging studies and visualization of the laryngeal area are the key to accurate diagnosis. Early recognition and appropriate treatment are essential because it can cause life-threatening airway obstruction. If diagnosis is delayed, it may lead to serious morbidity, moreso if left undiagnosed.

P-L-004

P-L-006

CONGENITAL CYSTIC ADENOMATOID MALFORMATION IN INFANCY

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Congenital cystic adenomatoid malformation (CCAM) encompasses a spectrum of variably sized pulmonary cysts with differing histology. These cystic lesions are non functional and may continue to enlarge postnatally forming macrocysts. We describe two infants with pulmonary macrocysts. The first case is a 7th month old male who came to our institution because of persistence of recurrent pulmonary infections. Patient was in mild respiratory distress with absent breath sounds on the left. Chest CT scan revealed multicystic structures on the left lung with mediastinal shift to the right. Left upper lobe lobectomy was done and biopsy revealed CCAM type 4. The second case is a 3 month old male with persistent tachypnea as the presenting symptom. Patient was admitted from another institution and managed as pneumonia with pneumothorax. CT Scan was done revealing large cystic lucencies on the left upper lobe with mediastinal shift to the right. Patient came in mild respiratory distress with absent breath sounds on the left. 2D echo revealed VSD. Patient underwent left upper lobe lobectomy. Biopsy revealed CCAM type 2. Both patients survived. In conclusion, CCAM can have varying presentations and the size of the lesion and the clinical course are not predictive of the specific lesion type. Tissue diagnosis is therefore essential.

PULMONARY AGENESIS IN A 5 YEAR OLD

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Pulmonary agenesis is a rare congenital anomaly with half of the cases associated with a variety of cardiac and non-cardiac malformations. Although more than fifty percent die before the first five years of age, some individuals may remain asymptomatic throughout their life with prognosis better in those with left sided malformation than those with right sided anomaly. We report a five year old girl who presented with recurrent respiratory infection due to left lung agenesis without any associated major cardiac or non-cardiac anomalies. She was diagnosed and managed as a case of tuberculosis yet remained to have recurrent lung infection. It is invaluable that children presenting with recurrent lung infection should be investigated for any congenital abnormality of the lung.

P-L-005

P-L-007

CLINICAL FEATURES AND OUTCOME OF EMPYEMA THORACIS FROM STREPTOCOCCUS PNEUMONIAE SEROTYPE 19A IN THAI CHILDREN

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Background: Streptococcus pneumoniae is the most common caused pathogen of complicated pneumonia including necrotizing pneumonitis and empyema thoracis. Serotype 19A is an emerged strain which associates with antibiotic resistance.

Methods: We describes clinical features and outcome of empyema thoracis from Streptococcus pneumoniae serotype 19A in Thai children.

Results: We reviewed 20 cases of invasive pneumococcal disease in children age from 5 months–7 years during year 2008–2013 in Bangkok Hospital. There were 3 cases of empyema thoracis caused from S. pneumoniae which ages ranged from 18 months to 7 years. All cases received combination antibiotics but failed to medical treatment. All cases underwent thoracotomy with decortications eventually. All blood culture or pleural fluid culture yielded S. pneumoniae with identified as serotype 19A. All cases responded well to decortications with defervescence within mean of 2.5 days without surgical complications. One case developed hemolytic uremic syndrome with upper gastrointestinal bleeding, microangiopathic hemolytic anaemia, thrombocytopenia and renal failure. All cases never received pneumococcal conjugated vaccine. Follow-up clinical and radiologic examinations returned normal pulmonary function after 6 months. All cases received 13-valent pneumococcal conjugated vaccine (PCV13) after clinical resolving.

Conclusion: Empyema thoracis is a severe complicated pneumonia with significant morbidity. Serotype 19A S. pneumoniae is detected as predominant emergence serotype associated with antibiotic resistance. Thoracotomy with decortications is safe and effective in combination with antibiotic treatment. Vaccination with PCV13 has potential to decrease the incidence of invasive pneumococcal disease and associated morbidity.

CLINICAL PROFILE OF SUSPECTED PAEDIATRIC CASES OF CHIKUNGUNYA CASES FROM ALAPPUZHA IN THE 2006 OUTBREAK

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Introduction: When Chikungunya fever (CGF), a benign Dengue – like viral illness occurring in epidemics, struck Kerala in 2006, the worst affected district was Alappuzha. In view of antigenic variations of virus of present epidemic modified clinical presentation was expected.

Aim of the Study: To study the clinical profile of paediatric CGF cases.

Materials and Methods: Suspected paediatric CGF cases admitted from September 2006 to December 2006 in TDMC Hospital, Alappuzha were studied. Data collected as per performa by interview and case sheet review. Patients were reviewed 3–7 months after illness.

Results: 110 cases were studied. Age varied from 32 days to 12 years (mean 8.2 yrs). M : F – 0.92:1. Maximum cases were from Cherthala taluk, the worst affected. Fever, the universal symptom, lasted 1–9 days (mean 3 days). Next commonest were cutaneous manifestation (89%). Characteristic facial flushing and ear erythema noted in 42.7%. Generalized diffuse erythema noted in 78%. Most subsided within 3 days. Joint symptoms like arthritis & arthralgia were seen in 2/3 cases – knee and ankle joints mainly and also small joints of hands and feet. They were transient, lasting 3 days in 80% cases. Persistent joint symptoms noted in two girls in whom the disease probably unmasked SLE and psoriatic arthritis. Other symptoms were myalgia (63.6%), conjunctival congestion (51%), headache, photophobia, generalized lymphadenopathy. CNS symptoms observed in nearly 1/3rd (29%) with febrile delirium in older children being the commonest. GI symptoms like vomiting, loose stools, abdominal pain noted in 71%. Bleeding manifestations and shock were not seen. Investigations: CBC did not show any typical changes nor PCV, LFT, CSF studies. IgM card test done from cases selected randomly showed positivity in 3/4th of samples. Mortality was nil.

Treatment: Essentially symptomatic and supportive. Infants and those with strong suspicion of Leptospirosis received antibiotics (4 & 12). Follow up showed residual symptoms in only 2, already mentioned.

Conclusion: The clinical profile of paediatric CGF was well in accordance with historically reported ones. Sequelae was minimal.

P-L-008

EFFECTS OF SEASON ON BIOMARKERS IN CHILDREN WITH EXACERBATION OF ASTHMA

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Background: Acute asthma exacerbation is defined as aggravation of asthma symptoms such as breathlessness, cough and wheezing. Several factors are known to cause asthma exacerbation but upper respiratory infection and exposure to aeroallergens are thought to be the most common cause. In our study, we compared seasonal difference in aeroallergen antibody titer and laboratory data between acute asthma exacerbation in fall and non-fall.

Methods: Study included 36 patients who visited Seoul St Mary's Hospital emergency department for mild to moderate asthma exacerbation between Sept 22, 2008 and Nov 8, 2010. We defined fall group as patients who visited emergency department in Sept, Oct, Nov and the rest were defined as non-fall group. We compared the clinical features, allergen specific IgE, cytokine, total IgE, eosinophilic cationic protein between fall group and non-fall group.

Results: Twenty-eight patients were included in fall group and 8 were non-fall group. Within the fall group, 14 (50%) visited emergency department in October. Mean age of fall group was 6.0 and 15 (58.3%) were male. Mean age of non-fall group was 5.6 and 6 (75.0%) were male. Total IgE was significantly higher in fall group; 787 IU/ml in fall group and 247 IU/ml in non-fall group. Antibody titer for *Dermatophagoides farinae* was 50.9 kUA/L and 11.9 kUA/L in fall group and non-fall group respectively. Antibody titer for *Dermatophagoides pteronyssinus* was 126.4 kUA/L and 27.1 kUA/L in fall group and non-fall group. Fall group showed significantly higher titers for house dust mite. Proinflammatory cytokines such as IL-1 β , IL-2, IL-6, G-CSF showed no significant difference between 2 groups. Antiviral cytokines such as IP-10 and IFN- γ showed no difference.

Conclusion: We found that in Korea, asthma exacerbation occurs most commonly in October. We also found that atopic tendency and sensitization to house dust mite plays an important role in asthma exacerbation rather than viral infection as previously thought. However, further study will be needed to clarify why such difference occurred.

P-L-009

THE STUDY OF GAMMA GLOBULIN TREATMENT EFFICACY IN CHILDREN BRONCHIAL PNEUMONIA

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Objective: To observe the therapeutic effects of Intravenous immunoglobulin (IVIg) on pneumonia of children.

Methods: Eighty children with pneumonia were randomly divided into treatment group and control group. Both of the groups were treated with anti-infection, anti-virus, cough relief, expectorant, inspire oxygen, glucocorticoid and other treatments. In addition to the above, the treatment group was additionally given IVIG 400 mg/kg/day for 3 days.

Results: The time to disappearance of cough in the treatment group (5.1 ± 0.13) is shorter than the control group (7.5 ± 0.40). The time to disappearance of the rale in the treatment group (5.5 ± 0.27) is shorter than the control group (6.9 ± 0.28). While the disappear time of tachypnea (3.36 ± 0.33) is shorter than the control group (6.29 ± 0.22). The time to disappearance of the cough, rale, and the shorten time of tachypnea of the two groups, have statistical difference ($P < 0.05$).

Conclusions: Using IVIG can reduce the course of disease and improve the rate of cure. IVIG is significantly efficacious on treating pneumonia of children.

POSTER PRESENTATION: PULMONARY CIRCULATION

P-M-001

THROMBOLYTIC TREATMENT (ALTEPLASE; RT-PA) IN ACUTE MASSIVE PULMONARY EMBOLISM AND CARDIOPULMONARY ARREST

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Patients with pulmonary thromboembolism (PE) often decompensate suddenly, and once hemodynamic compromise has developed, mortality is extremely high. Currently, thrombolytic therapy for PE is still controversial. We retrospectively evaluated 34 patients with PE between January 2010 and December 2013 in Samsun Medicalpark Hospital, Department of Pulmonary Medicine, Samsun, Turkey. The demographic and disease characteristics of patients who receiving thrombolytic treatment were retrospectively analyzed. The female to male ratio was 19/15 and the mean age was 63.1 ± 13.2 years. PE diagnosis were made: echocardiography (64.7%) and contrast enhanced-thorax CT with echocardiography (32.4%). 22 (64.7%) of patients went into the cardiopulmonary arrest due to massive PE and 17 (50%) of total patients recovered without sequelae. 11 (32.4%) of patients were diagnosed massive PE during cardiopulmonary arrest with clinical and echocardiographic findings. Alteplase (rt-PA) was administered during CPR and 4 (36.3%) patients responded to the CPR and they remained alive without sequelae. The complications of rt-PA treatment were haemorrhage in 5 (14.7%) patients and allergic reactions in 2 (5.9%) patients. There was no mortality due to complication of rt-PA treatment. In conclusion, mortality due to massive PE is much more than estimated and alteplase can be used safely in patients with massive PE. The thrombolytic treatment was not associated with any fatal haemorrhage complication. If there is any sign of acute PE, echocardiography should be used during cardiopulmonary arrest/instability and alteplase should be given in patients with suspected massive PE.

P-M-002

CLINICAL CHARACTERISTICS OF 99 PATIENTS WITH PTE

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Objective: We analyzed the clinical characteristics of 99 pulmonary thromboembolism (PTE) patients of the Second Affiliated Hospital of Jilin University, providing new perspectives for diagnosis and treatment of PTE.

Methods: Clinical data of 99 cases with PTE diagnosed by CT pulmonary angiography (CTPA) were collected from 2009 to 2013 in the Second Affiliated Hospital of Jilin University. We identified and analyzed the clinical data of these PTE patients, mainly on the general information, risk factors, clinical symptoms, examination and treatment.

Results

1. The risk factor for PTE includes old age, 46 cases were over the age of 60 (46.4%).
2. The aetiologies of 77 cases (77.8%) are clear, mainly post-operation, post-trauma fracture and deep venous thrombosis.
3. Clinical manifestations were not obvious in PTE patients and only 9 cases had typical chest pain, haemoptysis, dyspnoea triad.
4. The results of echocardiography indicated 22.2% of these patients had increasing pulmonary artery pressure; Lower extremity vascular ultrasound showed that 64.6% of these patients had lower extremity deep venous thrombosis; ECG showed that 4% patients had typical SI QIII TIII changes; D-dimer, 98 cases were positive (98.9%).
5. 84 cases were administered warfarin combined with low molecular heparin for anticoagulation after thrombolysis.

Conclusions

1. The risk factors of PTE include age and smoking.
2. Physicians should diagnose PTE combining with various examinations to improve the diagnosis rate owing to the atypical clinical manifestations of PTE.
3. Warfarin combined low molecular heparin used for anticoagulation is a safe and effective approach for PTE patients.

A CASE REPORT ON BRONCHIAL TO PULMONARY ARTERIAL-ARTERIAL FISTULA PRESENTING AS MASSIVE HAEMOPTYSIS

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Background: The phenomenon of systemic and pulmonary vascular communication occurs normally through the capillary bed surrounding the respiratory bronchioles. A direct anastomoses between two arterial to arterial circulations is a rare pulmonary vascular disorder which can suddenly lead to life threatening complications.

Objective: To be able to present a rare case of bronchial to pulmonary artery fistula in a 22 year old who presented with life-threatening haemoptysis.

Case: This a 22 year old male who presented with life-threatening haemoptysis. Work-up for tuberculosis, pneumonia or bronchiectasis revealed negative results. Chest CT angiography and pulmonary arteriogram failed to show distinct signs of AV malformation or aneurysm involving the pulmonary arterial system. Bronchial arteriogram revealed an isolated anomalous communication between a bronchial artery and pulmonary artery. The patient was initially managed by placing a fogarty catheter to provide endobronchial tamponade. The patient subsequently underwent embolization using a standard coil, completely occluding the supplying branch from the right bronchial to pulmonary arterial-arterial fistula in the medial basal segment of the right lower lobe. The patient was eventually discharged stable without recurrence of haemoptysis.

Conclusion: Systemic to pulmonary vascular communication should be considered in the differentials for a variety of conditions causing haemoptysis. Awareness of these disease entities promote earlier recognition of the cause of haemoptysis, and facilitates management and definitive treatment.

P-M-004

RISK CHARACTERISTICS OF VENOUS THROMBOEMBOLISM IN CHINESE PATIENTS

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Background and Objectives: There is little report concerning the risk characteristics of Chinese VTE patients. The present study was designed to investigate the risk characteristics in Chinese VTE patients through a retrospective study.

Methods: A total of 1,048 registry patients with VTE in recent 10 years was analyzed retrospectively with respect to underlying diseases or predisposing factors.

Results: The incidence of VTE in both male and female has been increasing in recent ten years and its prevalence in men was more than in women. 885 patients (73.0%) were more than 50 years and the mean age of the patients at diagnosis was 58.8 ± 15.7 years with 57.1 ± 15.4 years for male ($n = 603$), younger than 59.7 ± 15.5 years for female ($n = 445$, independent-samples *t* Test, $p < 0.05$). Main risk factors were a prolonged immobilization (11.9%), malignant tumours (10.4%) and infections (4.1%), which were different from western patients. Among all the tumours, lung and liver cancers were the dominant malignant tumours in male VTE patients, while uterus and lung cancers in female.

Conclusions: This registry demonstrated the different risk characteristics in Chinese from western patients. Our results will be available for establishing the prevention for VTE in China.

P-M-005

VATS LOBECTOMY FOR PULMONARY ARTERIOVENOUS MALFORMATION: A CASE REPORT

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Introduction: Pulmonary arteriovenous malformations (PAVM) are rare pulmonary vascular anomalies that caused by abnormal communications between arteries and veins. Due to evidence of progressive enlargement over a period of time and high morbidity rate, treatment should be done in order to prevent severe complications for all patients.

Case Report: A 37-year old woman presented with cyanosis on her lips and fingers and dyspnoea. This symptoms have been present for the past ten years. The chest X-ray revealed the specific findings compatible with PAVM on the right lower zone. In her blood gas analysis the oxygen saturation was 82.9%, pH: 7.472, PaO₂: 43.1 mmHg, PCO₂: 27 mmHg. Her blood analysis was normal except seconder erythrocytosis. Her brain CT was normal and there was no lesions compatible with Hereditary Haemorrhagic Telangiectasia (HHT). There was a massive AVM in the right lower lobe. It has two large feeding arterial vessels originating from pulmonary artery. She underwent embolization for two large feeding vessels. The embolization procedure was achieved uneventfully. However she does not relief probably due to two large size of the proximal feeding artery and her oxygen saturation was around 90% by pulse oximetry after one months from transcatheter embolization. Her cyanosis was not resolved. We discussed about any surgical intervention for patients including lobectomy if necessary. There was no target area that will be curative when we performed wedge resection. Therefore, we performed VATS lobectomy without any difficulty. Chest tube was removed on 4th postoperative day and the patient was discharged uneventfully. Her blood gas analysis was normal. The oxygen saturation was 98.8%, pH: 7.456, pO₂: 98.1 mmHg, pCO₂: 29.7 mmHg four months after surgery.

Conclusion: The benign diseases of the lung should be treated curatively with minimally invasive manner and less morbidity rate. VATS lobectomy can be accepted as a safe and minimally invasive procedure for patients with PAVM especially when it was performed after transcatheter embolization.

P-M-003

P-M-006

CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION OF 20 YEAR OLD FEMALE

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Background: Chronic thromboembolic Pulmonary Hypertension (CTEPH) is defined as mean pulmonary artery pressure greater than 25 mmHg that persists 6 months after pulmonary embolism is diagnosed and has emerged as one of leading cause of severe pulmonary hypertension. The incidence and prevalence of CTEPH are yet to be accurately determined and may be significantly underestimated. Historically, the occurrence of CTEPH in patients diagnosed with acute pulmonary embolism (PE) has been considered rare. Data from autopsy studies estimated the incidence of CTEPH at 1–3% overall and at 0.1–0.5% in patients surviving acute PE.

Method: A 20 Year old female admitted to Wahidin Sudirohusodo Hospital with progressively worsening Shortness of breath since 1 year ago. She had history of hospital admission and diagnosed with pulmonary hypertension with unknown aetiology. Physical examination revealed blood pressure 100/60 mmHg, tachypnea, tachycardia, jugular venous distention, Systolic murmur grade 3/6 on left lower sternal border, accentuated second heart sound and pitting oedema in lower extremities. ECG showed Sinus tachycardia, Right axis deviation and Right ventricle hypertrophy. Blood test revealed D-dimer 2.2 µg/ml. Chest X-ray revealed enlargement of the right ventricle and pulmonary artery. Transthoracic Echocardiography showed enlarged right chambers, severe tricuspid regurgitation, thrombus in the enlarged pulmonary artery and severe pulmonary hypertension. Contrast enhanced Multislice CT scan showed dilatation of Pulmonary Artery, thrombus mainly at right pulmonary artery with right lung infarction. Patient treated with thrombolytic agent (actylase) anticoagulant, oral fibrinolytic agent, phosphodiesterase type 5 inhibitors and prostacyclin analogue. Patient in stable condition with symptom relieved.

Result: A case of Chronic Thromboembolic Pulmonary Hypertension has been reported.

Conclusion: As one of the causes of severe Pulmonary Hypertension, Chronic Thromboembolic Pulmonary Hypertension should be specifically considered in the diagnosis workup of patients with pulmonary hypertension.

P-M-007

SEVERE PULMONARY FAILURE WITH PULMONARY ARTERIO-VEIN FISTULA DUE TO HEREDITARY HAEMORRHAGIC TELANGIECTASIA SUCCESSFULLY TREATED WITH COIL EMBOLIZATION IN A WOMAN JUST AFTER DELIVERY AND HER FATHER WITH IGG4-RELATED DISEASE

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Hereditary haemorrhagic telangiectasia (HHT), also known as Osler–Weber–Rendu disease, is an autosomal dominant genetic disorder that leads to arteriovenous (AV) fistula in the lung, liver and brain. We report two cases of HHT with severe pulmonary failure due to pulmonary AV fistulae that were successfully treated with coil embolization.

Case 1: A 30-year-old woman, just after a delivery via Caesarean section, showed pulmonary failure with 80% of SpO₂ under oxygen 15 L/min with mask reservoir bag. She had been diagnosed with HHT and her pulmonary AV fistulae had been treated with coil embolization 8 years before, and oxygen 2 L/min by nasal cannula had been administered until the delivery. To treat the severe pulmonary failure, we performed pulmonary catheterization and coil embolization in the eight AV fistulae, and her SpO₂ shows 89% under oxygen 2 L/min with nasal cannula. Additionally PaO₂ was improved to 236.2 Torr from 100.2 Torr under 100% oxygen after the coil embolization. Her physical ability recovered as before delivery.

Case 2: A 64-year-old man, the father of Case 1, also had a pulmonary AV fistula 4 cm in diameter for more than 30 years, and his SpO₂ showed 86% under room air. He has a history of cerebral infarction. Recently, pleural effusion, systemic lymphadenopathy and pulmonary nodules were found and he was diagnosed with IgG4-related disease. Corticosteroid was administered to treat IgG4-related disease with success, and then coil embolization was applied to pulmonary AV fistulae in the right lower and left lower lungs. PaO₂ was markedly improved to 441.5 Torr from 153.8 Torr under 100% oxygen.

Here we report two pulmonary failure cases of HHT with pulmonary AV fistulae that were successfully treated with coil embolization – in a woman just after delivery and her father with IgG4-related disease.

P-M-008

AN INTERESTING CASE OF SECONDARY POLYCYTHEMIA

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Introduction: Pulmonary arteriovenous malformations (PAVM) are rare pulmonary vascular anomalies. We present a case of PAVM which is unique because of its location being in close proximity to Left atrium.

Case Presentation: A 17 year old male patient was referred by a Haematologist for evaluation of secondary polycythemia with erythropoietin levels raised (392). All other investigations for secondary polycythemia like 2DECHO, JAK-2 Mutation, Methemoglobin levels, S.Iron, TIBC were within normal limits. On presentation, patient had exertional dyspnea grade 4 since 1½ months. No other significant past history except syncopal attacks twice before presentation. On examination, he was tachypneic, centrally cyanosed, clubbing grade 4 present, SpO₂-60% on Room air and 78% on High flow O₂. All other vital parameters within normal limits. Respiratory and cardiovascular system examination was unremarkable. Chest XRay PA view showed mild cardiomegaly and lung fields were normal. In view of persistent Hypoxia in spite of O₂ support, a double bubble contrast 2DECHO was done which was suggestive of Pulmonary AV Fistula. Later a HRCT Pulmonary angiography revealed large AV Fistula between Right Lower Lobe pulmonary artery and lower lobe pulmonary vein with right lower lung oligemia and dilated Left atrium. The feeder Pulmonary artery measured 1.7 cm in diameter. Because of its location and size, surgery was performed with high risk explained to the patient. Patient improved significantly symptom-wise immediately after surgery. His SpO₂ immediately improved upto 98% as soon as the AVM sac was ligated intraoperatively.

Discussion: PAVMs occur more frequently in women and around 10% of the cases are identified in infancy or childhood, followed by a gradual increase in the incidence through the fifth and sixth decades. Embolotherapy is the treatment of choice for most PAVM. For large and centrally localized lesions with large feeding vessels, surgery is proposed treatment modality. Embolotherapy was not advisable in this case because of close proximity of AVM sac to Left atrium and large size of AVM (4.3*4.2*4.4 cm).

Conclusion: Pulmonary AV malformation is a rare disorder. To our knowledge we report the first case of AVM diagnosed in a young male patient which was in close proximity to the left atrium but was still operated successfully.

POSTER PRESENTATION – RESPIRATORY INFECTIONS (NON-TUBERCULOSIS)

P-N-002

P-N-001

COMPARING CURB-65 AND SOAR CRITERIA IN THE PREDICTION OF ALL CAUSE IN-HOSPITAL MORTALITY IN ADULT COMMUNITY ACQUIRED PNEUMONIA AT THE DELOS SANTOS MEDICAL CENTER: A RETROSPECTIVE STUDY

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Background: The two clinical prediction rules for mortality in community acquired pneumonia (CAP) namely the CURB-65 and the SOAR criteria have been evaluated.

Objective: To compare the accuracy and reliability of CURB-65 versus the SOAR criteria in predicting all-cause 30-day mortality in moderate to severe community acquired pneumonia.

Design: Retrospective validation study.

Materials and Methods: A total of 117 adult patients diagnosed with CAP and admitted to since 2011 to 2013 were reviewed in terms of outcomes. Independent scoring using CURB-65 (confusion, urea >19 mg/dL, respiration \geq 30, blood pressure and age >65) were compared to SOAR criteria (systolic pressure, oxygenation, age and respiratory rate). Accuracy ratings for each index' cut-off score were compared.

Results: A total of 52 deaths and 65 survivors were analyzed. The overall area under the curve for CURB-65 was superior (AUC = 85.1%, 95% CI 78–92.3, $p = .001$) than the SOAR criteria was (AUC = 76.5%, 95% CI 67.7–75.3, $p = .001$). Using CURB-65, confusion, urea level, systolic BP less than 90 mmHg, age (>65) and tachypnea (RR \geq 30) in that order were predictive death. In the SOAR criteria, systolic BP and low oxygenation had the highest predictive odds.

Conclusion: The two clinical prediction rules are simple use in the rapid prognostication of moderate to severe CAP. CURB-65 shares many advantages over the SOAR criteria.

VIRAL AETIOLOGY OF COMMUNITY-ACQUIRED PNEUMONIA IN HOSPITALIZED PATIENTS IN UKRAINE

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Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community. The range and relative impact of microbial pathogens, particularly viral pathogens, as a cause of community-acquired pneumonia (CAP) in hospitalized adults has not received much attention in Ukraine. The aim of this study was to determine the microbial and viral aetiology of CAP in adults and to identify the risk factors for various specific pathogens. We prospectively studied 112 male patients with age of 19 to 25 years old from closed military community, who had hospitalized for CAP to identify its aetiology. Laboratory studies were provided during seasonal increase of acute respiratory diseases during the autumn and winter seasons of 2009–2010 against the backdrop of a pandemic influenza virus A/California/7/2009 (H1N1). It was confirmed diagnosis of CAP, occurred after acute respiratory viral diseases and influenza. For the detection of viral and bacterial agents it was used multiplex RT-PCR and rapid tests. Laboratory investigations showed that the main bacterial agent, detected in patients with CAP, was *S. pneumoniae*. It was identified in 40.9% of cases. *H. influenzae* was the second significant agent, which led to the disease in 15.3% of cases. It was studied by RT-PCR the aetiological structure of respiratory viruses, identified in 95 nasopharyngeal washings (84.8%). Influenza A virus, especially its pandemic variant was usually detected as mono-infection. It was identified in 30.3% of cases (34 patients), including highly pathogenic influenza A (H1N1) California – 20% of cases. Results of the research on detection of viruses were compared with our next studies among patients with CAP in interseasonal period (106 patients, March-June 2013). It was shown a minor role of influenza (3.4%) during this time of year. It was relevant for patients with moderately severe pneumonia only. In addition parainfluenza viruses, adenoviruses, RS viruses, rhinoviruses and coronaviruses played significant role in the ideological spectrum of CAP. So with the use of the modern diagnostic tools it was determined the spectrum of respiratory viruses and bacterial agents in patients with CAP in Ukraine. *S. pneumoniae* remains to be the most frequent pathogen in adults with CAP and should be covered with empirical antimicrobial treatment. Viruses, particularly influenza, were the second most common aetiological agent and should be tested for, especially in fall or winter, both in young and elderly patients who are hospitalized with CAP.

P-N-003

MULTICENTRE, COMPARATIVE STUDY OF LEVOFLOXACIN HIGH-DOSE, IV ORAL SEQUENTIAL THERAPY FOR CAP WITH MOXIFLOXACIN IN INDONESIA

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To evaluate efficacy and safety of high-dose levofloxacin (LVFX, 750 mg) of IV oral sequential therapy, we conducted a randomized, open-label, clinical study comparing with Moxifloxacin (400 mg) sequential therapy in 72 moderate to severe CAP patients. LVFX group showed comparative high clinical success rate (87% vs 84%) with shorter total treatment period (5.8 ± 2.07 days vs 9.3 ± 2.93 days).

P-N-004

METALLO-BETA-LACTAMASE-PRODUCING MULTIDRUG RESISTANT NOSOCOMIAL BACTERIAL ISOLATES CAUSING VENTILATOR-ASSOCIATED PNEUMONIA IN TERTIARY CARE HOSPITAL, NEPAL

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Introduction: Ventilator-associated pneumonia (VAP) caused by multidrug resistant pathogens producing metallo-beta-lactamase (MBL) is a major threat in the intensive care unit (ICU) patients which are increasing in numbers in a developing country, Nepal.

Objective: This study aimed to determine the aetiology of VAP along with multidrug bacterial strains producing MBL.

Methods: A total of 24 endotracheal secretions from the patients diagnosed of VAP from ICU were studied during March 2011-February 2012 at Department of Microbiology, TUTH as described by American Society for Microbiology (ASM). Antibiotic sensitivity tests were determined by modified Kirby-Bauer disc diffusion method. A combination disk method and E-test MBL were done for the detection of MBL-producing isolates.

Results: Twenty nine bacteria were isolated in which *Acinetobacter calcoaceticus baumannii* (Acb) complex was found to be more predominant (44.8%), which was followed by *Pseudomonas aeruginosa* (24.1%) and *Klebsiella pneumoniae* (20.7%). 46.4% of bacterial strains were found to be MBL producer in which Acb complex showed 84.6% and all were resistant to amikacin.

Conclusions: We found a higher rate MDR bacterial strains producing MBL in our hospital which prompts a special attention for the management of such patients as well as urgent need for implementation of infection control strategies.

P-N-006

DISEASE BURDEN OF PNEUMONIA IN KOREAN ADULTS AGED OVER 50 YEARS STRATIFIED BY UNDERLYING COMORBIDITIES

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Background and Aims: Community-acquired pneumonia (CAP) shows high mortality rate despite antibiotics treatment but there are no sufficient data on disease burden of pneumonia in Korea. This study was conducted to assess disease burden of pneumonia in adults according to underlying diseases types and age groups.

Methods: We performed a multi-centre, retrospective, observational study and collected data targeting for CAP patients (≥ 50 yr) from 11 hospitals. Data were assessed by retrospective review of patient medical records. Disease burden was defined as measured by total per-capita medical fee, severity, hospital length of stay (LOS), and mortality. Medical fee was calculated by multiplying the total use of the medical resource item during the hospital LOS with the medical cost unit price for the item. (1 USD = 1,100 Korean Won).

Results: A total 693 patients were included and 83.4% had the underlying disease. Total per-capita medical fees were the highest and the hospital LOS was the longest when the patients had chronic renal disease (USD 2,060 \pm 1,309, 10.72 days). If the patients had CNS disorder, the severity level by CURB 65 score and the mortality rate were the highest (1.88, 9.4%). The disease burden was higher markedly with advancing age. Also, having any kinds of underlying disease with pneumonia was significantly contributed to the burden of disease.

Conclusions: In Korea, the appropriate prevention of pneumonia should be considered as effective strategy, especially the patients with having underlying disease or older age group.

P-N-007

PROPHYLACTIC ADMINISTRATION OF SULFAMETHOXAZOLE-TRIMETHOPRIM ELIMINATES AIRWAY COLONIZATION OF PNEUMOCYSTIS JIROVECI

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Background: The mortality rate of Pneumocystis pneumonia is high without early diagnosis and prompt therapy. Reactivation of a latent infection is considered the main mechanism of the development of Pneumocystis pneumonia in immunosuppressed patients. However, it is still unknown whether prophylactic administration of sulfamethoxazole-trimethoprim has an efficacy on airway colonization of Pneumocystis jirovecii.

Objective: To determine the effect of prophylactic administration of sulfamethoxazole-trimethoprim for development of Pneumocystis pneumonia and for airway colonization of Pneumocystis jirovecii.

Method: We retrospectively assessed the effect of prophylactic administration of sulfamethoxazole-trimethoprim in the patients who had been examined to diagnose or rule out Pneumocystis pneumonia. To detect Pneumocystis jirovecii using the patients' bronchoalveolar lavage fluids or sputa, polymerase chain reaction assay was performed.

Result: There were 60 consecutive patients (mean age; 63-year-old, 38 males and 22 females) between 2004 and 2012. Not all of patients who had received prophylactic administration of sulfamethoxazole-trimethoprim (n = 11) developed Pneumocystis pneumonia nor did they show airway colonization of Pneumocystis jirovecii. None of patients who developed Pneumocystis pneumonia (n = 9, including 3 patients with AIDS) or showed colonization (n = 10) had received the prophylaxis.

Conclusion: The prophylactic administration of sulfamethoxazole-trimethoprim was effective not only on preventing Pneumocystis pneumonia but also on eliminating airway colonization of Pneumocystis jirovecii. Further studies targeting a large cohort of patients with a variety of underlying diseases are required to provide recommendations of prophylactic administration of sulfamethoxazole-trimethoprim.

P-N-005

IN VITRO ANTIBACTERIAL EFFECTS OF EUGENOL AND CINNAMALDEHYDE ON LEGIONELLA PNEUMOPHILA

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Objective: To investigate the antibacterial activity of eugenol and cinnamaldehyde on Legionella pneumophila (Lp) in vitro.

Methods

1. Determining the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of eugenol and cinnamaldehyde on Lp by broth microdilution method, and drawing the time-kill curve of the two drugs on Lp.
2. Fractional inhibitory concentration index was assayed when eugenol and cinnamaldehyde was used in combination.
3. The biofilm model was prepared and used to determine the inhibitory activity of eugenol and cinnamaldehyde on biofilms.

Results

1. The MIC was equal to MBC for eugenol with the concentration of 0.025%, the MIC of cinnamaldehyd was 15–30 μ g/ml, MBC was 30–60 μ g/ml, both were bactericidal.

2. The two drugs had a synergistic effect when used in combination.

3. Eugenol of 1/2MIC, 1/4MIC concentration could effectively inhibit the formation of biofilms of Lp, while cinnamaldehyde showed no significant inhibitory effect on biofilm formation.

Conclusion: Eugenol, cinnamaldehyde had an excellent antibacterial effect on Lp, there was a synergistic antibacterial effect against Lp when eugenol and cinnamaldehyde used as combination. Eugenol demonstrated a strong inhibitory effect against the biofilm formation and Lp in the biofilm, while cinnamaldehyde did not.

P-N-008

CLINICAL UTILITY OF A RAPID ANTIGEN TEST FOR DETECTING HUMAN METAPNEUMOVIRUS: USAGE EXPERIENCE DURING AN OUTBREAK IN A LONG-TERM CARE FACILITY IN OKINAWA, JAPAN

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Background: Human metapneumovirus (hMPV) is a recently described virus and causes upper and lower respiratory tract infection. A Rapid antigen test using immunochromatography for detection of this virus was developed recently and has been available commercially in Japan since 2012. There are very few reports evaluating the utility of rapid antigen test in the clinical setting, especially in adults. In the present study, we discussed the clinical utility and limitation of the rapid antigen test based on the usage experience during an outbreak in a long-term care facility.

Methods: Nasopharyngeal swabs were obtained from a subset of patients and the samples were tested with the multiplex PCR kit (Seeplex RV15 OneStep ACE Detection, Seegene, South Korea) and the rapid antigen test (CHECK hMPV, Meiji Seika Pharma, Japan). We retrospectively evaluated medical records to find out their background.

Results: An Outbreak in a long-term care facility in Okinawa, Japan was occurred between April 12th and 30th in 2013. During the outbreak, 22 patients had symptoms such as rhinorrhea, cough, and fever. We collected nasopharyngeal swabs from 11 patients and examined with both PCR and rapid antigen test. The number of patients with a positive for the PCR and rapid antigen test were 11 (100%) and 6 (55%), respectively. Thus, the 11 patients were confirmed as hMPV infection and the sensitivity of rapid antigen test was 55%. There was no difference between rapid antigen test positive and negative cases in their median age (92.5 vs 91; NS) and prevalence of pneumonia (83% vs 80%; NS). The average days from the onset of symptoms to sample collection was significantly shorter in rapid antigen test positive patients than that in negative patients (4.8 vs 11.2 days; $p < 0.001$). All cases were negative for the rapid antigen test if the samples were collected 9 days after the onset of symptoms.

Discussion: A previous report showed a good performance of the rapid antigen test during an outbreak in a long-term care facility. In the article, all patients were checked with the rapid test within 4 days from the onset of symptoms at longest. Our data suggests the sensitivity of rapid antigen test is decreased if sample collection is delayed from the onset of symptoms.

P-N-009

DEVELOPMENT OF A SINGLE TUBE REAL-TIME FLUORESCENCE LOOP-MEDIATED ISOTHERMAL AMPLIFICATION ASSAY FOR DETECTION OF STREPTOCOCCUS PNEUMONIAE

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Background and Aim of Study: Streptococcus pneumoniae was recognized as a major cause of pneumonia, and is issued as part of many humoral immunity studies. Diagnosis is generally built on clinical suspicion along with a positive culture from a sample from virtually any place in the body. But the testing time is extremely long. This study aims to develop a rapid diagnostic method to identification of Streptococcus pneumoniae.

Methods: Our laboratory has in recent years developed a new platform called RealAmp, which combines loop-mediated isothermal amplification (LAMP) with a portable tube scanner real-time isothermal instrument for the rapid detection of Streptococcus pneumoniae. Two pairs of amplification primers required for this method were the result of a conserved DNA sequence unique to the Streptococcus pneumoniae. The amplification was performed at 63 degree Celsius using SYBR Green for 60 minutes with the tube scanner set to collect fluorescence signals. Clinical samples of Streptococcus pneumoniae and other bacteria were applied in the preparation of the sensitivity and specificity of the primers by comparing with traditional culture method.

Results: The latest set of primers consistently detected in laboratory-maintained isolates of Streptococcus pneumoniae from our hospital. The new primers also showed to be more sensitive than the published species-specific primers specifically developed for the LAMP method in detecting Streptococcus pneumoniae.

Conclusion: This study demonstrates that the Streptococcus pneumoniae LAMP primers developed here have the ability to accurately detect Streptococcus pneumoniae infections by real-time fluorescence loop-mediated isothermal amplification.

P-N-010

RAPID DETECTION OF HAEMOPHILUS INFLUENZAE BY REAL-TIME FLUORESCENCE LOOP-MEDIATED ISOTHERMAL AMPLIFICATION

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Background and Aim of Study: Haemophilus influenzae is a bacterium that can cause a severe infection, occurring mostly in infants and children younger than five years of age. It can cause lifelong disability and be deadly. Diagnosis is generally built on clinical suspicion along with a positive culture. But the testing time is extremely long. This study is to develop a rapid diagnostic method to identification of Haemophilus influenzae.

Methods: Our laboratory has recently developed a new platform called RealAmp, which combines loop-mediated isothermal amplification (LAMP) with a portable tube scanner real-time isothermal instrument for the rapid detection of Haemophilus influenzae. Two pairs of amplification primers required for this method were the product of a conserved DNA sequence unique to the Haemophilus influenzae. Amplification was performed at 63 degree Celsius using SYBR Green for 60 minutes with the tube scanner set to collect fluorescence signals. Clinical samples of Haemophilus influenzae and other bacteria were used for the preparation of the sensitivity and specificity of the primers by comparing with traditional culture method.

Results: The latest set of primers consistently detected in laboratory-maintained isolates of Haemophilus influenzae from our hospital. New primers also showed to be more sensitive than the published species-specific primers specifically developed for the LAMP method in detecting Haemophilus influenzae.

Conclusion: This study demonstrates that the Haemophilus influenzae LAMP primers developed here have the ability to accurately detect Haemophilus influenzae infections by real-time fluorescence loop-mediated isothermal amplification.

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P-N-011

SECULAR TRENDS OF INCIDENCE AND CLINICAL CHARACTERISTICS OF VENTILATOR-ASSOCIATED PNEUMONIA IN THE INTENSIVE CARE UNIT AT ONE UNIVERSITY HOSPITAL

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Purpose: This study was designed for analyzing secular trends of incidence and clinical characteristics for ventilator-associated pneumonia (VAP) in the intensive care unit (ICU) at one university hospital.

Methods: Study population was 97 patients who were diagnosed as VAP at ICU from 2007 to 2012. VAP incidence use discharge patients, patient-days, and ventilator-days as each denominator. We compared VAP rates by Poisson regression. ICU inpatients' and VAP patients' characteristics were analyzed by descriptive statistics.

Results

1) Mean age was 59.36 +/- 17.34 and male was 74(76.3%). Common initial diagnoses were cerebrovascular and neurologic diseases (37.1%) followed by cardiovascular diseases (20.6%).

2) The overall rate of VAP was 3.35% per 100 discharge patients, 1.23 episodes per 1,000 patient-days and 3.40 episodes per 1,000 ventilator-days. The rate decreased from 4.92 in 2009 to 1.73 per 100 discharge patients in 2012 (p = 0.012, RR 0.858, CI 0.160-0.815). 1.75 in 2009 to 0.65 per 1,000 patient-days in 2012 (p = 0.038, RR 0.882, CI 0.784-0.993) and 4.41 in 2009 to 2.01 per 1,000 ventilator-days in 2012 (p = 0.201, RR 0.925). The most commonly isolated pathogens were Acinetobacter baumannii (47.4%), and Pseudomonas aeruginosa (11.8%).

Conclusion: The annual incidence of VAP was decreasing, which could be explained by active surveillance and infection control measures.

P-N-012

RAPID PATHOGEN IDENTIFICATION USING MALDI-TOF MS FOR CRITICALLY ILL PATIENTS WITH PNEUMONIA

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Background: Rapid pathogen identification and appropriate antibiotics therapy is important to treat critically ill patients. This study was conducted to evaluate the usefulness of Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass spectrometry (MALDI-TOF MS) for rapid pathogen identification for critically ill patients with pneumonia.

Methods: We conducted a retrospective study in the intensive care unit (ICU) at Pusan National University Hospital in Korea from May 2012 to February 2014. Patients who performed microbial culture and organism identification of endotracheal aspirate while receiving ventilator care were enrolled.

Results: A total 50 patients were included final analysis. Pathogen identification was performed using MALDI-TOF MS in 27 patients (MS group) and conventional methods in 23 patients (Conventional group). There were no differences in demographic characteristics and disease severity between two groups. When comparing two groups, the average time between endotracheal aspirate sample collection and pathogen identification (with antibiotics susceptibility test result) was shorter in MS group than conventional group (51.9 ± 10.8 hr vs. 70.5 ± 28.2 hr, p < 0.05). Thirty-seven patients changed antibiotics according to the identification results (21 patients in MS group, 16 patients in conventional group). The average time between sample collection and antibiotics change was shorter in MS group than conventional group (55.8 ± 10.6 hr vs. 74.9 ± 29.8 hr, p < 0.05). However, there were no significant differences in duration of mechanical ventilation, length of hospital stay and hospital mortality between two groups.

Conclusions: Pathogen identification and antibiotics change was faster when using MALDI-TOF MS in critically ill patients with pneumonia. Further investigation is needed to evaluate the impact of rapid pathogen identification on clinical courses of critically ill patients.

P-N-013

P-N-015

A FUNGAL INFECTION MIMICKING ENDOBRONCHIAL MASS

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A 68 year-old immunocompetent female patient was admitted for cough, sputum, and dyspnea for 4 months. The chest x-ray showed consolidation at right lower lobe. In thorax CT, there was a solid mass lesion extending through right lower lobe. Fiberoptic bronchoscopy showed mucosal infiltration extending right intermedial bronchus to the lower lobe. The histopathological examination of bronchus biopsy and transbronchial needle aspiration revealed fungus hyphae and dense inflammation. In thorax CT after a month of antifungal treatment the lesion regressed. This case was presented because fungal infection mimicked endobronchial mass lesion.

EVALUATION OF CHEMOTHERAPY FOR PULMONARY NON-TUBERCULOUS MYCOBACTERIAL DISEASE

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Background: Pulmonary non-tuberculous mycobacterial disease (NTM) is a progressive respiratory infection that sometimes causes chronic respiratory failure; however, it is still controversial when to start chemotherapy for NTM.

Aim: The aim of this study is to evaluate the factors that affect antimicrobial chemotherapy for NTM. **METHODS:** Patients were eligible for this study if they were diagnosed with pulmonary NTM in Yamagata University Hospital from 2007 through 2014. Pulmonary NTM was diagnosed by the following criteria: pulmonary nodules or infiltrates in chest X-ray; isolation of non-tuberculous mycobacteria once or more from sputum or bronchial aspirate cultures. Patients were divided into two groups; treated group and untreated group. Clinical parameters (e.g. patient characteristics, underlying diseases, results of clinical laboratory tests, and microbiological tests) were assessed retrospectively to determine the factors that affect the decision of starting chemotherapy for NTM.

Results: A total of 101 patients (39 men and 62 women) were enrolled in this study. The median age of the patients was 72 years (41 to 94 years). Of these 101 patients, 68 cases were positive cultures for *Mycobacterium avium*, 17 were *M. intracellulare*, and 16 were other mycobacteria. Twenty-four patients had undergone chemotherapy for NTM (7 men and 17 women, treated group), whereas 77 patients had not undergone any therapies (32 men and 45 women, untreated group). Standard combination of antimicrobials were given in most cases of treated group in accordance with the guidelines for chemotherapy of pulmonary NTM by the Japanese Society for Tuberculosis and the Japanese Respiratory Society. The age of patients were significantly younger in the treated group (61.9 years vs. 72.3 years, $p < 0.05$, Wilcoxon test). There were significantly more patients that showed positive results for acid-fast staining of sputum in the treated group (41.7% vs. 10.5%, $p < 0.05$, Chi-square test). Serum albumin levels were higher in treated group than untreated group (4.0 g/dl vs. 3.7 g/dl, $p < 0.05$, Wilcoxon test). There were no significant differences in other parameters including patient characteristics, underlying diseases, or other results of clinical laboratory tests. Multivariate analysis indicated that younger age of the patients and positive sputum smear test of acid-fast staining were the independent deciding factors in terms of antimicrobial chemotherapy for NTM.

Conclusion: Our study suggested that relatively younger patients with active pulmonary NTM would have a good indication for antimicrobial chemotherapy.

P-N-014

THE RELATIONSHIP BETWEEN PROCALCITONIN AND PNEUMONIA SEVERITY INDEX (PSI) SCORES TO ASSES THE SEVERITY OF COMMUNITY ACQUIRED PNEUMONIA (CAP) IN ADAM MALIK GENERAL HOSPITAL MEDAN

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Background: Procalcitonin as a biomarker for acute bacterial infection which is commonly used recently. This study is trying to find the relationship between Procalcitonin and PSI scores to assess the severity of CAP.

Methods: This study used longitudinal data collection approach without a control group. Patients with a diagnosis of Community Acquired Pneumonia were checked of their Procalcitonin levels and measured of their PSI scores on the first and third day of hospitalization.

Results: There was a total of 30 research subjects. The first day of the study found 12 subjects with increasing Procalcitonin levels > 0.5 ng/mL, where as much as 9 subjects had low PSI scores and 3 subjects had moderate PSI scores. Also found were 18 subjects with Procalcitonin levels < 0.5 ng/mL, where only one subject had moderate PSI scores and 17 subjects had low PSI scores ($p = 0.435$). On the third day of the study, 15 subjects encountered Procalcitonin levels > 0.5 ng/mL, where there were 13 subjects with low PSI scores, 2 subjects with moderate PSI scores. Also found were 15 subjects with Procalcitonin levels < 0.5 ng/mL, which contained 14 subjects with low PSI scores and 1 subject with moderate PSI scores ($p = 0.249$).

Conclusion: There is no correlation between Procalcitonin and PSI scores to assess the severity of Community Acquired Pneumonia.

P-N-016

PROGNOSTICATION SYSTEMS IN COMMUNITY ACQUIRED PNEUMONIA: UNIFORMITY IN DETERMINING SITE OF CARE

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Background: Pneumonia is the third leading cause of morbidity and mortality in the Philippines. Prognostication systems such as CURB-65, Pulmonary Severity Index, ATS/IDSA 2007 severity criteria, and SCAP score aid physicians assess the severity of community acquired pneumonia and recommend their corresponding site-of-care. The objective of this study is to determine the University of Santo Tomas Hospital patients' site-of-care based on prognostication systems for CAP and to see if UST Hospital adheres to the recommendations of what system USTH follows.

Methods: This research is retrospective descriptive or observational. USTH treatment room's medical records were reviewed. Excluded were patients transferred in from another hospital, who were to undergo surgical procedures, and post arrest patients. CURB-65, Pulmonary Severity Index, ATS/IDSA 2007 severity criteria, SCAP score, and the management-oriented risk stratification for CAP were applied to every case to determine their uniformity in recommending site-of-care.

Results: A total of 428 patients were seen at the emergency room pay division with the diagnosis of community acquired pneumonia (39%), CAP low risk (25%), CAP moderate risk (33%), and CAP high risk (3%). Fifty-eight percent of the patients were admitted to a regular room and four percent to an intensive care unit, while thirty-eight percent of the cases were discharged from the emergency room. The prognostication tools did not show uniformity in recommending site-of-care for CAP. The most common reason for non-adherence to the USTH's community acquired pneumonia algorithm is patient-related.

Conclusion: The treatment and decision for site-of-care of community acquired pneumonia must be based from the locally available prognostication tool to provide uniformity in its management.

P-N-017

PULMONARY BLASTOMYCOSIS, OCCURRING AS A FUNGAL BALL; FIRST DOCUMENTED CASE IN SRI LANKA

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In 1894, Gilchrist first described blastomycosis in the United States. It is a pyogranulomatous fungal infection caused by *Blastomyces dermatitidis*, caused by aerosolized conidial forms of the fungus from its natural soil habitat. Acute respiratory symptoms are varied in nature ranging from a flulike illness to pneumonia. Chronic pulmonary infection mimics chronic infections like tuberculosis or neoplasm. We report a case of pulmonary blastomycosis, in its chronic form.

Case Report: A 66 year old male presented with three months history of cough with scanty haemoptysis, constitutional symptoms without significant breathlessness. There was no past history or contact history of tuberculosis and no significant travel or exposure history. He was a heavy smoker of thirty pack years. Clinical examination was unremarkable. His oxygen saturation on air was 98%. His full blood count, serum electrolytes, renal, and hepatic functions were normal. ESR was 80 mm 1st hour, mantoux test was positive at 13 mm. CRP, Sputum Smears for acid fast bacilli, and HIV serology were negative. The chest x-ray showed a left upper zone ill defined mass with an air crescent. The CT scan revealed a thin walled cavity in the left upper zone with an intra cavitary body. At bronchoscopy, left upper lobe bronchus was found to be oedematous with contact bleeding. Broncho alveolar lavage was performed. The lavage fluid was negative for malignant cells and acid fast bacilli including atypical mycobacteria. Fungal staining of the BAL fluid culture revealed thin walled broad based budding yeasts on PAS staining, which was consistent with *Blastomyces* spp. A diagnosis of pulmonary blastomycosis was made and the patient was started on a course of oral itraconazole 200 mg twice daily for a total of six months with remarkable improvement.

Discussion: An uncommon fungal infection in routine practice. As its clinical spectrum mimics common pulmonary infections and neoplasms there is a tendency to under diagnosis leading to local complications and dissemination of the infection. It may also cause unnecessary exposure to toxic medications like anti tuberculous treatment. This case illustrates pulmonary blastomycosis mimicking pulmonary tuberculosis in an otherwise healthy individual. Although epidemiologically blastomycosis is rare in this region, this case indicates that blastomycosis does exist in our region and should be considered in all cases of chronic lung infections.

P-N-018

DIFFUSE PANBRONCHIOLITIS: FIRST CASE REPORT FROM SRI LANKA

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Introduction: Diffuse Panbronchiolitis (DPB) is an idiopathic inflammatory disease, principally affecting the respiratory bronchioles, causing a progressive suppurative and severe obstructive respiratory disorder. If left untreated, DPB progresses to bronchiectasis, respiratory failure and death. We report a case of Diffuse Pan Bronchiolitis, very rare in this region and hitherto unreported in Sri Lanka. A 67 year old male on treatment for bronchiectasis for four years, presented with progressive exertional dyspnoea for six months duration, productive cough, dyspnoea scale of MRC grade 2 and no constitutional symptoms. No significant exposure to inorganic or organic substances and an exsmoker of five pack years. Clinical examination revealed averagely built, no clubbing or lymphadenopathy. Auscultation revealed Bibasal Fine Crepitations and no Ronchi. Other systems were unremarkable and Sao2 on air was 97%. Full blood count, serum electrolytes, renal, hepatic and thyroid function were normal. ESR was 40 mm 1st hour. CRP, Sputum Smears for AFB, mantoux test and HIV serology, auto immune screening, 2 Decho were negative. Skin prick test for aero allergens were negative, including aspergillous spp. Serum IgE was 50 u/l (<53). The lung function tests were normal. Fibre optic bronchoscopy and BAL was normal with negative for malignancy and infections. Chest radiograph revealed subpleural asymmetrical fibrosis, nodules and areas of bronchiectasis bilaterally. A HRCT showed ill defined nodules, patchy consolidations and areas of bronchiectasis involving bilaterally and tree in bud appearance in peripheral part of the lower zones in both lungs and patchy ground glass opacities. An open lung biopsy showed collections of inflammatory cells and lymphoid cells around the bronchioles, consistent with diffuse panbronchiolitis. A diagnosis of diffuse panbronchiolitis was made according to the clinical radiological and histological evidence. He was started on a prolonged course of oral corticosteroids, 0.5 mg/kg/BW, together with azithromycin 250 mg bd. At three months of follow up patient showed significant clinical improvement and continues to be regularly followed up at the clinic.

Discussion: DPB can mimic common disorders like bronchial asthma, tuberculosis and other chronic lung infections. However if diagnosed early, it can be treated with a significant improvement and good prognosis. The detection of a case of DPB which is rare in this region emphasizes the importance of maintaining the clinical suspicion and doing the relevant investigations in order to make a diagnosis in the appropriate clinical setting.

P-N-020

P-N-021

DISH SCORE AS A PREDICTION MODEL FOR IN-HOSPITAL MORTALITY OF INDONESIA PATIENTS WITH HOSPITAL ACQUIRED PNEUMONIA

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Background: Mortality due to Hospital Acquired Pneumonia (HAP) is high, in certain part of the world it may reach up to 50% and currently Indonesian data showed similar proportion. As far as our concern, there are too few published studies about the mortality and predictors of mortality in Indonesian HAP patients. These data are important to improve the management of HAP in order to decrease mortality.

Objectives: The aims of this study were to identify predictors of in-hospital mortality in HAP patients and develop a scoring system as a prediction model of mortality.

Methods: This was a retrospective cohort study. Subject's data were taken from medical records from January 2006 to December 2012 of Cipto Mangunkusumo National Referral Hospital, Jakarta, Indonesia. Independent variables consisted of age over 60, decrease of consciousness, shock, sepsis, hypoalbuminemia less than 3 g/dL, immune-compromised, late onset HAP. We used logistic regression test, with backward LR method for multivariate analysis. We developed the scoring system by analysing the area under the receiver operating curve (AUROC) and the Hosmer-Lemeshow test.

Results: There was 204 HAP patients included with all completed data. The mortality proportion of our HAP patients was 44.1%. Multivariate analysis showed that the predictors of mortality in patients with HAP were decrease of consciousness ($p < 0.0001$ OR 7.86 95%CI 3.363–18.36), shock ($p 0.012$ OR 3.80 95%CI 1.342–10.742), immune-compromised ($p < 0.0001$ OR 3.36 95%CI 1.738–6.483) and hypoalbuminemia ($p 0.009$ 95%OR 2.78 95%CI 1.298–5.958). Hosmer-Lemeshow showed $p = 0.334$ implied good accuracy and AUROC showed $p = 0.767$ implied good discriminating ability. We used the acronym DISH as in Decrease of Consciousness (score 2), Immune-compromised (score 1), Shock (score 1), and Hypoalbuminemia (score 1). Score 0 predicts mortality of 10%, score 1,2,3,4 predict mortality of 25,50,75,90 % respectively, and score 5 predicts mortality as high as 96%.

Conclusions: Predictors of mortality in patients with HAP were decrease of consciousness, shock, immune-compromised and hypoalbuminemia. We have developed a clinically practical scoring system to predict HAP mortality in Indonesian patients, the DISH score.

THROMBOCYTOPENIA PREDICTS IN-HOSPITAL MORTALITY IN PATIENTS WITH HOSPITAL ACQUIRED PNEUMONIA

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Background: Hospital Acquired Pneumonia (HAP) is a lethal disease, with increased morbidity and mortality around the globe. Indonesian local data in Jakarta showed proportion of HAP mortality as high as 44.1%. Previous study had identified several risk factors related to mortality of HAP. Platelets are inflammatory cells with an important role in antimicrobial host defenses. Other studies had demonstrated in the setting of Community Acquired Pneumonia (CAP) patients that low platelet was associated with mortality in CAP patients. To our knowledge, there is no study ever conducted to investigate similar effect in the HAP patients. We hypothesized that a decreased platelet count (less than 100,000/L) may be a predictor of in-hospital mortality in patients with HAP.

Objective: Current study was aimed to investigate the relationship between decreased platelet count at diagnosis of HAP and clinical outcome of mortality in hospital.

Method: We performed a retrospective cohort study with patients' data were taken from medical records from January 2006 to December 2012 of Cipto Mangunkusumo National Referral Hospital, Jakarta, Indonesia. Independent variable was platelet count at diagnosis of HAP (less than 100,000/L and 100,000/L or more), while dependent variable was all-cause in-hospital mortality stated in the medical records. We used the Pearson-chi square for statistical test and p value of < 0.05 is considered statistically significant.

Result: Low platelet count (thrombocytopenia less than 100,000/L) was associated with increased risk of in-hospital mortality ($p = 0.024$, RR = 1.5, 95%CI 1.093–2.058).

Conclusion: Thrombocytopenia less than 100,000/L is associated with increased risk of mortality (1.5 times higher) in patients with HAP. We suggest to include thrombocytopenia into the HAP scoring system of mortality prediction model.

P-N-022

25 YEARS OLD MAN WITH NON TUBERCULOUS MYCOBACTERIUM (NTM) LUNG DISEASE, CHRONIC LIVER DISEASE, AND DILATED CARDIOMYOPATHY

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Background: Pulmonary infections due to NTM are increasingly recognized worldwide. NTM could affect many organ systems, especially pulmonary diseases. There are lacks of data that report the relationship between NTM and cardiovascular disease, in this case cardiomyopathy.

Case Report: A 25 years old man admitted to Wahidin hospital due to shortness of breath since 3 months ago, he diagnosed as TB but didn't complete the TB treatment. The patient was composmentis, poor nourished, elevated jugular vein, right hemithorax pleural effusion, cardiomegaly, ascites, bilateral pretibial and dorsum pedis oedema. The first CXR showed infiltrates in almost all of right lung, with normal heart imaging. Two months later, CTI increased 2x. Echocardiography result dilatation of all cardiac chamber, global hypokinetic, LV systolic and diastolic dysfunction with EF 30% LVSEC +, MR moderate TR severe, PH moderate, mild pericardial effusion. AFB positive. Not only ALT, AST but also his Bilirubin raising rapidly more than 3x and the TB drugs were stopped. Sputum Culture is Non Mycobacterium (NTM).

Discussion: There are no pathognomonic clinical symptoms for pulmonary NTM diseases. In this patient the NTM infected the lung as Mycobacterium tuberculosis did, and the clinical manifestation as well. The OAT regimen didn't make any better condition, because the NTM needed special combination regimen to be eradicated. Beside the clinical symptoms, the CXR also showed normal heart until 2 months later the heart size was much larger than before. The echocardiography proved the dilatation of all cardiac chamber LVSEC+, LV systolic and diastolic dysfunction, EF 30%, and mild pericardial effusion. The risk factor for heart disease in this patient is smoking. The alcohol consumption in 3 years, and had been stopped drinking for 2 years made the alcohol cardiomyopathy less possible, based on the literature had reviewed.

Conclusion: 25 years old man with NTM, chronic liver disease, and dilated cardiomyopathy due to NTM had been reported. The clinical sign and symptoms in this patient were similar to pulmonary TB. The diagnosis of NTM pulmonary disease was made after there was the sputum culture result. It suspected affect not only the lung but also the heart, based on CHF occur later and within 2 months after he had been diagnosed pulmonary TB (first time, before culture) the heart's size was getting bigger significantly on serial CXR and the echocardiography showed dilatation of all cardiac chamber, with poor LV function.

P-N-023

QUALITY OF IMPLEMENTATION OF THE VENTILATOR ASSOCIATED PNEUMONIA BUNDLES OF CARE IN THE UNIVERSITY OF THE PHILIPPINES – PHILIPPINE GENERAL HOSPITAL CENTRAL INTENSIVE CARE UNIT AND MEDICAL INTENSIVE CARE UNIT: A TWO-MONTH PROSPECTIVE SURVEY

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Introduction: Prevention methods play a key role in reducing VAP incidence, and these require significant educational commitments and high rates of compliance in order to achieve reduction in the incidence of VAP. The success of the bundle depends largely on the way it is implemented; therefore, performance of these must always be under constant review with surveillance compliance. The main purpose of the study is to evaluate the compliance of healthcare workers and to evaluate the actual practice of doctors and nurses, including determination of barriers and obstacles.

Objectives: To evaluate VAP bundles of care compliance of the University of the Philippines – Philippine General Hospital health care workers in the Central and Medical Intensive Care Unit through direct observation, chart review of patients and a survey questionnaire in a two-month period. To identify barriers and obstacles in the implementation VAP bundles of care through a questionnaire given to the primary care givers of the patients included.

Methods: This is a cross sectional study involving adult intubated patients in the Central and the Medical ICU and the healthcare workers in the two-month period. The following data were analyzed: 1. Direct observation of intubated patients – noting head of bed elevation, daily oral hygiene and DVT prophylaxis; 2. Chart review of admitted patients – presence of VAP prevention bundle checklist, VAP prevention bundle or components ordered by the physician; and 3. VAP bundles carried out by the nurses written on nurses notes and monitoring sheet. Survey questionnaires were also administered to health care workers to determine baseline knowledge of the VAP prevention bundles, including training received, perceived compliance and factors in its implementation. A second set of questionnaires were distributed to determine barriers and obstacles to the implementation of each of the components of the bundles of care.

Results: A total of 62 admitted patients were included in the study; 26 from the medical ICU and 36 patients from the central ICU. Compliance to the bundles were computed as follows: number of vented patients receiving all components of bundle/ total number of patients on ventilator for the day of the prevalence sample x 100, result of which is 38.71%.

Conclusions: The general compliance to the VAP prevention bundle showed a rate of 38.71%. The two components with the lowest conformity were DVT prophylaxis and assessment for readiness to wean/sedation holidays. In order to improve the compliance to the prevention bundle, it is important to include the provision of needs and funds for medications needed for stress ulcer and DVT prophylaxis. It is imperative to improve the facilities, especially repair of non working beds; periodic evaluation and assessment of the medical and nursing staff. Equally important is the stipulation of the VAP checklist and protocol as well as guidelines for weaning and sedation.

P-N-024

CRYPTOGENIC ORGANIZING PNEUMONIA ASSOCIATED WITH INVASIVE PULMONARY ASPERGILLOSIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Concomitant occurrence of invasive pulmonary aspergillosis (IPA) with cryptogenic organizing pneumonia (COP) are scarce. Here, we report a case where COP was a presenting feature in a patient with diagnosed IPA, and review additional 58 COP patients reported in the literature from 1988 through 2013.

Case Presentation: The study was reviewed and approved by the Institutional Ethics Committee of Shanghai Tenth People's Hospital of Tongji University and was conducted in compliance with the Helsinki Declaration. Written informed consent was obtained from patient. A 56-year-old man presenting with productive cough for several weeks and unremitting high fever for a week was hospitalized with an initial clinical diagnosis of pneumonia, for which antibiotics were prescribed but did not work. Seeing that the condition progressed both clinically and radiographically, bronchoscopy, bronchoalveolar lavage and lung biopsy were performed, and the diagnosis of cryptogenic organizing pneumonia (COP) and invasive pulmonary aspergillosis (IPA) co-existence was made. Initially, the patient responded to steroid pulse therapy and voriconazole treatment, and his condition was partially improved. However, the patient's condition deteriorated progressively 5 months after the disease onset and the patient died during the third admission due to respiratory failure and the adverse reactions of coriaceous hormone therapy.

Conclusion: The diagnosis of cryptogenic organizing pneumonia (COP) and invasive pulmonary aspergillosis (IPA) co-occurrence depends on clinical, radiological and histological presentations. Similarities with other disease processes could lead to a delayed diagnosis or maldiagnosis. The present case suggests that clinicians should be alert to this disease in their clinical practices.

Key Words: cryptogenic organizing pneumonia, invasive pulmonary aspergillosis, bronchiolitis obliterans organizing pneumonia.

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P-N-025

PHARMACOKINETICS OF LANINAMIVIR OCTANOATE, A LONG-ACTING NEURAMINIDASE INHIBITOR, IN ALVEOLAR MACROPHAGES AND THE CONTRIBUTION OF ACYL-PROTEIN THIOESTERASE 1 TO FORM AN ACTIVE METABOLITE, LANINAMIVIR

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Introduction: Bronchoalveolar lavage (BAL) of human subjects by use of a flexible bronchofiberscope offers an easy, low-risk means of sampling fluids and cells from the respiratory tract. Intrapulmonary pharmacokinetics of laninamivir octanoate (LO), a long-acting neuraminidase inhibitor, in healthy volunteers has been clarified by measuring the drug concentrations in epithelial lining fluid (ELF) and alveolar macrophages (AM) obtained from BAL fluid to support its long lasting efficacy to treat patients with influenza virus infection by the single inhalation. While intrapulmonary pharmacokinetics of LO and laninamivir has been clarified, the metabolic enzymes to form laninamivir and their contribution to overall elimination of LO in AM have not been fully evaluated.

Methods: A single-centre, open-label study was performed in adult healthy volunteers. Seven subgroups of five subjects each underwent BAL at specified time intervals up to 240 hrs following a single inhaled administration of LO (40 mg). Plasma, BAL fluid and AM were analyzed to determine LO and laninamivir concentrations using validated LC-MS/MS methods. Microautoradiographic localization in the respiratory tissues was also evaluated after a single intranasal administration of radio-labelled LO to mice. LO-hydrolyzing enzymes were identified using proteomic correlation profiling and the immunohistochemical assay was performed in human pulmonary tissue.

Results and Discussion: In healthy volunteers, the peak plasma concentrations of laninamivir in AM occurred at 8 hrs after inhalation and decreased with the half-life of 89.9 hrs. Laninamivir concentrations in AM were much higher than those in plasma and ELF, and decreased with a longer half-life (~6 days) than that in plasma. The distribution of radioactivity was observed mainly on the epithelial cells of the airway tracts for a long period after radio-labelled LO administration in mice. S-formylglutathione hydrolase (ESD) and acyl-protein thioesterase 1 (APT1) were identified which would be primarily involved in the bioactivation of LO in human pulmonary tissue. Both enzymes were mainly localized in the pulmonary epithelia and would contribute to form laninamivir after an inhaled administration of LO. In addition, the positive staining of APT1 was also observed in the alveolar macrophage, indicating that APT1 would contribute to metabolize LO to laninamivir in AM. Prolonged high retention of LO in AM supports to supply laninamivir in AM and may support its long lasting efficacy to treat patients with influenza virus infection by the single inhalation.

P-N-026

RAPIDLY PROGRESSIVE CAP, LUNG ABSCESS AND BACTERAEMIA CAUSED BY ACINETOBACTER URSINGII

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We describe a case of rapidly progressive CAP, lung abscess and bacteraemia caused by *Acinetobacter ursingii*, which was confirmed by the 16S rRNA gene sequence. This report highlights *Acinetobacter ursingii* can cause infiltration and necrotic cavity on lung, irreversible lung damage and secondary bacteraemia on healthy host occasionally, though it is known as a conditioned pathogen. Meanwhile, *Acinetobacter ursingii* shows a changeable resistance to antibiotics containing β -lactamase inhibitors, but still sensitive to imipenem.

P-N-027

AETIOLOGY OF VIRAL PATHOGENS IN PATIENTS WITH INFLUENZA-LIKE ILLNESS DURING AN INFLUENZA SEASON AT THE UNIVERSITY HOSPITAL IN OKINAWA, JAPAN

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Background: PCR method enables us to diagnose respiratory viral infections with higher sensitivity and specificity than conventional methods. Multiplex PCR (mPCR) is designed to examine multiple pathogens simultaneously and our department has introduced this detection system to clinical practice since 2012. Although there are some reports showing viral aetiology of influenza-like illness, such data in Japan is very few. In the present study, we investigated viral aetiology during an influenza season at the university hospital in Okinawa, Japan.

Methods: Nasal swabs were collected from patients with influenza-like illness and rapid antigen test for influenza A/B was performed first and the nucleotide was eluted with commercially available kit from the residual liquid of the rapid test. A commercially available mPCR kit (Seeplex RV15 OneStep ACE Detection, Seegene, South Korea) was used to screen 15 respiratory viruses simultaneously. Data about patient's symptoms were analyzed retrospectively.

Results: Between January and March 2013, 195 patients were examined and 88 cases (45.1%) were positive with mPCR. Detected viruses were; influenza virus A: 33 cases (37.5%), influenza virus B: 2 cases (2.2%), rhinovirus: 25 cases (28.4%), RS virus: 8 cases (9.1%), Coronavirus: 7 cases (8.0%), parainfluenza virus: 7 cases (8.0%), adenovirus: 6 cases (6.8%), bocavirus: 4 cases (4.5%), enterovirus: 2 cases (2.3%), metapneumovirus: 1 case (1.1%). Co-infection was observed in 6 patients (double infection in 5 patients and triple infection in one patient). Myalgia and arthralgia, which are known as influenza-like symptoms, were often observed in patients with other than influenza, such as rhinovirus, RS virus, corona virus, and parainfluenza virus. In terms of influenza virus, positive and negative agreement rate between rapid antigen test and mPCR were 89.5% and 99.4%, respectively.

Discussion: Although influenza epidemic was occurred in Okinawa during the investigation period, respiratory viruses other than influenza were detected more often than we expected. Since rapid antigen test for influenza virus is not able to detect early phase influenza infection, physicians sometimes prescribe influenza neuraminidase inhibitor based on the clinical diagnosis even if rapid antigen test is negative. Since our data and previous report showed that influenza-like symptoms were often observed in patients with respiratory viral infections other than influenza virus infection, clinical diagnosis based on the symptom seems not to be reliable. The current data indicates that we have to be careful when we prescribe the influenza neuraminidase inhibitor to clinically diagnosed patients even in the influenza season.

P-N-028

ASPERGILLUS EMPYEMA WITH ASPERGILLUS-RELATED EOSINOPHILIC PNEUMONIA: A CASE REPORT AND REVIEW OF THE LITERATURE

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A 51-year-old man was admitted with cough and high fever. Chest radiography and chest computed tomography showed cavitary lesions and extensive consolidation in the right upper lobe. A marked increase in eosinophils was seen in the peripheral blood and bronchoalveolar lavage fluid (BALF), and *Aspergillus fumigatus* was detected in BALF. This case was diagnosed as *Aspergillus*-related eosinophilic pneumonia. Antifungal drugs and systemic corticosteroids were administered, and his symptoms improved; however, he subsequently developed *Aspergillus* empyema with a pulmonary fistula. Chest tube drainage and another antifungal drug were started. The pleural fluid culture tests for fungus became negative. Despite chest tube drainage, air leakage did not cease. To control fungal infection and close the pulmonary fistula, a right upper lobectomy and decortication were performed. In follow-up, the patient had no clinical signs of recurrence, and this *Aspergillus* empyema was treated successfully. We report the case and review the literature regarding *Aspergillus* infection with hypersensitivity reaction to *Aspergillus* antigen.

P-N-029

VALIDITY OF THE ST. GEORGE'S RESPIRATORY QUESTIONNAIRE AND COPD ASSESSMENT TEST IN ASSESSING HEALTH STATUS IN PULMONARY INFECTION WITH NONTUBERCULOUS MYCOBACTERIUM

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Background: The influence of pulmonary infection with nontuberculous mycobacterium on health-related quality of life (HRQL) has not been quantified. The St. George's Respiratory Questionnaire (SGRQ) is widely used for several chronic pulmonary diseases, and COPD Assessment Test (CAT) is used for COPD. We investigated validity of SGRQ and CAT in pulmonary nontuberculous mycobacterium (pNTM) infection.

Methods: 52 patients with pNTM infection completed the SGRQ, CAT, the Short Form-36 Health Survey (SF-36) and pulmonary function test. We investigated correlation between SGRQ or CAT and SF-36, as well as correlation between SGRQ or CAT and pulmonary function test.

Results: The mean age was 67 years, and female was 96 % (50/52). The SGRQ total score, each SGRQ components (symptom, activity, impact) and CAT total score were moderately to strongly correlated with SF-36 physical component summary score (PCS) and mental component summary score (MCS). In pulmonary function test, %DLco was strongly correlated with SGRQ and CAT, and 6MWD was weakly correlated with SGRQ and CAT.

Conclusions: SGRQ and CAT demonstrated a significant validity in assessing HRQL in patients with pNTM.

P-N-030

P-N-032

RELATIONSHIP BETWEEN NUTRITIONAL STATUS, RESPIRATORY SYMPTOMS AND LUNG FUNCTION IN ELEMENTARY SCHOOL CHILDREN IN BOTH PRIVATE AND PUBLIC SCHOOL

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Background: Lung Function tests is a measure of respiratory status. These tests were affected by factors affecting the growth and development in children and are influenced by age, sex, race, nutrition and socioeconomic status.

Objective: To determine the relationship between nutritional status, lung function and respiratory symptoms of elementary school children enrolled in both public and private schools.

Materials and Methods: This is a cross sectional study done among elementary school in both public and private school in Quezon City. School children ages 7–12 years old were recruited to participate in this study. Once informed consent was obtained from the children, parents and guardians were interviewed to elicits the respiratory symptoms of all subjects. The body mass index were calculated to determine the degree of nutrition. All subjects underwent a pulmonary function test using a microloop.

Results: A total of 161 patients were enrolled in the study. The study groups were divided into 3 main categories: normal weight, wasted and overweight. Different degrees of malnutrition have its effect on the pulmonary function tests. Both wasted and overweight groups showed significant degrees in FVC (P -value = 0.0006) and FEV1 (P -value = 0.0009). Both the wasted and overweight children were most likely to develop respiratory symptoms. Wasted children were found to be at risk of having restrictive lung function as well as obstructive ventilatory defect.

Conclusion: We showed that the BMI has significant effects on all lung functions and the greatest effects were on the FVC and FEV1. The reduction in the lung volumes and flow rates could be due to their poor nutritional status. The wasted and overweight children had higher susceptibility to suffer from respiratory symptoms.

A USEFUL COMPOSITE SCALE OF PCR AND THE (1→3)-B-D-GLUCAN ASSAY FOR DIAGNOSING PNEUMOCYSTIS PNEUMONIA IN IMMUNOCOMPROMISED PATIENTS WITH ACUTE LUNG DISEASE

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Background: The usefulness of PCR-based detection of Pneumocystis pneumonia (PCP) from bronchoalveolar lavage fluid (BALF) has been demonstrated in many studies. However, the differentiation of PCP from colonization is essential for an accurate diagnosis in cases of Pneumocystis jirovecii-positive BALF PCR-positive. Some reports have shown (1→3)-β-D-glucan to be a reliable marker for PCP diagnosis. We assessed the utility of a composite scale using both the β-D-glucan assay and PCR.

Methods: Between June 2010 and June 2014, we identified 178 adult immunocompromised patients admitted at Osaka City General Hospital who had diffuse ground-glass opacity, acute lung disease, and were suspected of having PCP. They were examined by PCR-based detection of *P. jirovecii* in BALF or induced sputum, as well as by the β-D-glucan assay and lactate dehydrogenase assay using retrospective chart review. We excluded patients who were misdiagnosed (e.g., having other fungal infections or congestive heart failure) or who were not examined comprehensively. A composite scale of PCR results and stratified β-D-glucan assay scores (<6.0, 6.0–14.0, ≥14.0) was compared with results of β-D-glucan assay alone and PCR alone.

Results: Of the 112 patients investigated (54 with PCP and 58 without PCP), 30 had inflammatory disease, 27 had HIV, 24 had haematological malignancy, 8 had solid tumours, and 4 had undergone organ transplantation. In multivariate analyses, PCR results and β-D-glucan assay scores are independent predictive factors for the diagnosis of PCP. The values for area under the receiver-operating characteristic curve of the β-D-glucan assay, PCR assay, and composite scale of both were 0.90 (95%CI: 0.85–0.95), 0.90 (0.85–0.96), and 0.97 (0.95–1.00), respectively. The diagnostic accuracy of the composite scale was significantly higher than that of PCR alone ($P = 0.01$) and β-D-glucan assay alone ($P < 0.01$). The sensitivity and specificity for PCP diagnosis were 79.6% and 98.3%, respectively, for PCR-positive cases with a cut-off value of 14.0 pg/mL for the β-D-glucan assay. For PCR-positive cases with a cut-off value of 6.0 pg/mL, the sensitivity and specificity for PCP diagnosis were 90.7% and 96.6%, respectively.

Conclusion: The composite scale of PCR results and β-D-glucan values is useful for diagnosing PCP, and in particular, for differentiating PCP from Pneumocystis colonization in immunocompromised patients with acute lung disease.

P-N-031

AMOEBIASIS EMPYEMA DEVELOPED FROM LIVER ABSCESS

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We report male, 47 years old being diagnosed with right thoracic empyema. He came to our emergency ward of Pulmonology and Respiratory Medicine General Hospital, had experienced symptoms of dyspnoea for one month and became worse on last one week, right chest pain that was not localized, mild fever, weight loss of 5 kg in 3 months and loss of appetite. He didn't complain other respiratory symptoms. History of smoking 24 cigarettes per day for 35 years. On physical examination we found dullness on right lung. Computed tomography scan of thorax showed encapsulated pleural effusion with air inside, consolidation in the segment 9 and 10 of the right lung, fibrosis in the right segment 2 and 3 and enlarged liver size with a hypodense lesion in the right lobe of the liver. On ultrasonography showed right pleural effusion and the liver showed hyperechoic with firm border indicated an abscess. Blood test analysis showed increased leukocytes 23.790 cell/microliter only. Pleural tapping was performed and found purulent pleural fluid. From pleural fluid analysis showed exudate with increased leukocyte 47.300 cell/microliter and PMN dominant. Tube thoracostomy was performed and 800 ml pus was evacuated. Microbiology test from pleural fluid found entamoeba histolytica. Patient was treated by given metronidazole 500 mg t.i.d for 14 days and liver abscess evacuated by percutaneous drainage.

P-N-033

CLINICAL CHARACTERISTICS AND PREDICTIVE FACTORS OF METHILLIN-RESISTANT STAPHYLOCOCCUS AUREUS INFECTION IN ELDERLY PATIENTS WITH NON-NOSOCOMIAL PNEUMONIA

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Background: Non-nosocomial methillin-resistant *Staphylococcus aureus* (MRSA) pneumonia has been reported severe and life-threatening disease, but data are limited. Also, optimal prediction for MRSA infection in non-nosocomial pneumonia have been not fully established. We aimed to evaluate the clinical features and risk factors of MRSA infection in elderly patients hospitalized with non-nosocomial pneumonia.

Methods: This study was retrospectively conducted in elderly patients with non-nosocomial MRSA pneumonia that were hospitalized in Jeju National University Hospital between January 2012 and December 2013.

Results: A total of 362 patients were enrolled and 16(4.4%) had MRSA infection. The MRSA group showed worse clinical parameters at onset, and PSI score were higher than in the MRSA group (144 vs. 117, $p = 0.007$). Total in-hospital mortality did not show a significant difference between the groups (31.2% vs. 13.8%; $p = 0.068$). But, other clinical outcomes including duration of antibiotic therapy (14 vs. 10 days; $p = 0.017$), the rates of antibiotics changes (75.0% vs. 23.6%; $p < 0.001$), use of inappropriate antibiotics (100% vs. 5.2%; $p < 0.001$), failure of initial antibiotics therapy (81.2% vs. 24.8%; $p < 0.001$), and length of hospital stay (14 vs. 9 days; $p = 0.021$) were significantly worse in the MRSA group. In a multivariate logistic regression analysis, a high PSI score was identified as a predictive factor for MRSA infection (Odds ratio = 1.014, $p = 0.037$). When used the ROC curve analysis, the cut-off score value that considering MRSA infection was 140, and its sensitivity and specificity were 73.7% and 62.5%, respectively. By contrast, the presence of healthcare-associated pneumonia or nursing home-acquired pneumonia, and CRP level were not risk factors for MRSA infection.

Conclusions: MRSA infection in elderly patients admitted with non-nosocomial pneumonia was associated with overall worsened clinical outcomes. And we suggested that the risk of MRSA infection might be related to a high PSI score more than 140.

P-N-035

UNILATERAL PULMONARY HYPOPLASIA IN A 24-YEAR OLD MALE

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Introduction: Pulmonary hypoplasia is a rare congenital anomaly. It is usually detected in infancy or childhood and rarely in adults. Presented is a case of an adult male who was diagnosed with unilateral pulmonary hypoplasia without other associated congenital anomalies.

Case Presentation: A 24 year-old man had been treated as asthma patient since childhood. He claimed to be stable until 2 years prior to admission, whereby there was an increase in the frequency of dyspnoea. Consults done and a diagnosis of Congestive Heart Failure secondary to congenital heart disease was made. A week prior to admission, he had increased shortness of breath, hence the admission. Seen at ER – tachypneic, tachycardic, anasarctous short man. Breath sounds decreased over the right lung field with note of RV heave and diastolic murmur. He was initially managed for heart failure secondary to congenital heart disease with pneumonia. A few hours after admission he became unstable, inotropes was started and he was shifted to BiPAP. Echocardiography showed concentric left ventricular hypertrophy with good wall motion and contractility and preserved overall systolic function. HRCT of chest revealed consolidation/atelectasis of right lower lobe, ipsilateral shift of mediastinal structures, bilateral pleural effusion, minimal pericardial effusion, cardiomegaly and pulmonary congestion. Bronchoscopy revealed a trachea skewed to the right. Right bronchopulmonary segments were not visualized: upon entry to right mainstem bronchus, 2 lobar bronchi visualized, one was not patent (probably the middle) and one revealed 2 bronchi (probably the lower). A right pulmonary hypoplasia was then confirmed. Sputum and blood cultures revealed no growth. Patient was then gradually weaned off from BiPAP and eventually discharged.

Discussion: Pure pulmonary hypoplasia is rare; usually accompanied by anomalies in other systems. Depending on the severity, patients may either be asymptomatic or with severe respiratory distress symptoms and cause mortality because of respiratory insufficiency or associated congenital disorders. Some patients survive into adulthood and usually have chronic lung problems, recurrent chest infections and impaired growth just like our patient. Diagnosis was confirmed with bronchoscopy, bronchography, CT scan, MRI or pulmonary angiography. Treatment in adults consists of control of recurrent infections, symptomatic treatment in form of expectorants and bronchodilators and management of other complications. Prophylaxis for respiratory syncytial virus, pneumococcus, and influenza infections are recommended. Prognosis depends upon the functional integrity of the remaining lung as well as upon the presence of associated anomalies.

Conclusion: Congenital unilateral pulmonary hypoplasia without other anomalies is rarely diagnosed in adulthood. Management options include control of recurrent infections and symptomatic treatments as well as immunizations.

P-N-034

AORTOBRONCHOPULMONARY FISTULA CAUSED BY LUNG ABSCESS

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A 76-year old woman presented with general weakness. Initial non-enhanced chest CT shows mass like consolidation with necrotic cavity showing air-fluid level in left lower lobe. Empiric broad-spectrum antibiotic therapy was started. On seventh hospital day, haemoptysis was developed. Aortic angiography and CT angiography confirmed shows the fistula between the descending aorta and the lung abscess. The patient refused endovascular repair and died of respiratory failure on twelfth hospital day.

P-N-036

PROCALCITONIN-GUIDED ALGORITHM IN NURSING AND HEALTHCARE-ASSOCIATED PNEUMONIA

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Background: The Japanese Respiratory Society (JRS) guideline recommends that patients with nursing and healthcare-associated pneumonia (NHCAP) who have a risk of drug-resistant pathogens are treated with broad-spectrum antibiotics covering them. In the preceding randomized controlled trial, however, antibiotic therapy according to JRS guideline could not show significant improvement in prognosis compared to antibiotic selection confined to ampicillin-sulbactam (SBT/ABPC) or ceftriaxone (CTRX). The aim of this study is to assess the validity of procalcitonin (PCT)-guided antibiotic therapy using only SBT/ABPC or CTRX in patients with NHCAP.

Methods: We adapted the algorithm, deciding duration of antibiotic therapy according to the PCT level, to patients with NHCAP admitted to our hospital. Primary endpoint was relapse of pneumonia and death within 30 days. Secondary endpoints were the initially prescribed antibiotics, the frequency of switching antibiotics, the duration of antibiotic therapy, and the detection rate of drug-resistant pathogens in sputum cultures.

Results: Sixty patients were enrolled in this study, 2 patients withdrew informed consent and excluded from all analysis. The rate of relapse and death within 30 days was 28%, which did not differ from the data performed in the preceding study. SBT/ABPC or CTRX were prescribed to 83% or 17% of patients with NHCAP, respectively, as initially prescribed antibiotics. The median duration of antibiotic therapy was 5 days. Although the detection rate of drug-resistant pathogens was 31%, there was no relevance to the switch to broad-spectrum antibiotics in 4 patients (7%). 14 patients (24%) the algorithm was deviated based on the judgement of treating physicians.

Conclusions: Our PCT algorithm could reduce not only prescription of broad-spectrum antibiotics but duration of antibiotic therapy without worsening prognosis. These results may show the validity of PCT algorithm in NHCAP treatment.

P-N-037

COMPARISON OF CLINICAL CHARACTERISTIC AND PROGNOSIS IN EACH ENTITY OF CHRONIC PULMONARY ASPERGILLOSIS

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Background and Aim of Study: In the Japanese guideline of invasive fungal infections published in 2007, chronic pulmonary aspergillosis (CPA) was categorized into simple aspergilloma or “Chronic Necrotizing Pulmonary Aspergillosis” (CNPA) by clinical information. However, the CNPA cases actually contained pathological components of CNPA and chronic cavitary pulmonary aspergillosis (CCPA) cases. Therefore, there was a mismatch in disease entities between Japanese and Infectious Disease Society of America guidelines. The new clinical disease concept named chronic progressive pulmonary aspergillosis (CPPA) which contains pathologically diagnosed CNPA and CCPA was proposed in new Japanese guideline of invasive fungal infections in 2014 in order to resolve this problem. Since there are few studies regarding the prognosis of CNPA and CCPA in Japan, we compared the clinical characteristics and prognosis of them in this study.

Methods: We retrospectively investigated medical records of CPA patients who were admitted to our hospital from April 2008 to September 2013. Although it was difficult to distinguish between CNPA and CCPA with radiological findings and clinical courses in the cases without pathological findings, we clinically classified them in terms of presence of pre-existing cavity or rapid exacerbation (within 3 months) of radiological findings and clinical symptoms in this study.

Results: Six and twenty four cases were diagnosed as clinically diagnosed CNPA and CCPA, respectively. Survival rates 3 month after diagnosis of them were 66.7 and 100%, respectively. The survival rate of clinical CNPA was significantly lower than that of clinically diagnosed CCPA by log rank test ($P = 0.0023$). Survival rates one year after diagnosis of them were 66.7 and 87.5%, respectively; there was no statistically significant difference ($P = 0.1286$).

Conclusions: The clinically diagnosed CNPA cases actually included many CCPA cases. The prognosis of CNPA cases might be underestimated because of this reason. In addition, we here report clinical characteristics and prognostic factors of each entity.

P-N-038

CLINICAL CHARACTERISTICS AND PROGNOSIS OF CHRONIC PULMONARY ASPERGILLOSIS

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Rationale: Chronic cavitary pulmonary aspergillosis (CCPA) is defined as cavitary lesions with significant systemic symptoms and considered to be associated with invasiveness of pulmonary aspergillosis infection from the simple aspergilloma. Although CCPA causes chronic destruction of the lung tissues causing significant morbidities, little is known about the optimal treatment strategies. This study investigated the clinical features at the diagnosis, focusing on the differences in patients' baseline characteristics, radiologic and serologic profiles between CCPA and simple aspergilloma and the treatment outcomes.

Methods: From January 2012 to August 2013, we reviewed the medial records of the patients with positive serum Aspergillus IgG or Aspergillus Ag or Aspergillus species isolated from respiratory specimens.

Results: A total of 35 patients with suspected pulmonary aspergillosis were identified, which included 4 ABPA, 3 CNPA, 8 IPA, 5 simple aspergilloma and 15 CCPA. 15 patients were males, median age of 57 years. 63.6% (n = 7) of the patients were ever smokers. Old pulmonary tuberculosis (n = 15) and emphysema (n = 4) were primary underlying lung conditions. Most frequent symptom was haemoptysis, 42.9% (n = 6). Comparing the asymptomatic simple aspergilloma, larger cavity size, pleural thickening, bronchiectasis, and BPF was more frequently found in chest computed tomography of CCPA. Aspergillus IgG titer was higher in CCPA. BMI, FEV1 (%), serum albumin, Aspergillus Ag titer, WBC count, ESR and CRP levels were not significantly different. Total 8 patients (57.1%) were treated with itraconazole (100%), amphotericin B deoxycholate (12.5%) and voriconazole (37.5%) for mean 134 days and 2 had curative operations. For median 206 days follow up periods, 66.7% (n = 6) had favourable responses in symptoms (44.4%) or radiologic findings (55.5%). During the treatment, serum Aspergillus IgG titer was decreased in patients with favourable responses (33.3%), whereas none with unfavourable responses or without the antifungal treatment.

Conclusions: Previous pulmonary tuberculosis infection and emphysema could be the risk factors for CCPA development. We suggest that patients with simple aspergilloma who present progressive symptoms with radiological changes and high serum Aspergillus IgG titer should be considered to use antifungal agents, anticipating favourable clinical outcomes.

P-N-039

VIRAL INFECTION IN PATIENTS WITH NURSING AND HEALTHCARE-ASSOCIATED PNEUMONIA (NHCAP)

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Background and Aim: Nursing and healthcare-associated pneumonia (NHCAP) is a new category that was defined by considering the medical environment in Japan. In Japan, many elderly and physically handicapped people are cared at home, long-term care facilities or hospitals. Pneumonia occurring in such patients has higher mortality and multidrug-resistant pathogens are isolated more frequently than community-acquired pneumonia (CAP). NHCAP is the category which met one or more of the following definitions: (1) resident in long-term care facilities; (2) discharged from hospital within recent 90 days; (3) elderly and physically handicapped, requiring nursing care at home, or (4) receiving continuous ambulatory intravascular treatment. Some studies on viral infection among CAP have been reported, but there are few reports among NHCAP. To clarify viral burden among NHCAP, we conducted prospective study.

Methods: From February 2012 to January 2013, NHCAP patients with written permission in Kameda Medical Center were enrolled. Clinical data was collected and all sputum samples underwent culture and multiplex polymerase chain reaction (PCR) for detecting 13 respiratory viral species.

Results: Two-hundred and fourteen patients were enrolled into the study, and 200 sputum specimens underwent assays. Among these 200 specimens, 62 (31%) showed positive virus PCR. Among the viruses detected, influenza A was 12, influenza B was 1, human metapneumovirus was 5, RS virus was 12, parainfluenza type1 was 4, parainfluenza type2 was 4, parainfluenza type3 was 4, rhinovirus was 24, coronavirus was 1, adenovirus was 2. Virus burden was higher in the cases that require nursing care compared with those who do not require (37% vs. 21%, respectively). Mortality rate was not statistically different regardless of whether virus was detected or not.

Conclusion: Although the viral infection was not few in NHCAP, it did not seem to contribute mortality.

P-N-040

THE USEFULNESS OF LOCAL ANAESTHETIC THORACOSCOPY FOR PARAPNEUMONIC PLEURAL EFFUSIONS

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Purpose: To examine the usefulness of local anaesthetic thoracoscopy (LAT) for the management of parapneumonic pleural effusions.

Methods: This retrospective study included 23 patients admitted to our hospital for parapneumonic pleural effusions between April 2009 and March 2013, who had undergone LAT. We investigated the patients' backgrounds, findings of pleural effusion, findings of computed tomography (CT), treatment (antibiotics, surgery, intrapleural administration of urokinase), outcome and LAT findings, using medical records. Finally, we examined the correlation between the findings of thoracic cavity and these data.

Results: LAT findings were classified into three types; pus predominant pattern (> 50% of pleura covered by pus, n = 5), fibrin predominant pattern (> 50% of pleura covered by fibrin, n = 10), and others (n = 8). Among three groups, patients with pus predominant pattern had higher rate of positive pleural fluid culture (especially, Streptococcus aureus, Staphylococcus pneumoniae and α -Streptococcus) than the other groups, however, the other characteristics of pleural effusions, patients' backgrounds and chest CT findings were not significantly different. Of 23 patients, six patients were received surgery; three of five pus predominant patients (60%), two of 10 fibrin predominant patients (20%), and one of eight other type patient (13%).

Conclusions: Our study showed that LAT might be useful to evaluate the necessity for surgery.

P-N-041

P-N-043

CLINICAL EVALUATION OF ASPIRATION PNEUMONIA IN A COMMUNITY HOSPITAL IN JAPAN

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Background: Aspiration pneumonia is a major medical problem especially in elderly persons in Japan. Aspiration is one of the most common causes of community-acquired pneumonia as well as hospital-acquired pneumonia. Patients with aspiration pneumonia are increasing in numbers year by year in community hospitals in Yamagata area.

Aim: The aim of this study is to evaluate clinical features of aspiration pneumonia in a community hospital in Yamagata, located in north-eastern Japan.

Methods: Patients were eligible for this study if they were 15 years or older, and were diagnosed with pneumonia in Yamagata City Hospital Saiseikan from October, 2012 through March, 2014. Patients were divided into two groups based on the clinical diagnosis by respiratory physicians: aspiration pneumonia and non-aspiration pneumonia. Clinical parameters (e.g. patient characteristics, administered antimicrobials, bacterial cultures, and prognosis) were assessed in both groups. Severity of pneumonia was evaluated by A-DROP scores: age; dehydration; respiration; orientation; and pressure.

Results: A total of 788 cases in 679 patients (443 men and 345 women) were enrolled in this study. The median age of the cases was 85 years (15 to 102 years). Of these 788 cases, 412 were aspiration pneumonia (227 men and 185 women; AP) and 376 were non-aspiration pneumonia (216 men and 160 women; NAP). The mean age of AP was significantly higher than NAP (86.0 vs. 74.3 years; $p < 0.05$, Wilcoxon test). AP showed more frequent of pneumonia recurrence (10.4 vs. 3.1%; $p < 0.05$, Chi-square test), higher severity by A-DROP scores (2.0 vs. 1.5; $p < 0.05$, Wilcoxon test), longer hospital stay (18.2 vs. 13.2 days; $p < 0.05$, Chi-square test), and higher mortality (8.9 vs. 4.1%; $p < 0.05$, Chi-square test). Additional antimicrobials were required for the treatment of AP other than empiric antimicrobial therapy compared to NAP (14.2 vs. 10.2%; $p < 0.05$, Chi-square test). There were more numbers of sputum MRSA carriers (6.5 vs. 2.4%) or *Candida* carriers (26.7 vs. 18.4%) in AP ($p < 0.05$, Chi-square test). Multivariate analysis indicated that the following independent factors were related to clinical features of AP: higher age; recurrent pneumonia; and *Candida* carriers in sputum cultures.

Conclusion: Clinical features of AP would be more severe than NAP in higher-aged patients in a community hospital, resulting in failure of initial empiric antimicrobial therapy and increasing overall mortality.

NEUTROPHIL TO LYMPHOCYTE RATIO TO PREDICT CLINICAL OUTCOMES IN PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA

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Background and Objectives: The neutrophil-lymphocyte count ratio (NLR) is an emerging inflammatory marker. Recently, several studies have demonstrated its predictive power in several infectious diseases. We herein sought to the prognostic value of serial NLR measurement in patients with community acquired pneumonia.

Method: A total of 177 patients with suspected lower respiratory infections who were admitted to the emergency department of the Dong-A university hospital were enrolled. Serum samples for NLR were collected at admission and at hospital day 4. The NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.

Results: The NLR at day 4 provided moderate prediction of clinical stability at day 4 (AUC: 0.749, 95% CI: 0.668 to 0.831, $p < 0.001$) and mortality (AUC: 0.740, 95% CI: 0.615 to 0.865, $p = 0.001$), whereas the NLR at admission did not show significant predictive value. A decrease in NLR between admission and day 4 was present in 84.1% (111 of 132) of patients who were stabilized at hospital day 4 and in 51.1% (22 of 45) of patients who were not stabilized ($p < 0.001$). An increase in NLR occurred more frequently in patients who died of pneumonia than patients who recovered (58.8% vs. 20.9%, $p = 0.002$). A change in NLR was found to be significant and independent predictor of clinical stability at hospital day 4 (OR: 4.88, 95% CI: 2.27 to 10.52, $p < 0.001$) and mortality (OR: 4.01, 95% CI: 1.39 to 12.03, $p = 0.10$) after adjusting for age, comorbid illness.

Conclusion: The NLR, especially a change of measurements, was a useful laboratory marker to predict clinical stability and mortality in patients with community acquired pneumonia.

P-N-042

ASSOCIATION BETWEEN NUTRITIONAL STATUS AND DISEASE SEVERITY BASED ON PSI AND OUTCOME PATIENT WITH CAP IN PULMONARY WARD, GENERAL HOSPITAL DR. M. DJAMIL PADANG

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Background: Malnutrition and infection had mutual influence. Malnutrition could accommodate and aggravate infection. The infection decreasing someone's immunity and in the other hand increasing severity of the disease. The aim of this study is to determine association between nutritional status and lower respiratory tract infection.

Matter and Methods: Cross sectional study We collected data from patients with community acquired pneumonia (CAP) including demographic data, disease severity based on Pneumonia Severity Index (PSI), nutritional status based on subjective Global Assessment SGA, and outcome. We analyzed data using inpaired t-test, with P value $< 0,05$ considered as significant.

Result: We found 30 subjects with CAP and most of them whose PSI scores mild 15 (50%) dan SGA scores C (malnutrition) 20 (70%). There was no statistically significant association between nutritional status and disease severity based on PSI scores ($p = 0,121$; CI 95%), nutritional status and length of stay ($p = 0,669$; CI 95%), nutritional status and outcome ($p = 0,197$; CI 95%).

Conclusion: There were no association between nutritional status with disease severity and outcome, but from this study patient with PSI score mild all SGA score was malnutrition.

P-N-044

INTRAVENOUS AZITHROMYCIN MONOTHERAPY FOR NON-SEVERE COMMUNITY-ACQUIRED BACTERIAL PNEUMONIA – A PROSPECTIVE, OPEN LABELLED, NON-COMPARATIVE STUDY

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Background and Aim: In Japan, because of emerging of macrolides-highly resistant strains of *S.pneumoniae*, macrolide antibiotics administration is avoided as empiric therapy for community-acquired bacterial pneumonia. Intravenous azithromycin is expected effective for community-acquired bacterial pneumonia because of its antibiotic spectrum and unique pharmacodynamics nature as a single agent, but there are few reports that evaluated its usefulness in our country. We conducted a prospective, single centre, open labelled, non-comparative study of azithromycin-intravenous monotherapy for non-severe community-acquired bacterial pneumonia in Japanese adults to evaluate clinical efficacy and safety. This study was approved by institutional review board in our hospital.

Patients and Methods: Adult mild-to-moderate community-acquired bacterial pneumonia patients with obtained written consent enrolled from January to December, 2013. Five hundred mg of azithromycin was intravenously administered once daily for 7 days. Switch to oral 500 mg of azithromycin once daily was enabled with discretion of attending physician. The primary end-points are efficacy rate in the Clinical Per Protocol Set (CPPS) at the end of trial (EOT) and drug related adverse events incidence. The secondary end-point is an eradication rate of the causative pathogen.

Results: A total of 17 cases were enrolled, and all of them received iv azithromycin. Four cases were excluded from the CPPS. For the 13 cases in the CPPS, mean iv AZM dosing was 6.8 days, and only 2 cases received oral azithromycin after iv treatment. The efficacy rate in the CPPS was 91.7% (11/12) at EOT. Causative pathogen was identified in 6 cases; *S.pneumoniae* (2 strains), *Haemophilus influenzae* (2 strains), *Moraxella catarrhalis* (1 strain) and *Pasteurellamutocida* (1 strain). Both 2 strains of *S.pneumoniae* isolates were resistant to azithromycin (MIC > 4 µg/mL). Concerning bacteriological response, eradication rate was 50% for both *S.pneumoniae* and *H.influenzae*, and was 66.7% for all the cases whose causative pathogen identified. Although causative pathogen remained at EOT concerning *S.pneumoniae* and *H.influenzae*, the efficacy rate was 100% for the cases these pathogens were isolated. All cases who received at least 1 dose of azithromycin were included in the safety analysis. Among the 17 cases, treatment related adverse events were observed in 7 (41.1%). The most common adverse event was transient abnormality in laboratory findings such as elevation of ALT/AST, and CK. The serious adverse events was not observed. No cases died in this study.

Conclusion: The 500 mg of intravenous azithromycin monotherapy is hopeful for mild-to-moderate community-acquired bacterial pneumonia even in Japan.

P-N-045

A CASE OF SUCCESSFUL SURGICAL MANAGEMENT FOR NECROTIZING PNEUMONIA

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Necrotizing pneumonia is characterized by pneumonic consolidation with multiple necrosis of the lung parenchyma. Medical therapy is usually mainstay of management. In rare cases, surgical treatment can be essential because this infection could be life-threatening. To date, there are no established surgical indications for necrotizing pneumonia. A 51-year-old man visited our emergency department due to necrotizing pneumonia in the right upper lung. The patient had co-morbidities such as diabetes mellitus and alcohol abuse, whose necrotizing pneumonia was not controlled by proper medical treatments with antibiotics but deteriorated progressively. The patient underwent surgical management and showed successful treatment outcomes. Early aggressive surgical management should be considered in achieving a curative treatment in patients with necrotizing pneumonia who are refractory to optimal medical treatments. This should also be accompanied by multidisciplinary approaches with clinicians in other specialty areas.

P-N-046

CLINICAL UTILITY OF MULTIPLEX PCR TO DIAGNOSE RESPIRATORY VIRAL PNEUMONIA

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Background: PCR method enables us to diagnose respiratory viral infections with higher sensitivity and specificity than conventional methods. Multiplex PCR (mPCR) is designed to examine multiple pathogens simultaneously and exerts its ability on screening respiratory viruses especially in patients with unknown aetiology. Although mPCR has been used mainly for research purpose, our department has introduced this system to clinical practice since 2012 and routinely checked respiratory specimens from patients with unknown aetiology. Here, we present 6 cases which respiratory virus was detected in a specimen from lower respiratory tract.

Methods: A commercially available mPCR kit (Seeplex RV15 OneStep ACE Detection, Seegene, Korea) was used in this study. This kit can screen 15 respiratory viruses simultaneously.

Results: Between August 2012 and November 2013, 54 specimens from lower respiratory tract were examined; 34 samples (63.0%) were bronchoalveolar lavage fluid (BALF), 18 samples (33.3%) were bronchial lavage fluid, and 2 samples (3.7%) were sputum in trachea. Among them, a virus was detected in 6 cases; parainfluenza virus type 3: 3 cases, parainfluenza virus type 1: 1 case, influenza virus A: 1 case, rhinovirus: 1 case. Underlying conditions of these patients were; cancer (haematological malignancy: 2 cases, solid cancer: 1 case), HIV: 1 case, immunosuppressive agent user: 1 case, none: 1 case. Three cases were diagnosed pure viral pneumonia based on the clinical and radiological findings. Within these 3 cases, ground glass opacity was observed in all patients and neutrophils in BALF were significantly elevated in 2 patients (41.7% and 20.9%). Viral pneumonia is frequently missed due to the limitation of conventional diagnostic strategy, mPCR is a powerful tool and must advance the quality of clinical practice in the field of respiratory diseases. We will present updated data with more cases which respiratory virus is detected in a specimen from lower respiratory tract at the congress.

P-N-047

P-N-048

A CASE REPORT OF PULMONARY NOCARDIOSIS CAUSED BY *N. CONCAVA*, AND REVIEW OF THE LITERATURES

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Nocardia concava is a new *Nocardia* species identified in 2005. There have been only 3 case reports of *N. concava* infection and the clinical characteristic has not been cleared. *Nocardia* spp. is aerobic Gram-positive bacteria of the order Actinomycetales. *N. asteroides* is the most common cause of nocardiosis, *N. brasiliensis*, *N. otitidiscaviarum*, and *N. farcinica* also cause human infection. *Nocardia* often enters through the respiratory tract, and the infection develops and spreads to any part of body. The antimicrobial sensitivity of *Nocardia* is depending on the species. Therefore, identifying *Nocardia* species is important to select antimicrobial agents. Here we report the case of an immunocompromised patient who developed pulmonary nocardiosis caused by *N. concava*, and review the previous case reports. A 68-year old male patient was admitted to our hospital with complaints of anorexia and leg pain. His urinary sediment showed many red cell counts (50–99/HPF). Laboratory tests showed renal dysfunction (creatinine 1.83 mg/dl, BUN 35 mg/dl), and increased MPO-ANCA (87.5 U/ml). He was diagnosed with ANCA-associated vasculitides by a renal biopsy. On hospital day 3, Steroid pulse therapy for three days at a dosage of 1000 mg/day was performed twice, and cyclophosphamide (500 mg/day) was administered via intravenous on 20th day. On 39th day, he complained of hemoptysis. Chest computed tomography (CT) showed a 22 mm cavitary lesion with wall thickness in the left upper lobe. A gram stain of his sputum showed branching Gram-positive filaments resembling *Nocardia* spp. Depending on his renal function, 320 mg of trimethoprim and 64 mg of sulfamethoxazole (TMP/SMX) was administered. Cultures from the sputum showed *Nocardia* species, and we were able to identify the species as *N. concava* using a sequence analysis of 16S rRNA. After initiation of therapy, his symptoms improved; the wall thickness of the cavity was reduced. The patient has recovered from the infection of *Nocardia*. There have been only 3 detailed reports of *N. concava* infection worldwide. All of them have been reported in Asian countries since 2011. All of them were disseminated infection cases, and patient's symptoms, infected organs, administered antimicrobial therapy were various. Here we present our case in detail, and review the literatures.

THE ASSOCIATION BETWEEN THE SEVERITY OF SWALLOWING IMPAIRMENT AND OUTCOMES OF ASPIRATION PNEUMONIA: A RETROSPECTIVE STUDY OF 321 CASES

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Objectives: Aspiration pneumonia (AP) is a major cause of morbidity and mortality among the elderly. Multiple risk or prognostic factors for pneumonia have been identified, but few studies have effectively compared the relative risk of factors in several different categories, including swallowing dysfunction. The aims of this study are to evaluate the correlation between the severity of swallowing dysfunction and clinical features and outcomes of AP.

Methods: We retrospectively analyzed 321 patients performed videofluorography (VF) to examine the swallowing function objectively between January 2011 and March 2013 in Nagasaki University Hospital.

Results: 20.2% (65/321 cases) of the patients have been developed pneumonia, of which 14.0%, 48.0%, and 38.0% were community-acquired pneumonia, hospital-acquired pneumonia and nursing and healthcare associated pneumonia, respectively. An infectious agent was detected in 34.0% of cases, of which 9.0%, 6.0%, and 4.0% were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*, respectively. 56.7% (182/321 cases) of the patients were detected swallowing dysfunction. The presence of swallowing dysfunction was not responsible for the risk factors of drug-resistant pathogens (prior hospitalization, immunosuppression, previous antibiotic use, use of gastric acid-suppressive agents, tube feeding, and non-ambulatory status) reported previously. The independent risk factors of swallowing dysfunction were low Performance Status (odds ratio [OR] 1.64; 95% confidence interval [CI], 1.27–2.11; $P = 0.0002$), head and neck tumour (OR 4.18; 95% CI, 2.00–8.19; $P = 0.0002$), and hypoalbuminemia (OR 0.82; 95% CI, 0.52–1.30; $P = 0.0019$). The independent risk factors of aspiration pneumonia were cerebral nervous diseases (OR 2.33; 95% CI, 1.25–4.32; $P = 0.0075$), post gastro-esophageal surgery (OR 2.43; 95% CI, 1.08–5.48; $P = 0.0327$), hypoalbuminemia (OR 0.40; 95% CI, 0.25–0.65; $P = 0.0020$) and severity of swallowing dysfunction (OR 0.79; 95% CI, 0.65–0.95; $P = 0.0119$). No significant correlations between the severity of swallowing dysfunction and severity of pneumonia were observed whereas the duration of antibiotics administration and hospitalization were significant prolonged according to the swallowing impairment. Hypoalbuminemia was only an independent risk factor for in-hospital mortality in the patients with swallowing dysfunction (OR 0.19; 95% CI, 0.06–0.58; $P = 0.0035$).

Conclusions: To estimate the swallowing function by the objective manner such as VF is clinically useful for making a prediction of the occurrence and outcome of aspiration pneumonia.

P-N-049

SUBGROUP ANALYSIS OF HEALTH CARE ASSOCIATED PNEUMONIA PATIENTS

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The main objective of this study is to determine clinical differences between the two subgroups of healthcare associated pneumonia (HCAP) patients. The secondary objective is to search the factors that may influence mortality in HCAP patients according to the comorbidity condition. The study is a retrospective cohort study and enrolled in patients hospitalized for HCAP pneumonia in a teaching hospital between 2011 and 2013. The patient's records were analyzed for demographic data, hospital stay, ICU admission, in-hospital mortality, infectious markers like CRP and WBC counts and isolated bacteria. The data of 130 patients (mean age 76 ± 9 , 88 male) hospitalized for HCAP were analyzed and the study population was divided in patients with neurological disorder (Group 1; n:90, mean age: 78 ± 8 , 60 male) and patients with chronic renal failure (Group 2; n:40, mean age 69 ± 9 , 28 male). The hospital stay was found in Group 1 and 2 as 14 ± 11 and 17 ± 11 days, respectively (p:0.12,ns). The ICU admission rate was higher in Group 2 (16/40; 65%) when compared to Group 1 (36/90;40%) (p < 0,05). There was no difference for WBC counts and CRP levels at admission between two groups. A causative bacteria was isolated in 25 patients in Group 1 and 8 patients in Group 2 (p : ns). The in-hospital mortality rate was found as 44% in patients with neurological comorbidity and 40% in patients with renal failure (p : ns). No relation was found between mortality and investigated parameters. The study demonstrates that there is no major difference between two subgroups of HCAP patients when analyzed for hospitalization days, mortality, WBC and CRP levels, causative agent isolation rate. ICU need was found higher in patients with chronic renal failure. At hospital admission, subgroups of HCAP patients do not show any difference upon in-hospital mortality but, patients with chronic renal failure need more ICU care. This data may be relevant when triage is needed.

P-N-050

CLINICAL FEATURES OF COMMUNITY-ACQUIRED PNEUMONIA(CAP) AND NURSING AND HEALTHCARE-ASSOCIATED PNEUMONIA(NHCAP) IN OUR HOSPITAL

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Objective: The mortality rates of pneumonia are far higher especially in elderly. In this study, we aimed to investigate the characteristics of CAP and NHCAP and its sputum culture data and mortality.

Methods: We studied consecutive 445 patients who were admitted to Showa University Fujigaoka hospital with diagnosis of pneumonia between October 2009 and December 2012 (219 cases were diagnosed CAP and 225 cases were NHCAP). The NHCAP group included patients who were hospitalized at a convalescent bed, residents in a nursing home or long-term care facility; patients hospitalized within 90 days of the study period; elderly or disabled people requiring care; patients receiving continuous intravenous therapy, including haemodialysis, antibiotic treatment, chemotherapy, and immunosuppressive treatment. We compared their laboratory findings, severity and mortality rates and especially initial treatment for patients who had *Pseudomonas aeruginosa* and MRSA in sputum. The guideline for NHCAP, the Japanese Respiratory Society documented and published, recommended anti-*P.aeruginosa* biotics for patients who had risk of having resistant bacteria (using antibiotics within 90 days and tube feeding) and who need intensive care for severe respiratory, and we studied their initial treatment and outcome. We also categorized the patients into the ADROP (0–5) risk strata and relationships between sensitivity and specificity were plotted in ROC curves.

Results: Patients with NHCAP were older and had many complication (cerebrovascular disease, neuromuscular disease, chronic heart failure etc.). And performance states (PS) score was more worse in patients with NHCAP. In clinical data, NHCAP group had more higher severity score (ADROP score 3–5). The 30 days mortality in the patients with NHCAP was significantly higher than with CAP (p < 0.0001). And ROC curves for 30 days mortality showed us that ADROP scoring system was more useful in patients with CAP. In 25 patients with *P.aeruginosa* who received no anti-*P.aeruginosa* biotics, 13 patients does not need anti-*P.aeruginosa* biotics. Similarly in MRSA, 18 patients does not need anti-MRSA biotics among 31 patients. We also analyzed initial treatment and outcome for the patients who recommended anti-*P.aeruginosa* biotics, the patients who failed for initial treatment are more severe ADROP score. Multivariate analysis identified low score of performance status (PS) and respiratory failure as predictors of pneumonia.

Conclusion: Mortality of pneumonia is significantly higher in NHCAP, because the patients with NHCAP were more elderly, had more complication, low PS score. Utility of ADROP risk strata for NHCAP was less than CAP. Many *P.aeruginosa* and MRSA were found in the patients with NHCAP, but that is not identified as predictors of pneumonia and the bacteria doesn't cause pneumonia in some cases.

P-N-051

NONTUBERCULOUS MYCOBACTERIA INFECTION, DIAGNOSED BY ENDOBRONCHIAL ULTRASOUND

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Introduction: In the 1980's, NTM was recognized as a common cause of disseminated infection in patients who were severely immunocompromised. In Thailand, a study reported that almost half of the disseminated NTM infections in HIV-negative cases were related to farming. NTM-contaminated soil and water lead to tissue invasion and disease causation. In the recent years, Bangkok Hospital Medical Center has observed a constant rise of patients diagnosed with NTM, with or without accompanying disease or infection. Diagnosing NTM has been made easier with the availability and aid of Endobronchial Ultrasound (EBUS) in collecting specimens for culture and sensitivity.

Objective: To illustrate 10 different cases and management of NTM.

Methodology: From 2012–2014, data of patients positive of NTM from culture and sensitivity results were collected.

Results: 10 HIV-negative cases of NTM were identified by bronchoscopy, EBUS-GS and sputum culture. The age ranged from 41 to 89 years old, with mean of 64 years. There were 8 females (80%), most were menopausal (87.5%), and 2 males (20%). Underlying conditions were diabetes mellitus (30%), coexisting tuberculosis (50%) and lung cancer (10%). All suffered from respiratory symptoms such as fever, dyspnoea, sputum production and abnormal chest X-ray and chest CT scan results. All were identified using EBUS (70%), sputum culture (20%) or bronchoscopy (10%). Bacterium recorded were *M. avium* complex (MAC) (30%), *M. intracellulare* complex (MIC) (10%) and 60% were unidentified NTM bacteria. All responded well to macrolide and quinolone treatment. Specimens obtained from EBUS are highly reliable with the right laboratory setting that can identify specific types of NTM.

P-N-053

FATAL MUCORMYCOSIS MEDIASTITIS IN AN IMMUNOCOMPETENT MALE

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Introduction: Mucormycosis is an emerging angioinvasive infection caused by ubiquitous filamentous fungi. It very rarely causes disease in immune competent host. Mediastinitis is a rare condition and usually occurs with predisposing conditions as a complication after odontogenic or cervicofacial infections or after cervical trauma spreading along the deep fascial planes into the mediastinum. We describe a case of an immunocompetent Saudi male who presented with Mucormycosis mediastinitis with fatal outcome reflecting on the diagnosis and radiological manifestation.

The Case: 34 year-old Saudi gentleman, not know to suffer from any chronic disease, presented with 2 days history of cough & fever. It was associated with pleuritic chest pain and dyspnoea. He gave a history of odynophagia 1 week prior to his presentation and intermittent headache. There was no haemoptysis, dysphagia or weight loss. On examination: T: 38.1°C, Bp: 140/82, pulse: 96 bpm, RR: 23/min and SpO₂: 99% in room air. There was decrease chest expansion in right mid to lower chest, decreased tactile vocal fremitus in the same side and dullness in the right lower zone with diminished air entry in the right lower zone. Abdomen: Soft, lax with no tenderness or organomegaly. He was treated as community acquired pneumonia with antibiotics which were adjusted depending on his response and radiology (CXR, US & CT) was done. He later developed nausea and vomiting with palpable mass in right iliac fossa. This became necrotic. Surgical debridement was done and cultures sent. He developed renal failure and was dialyzed. The patient developed septic shock and was intubated, put on inotropic support but later died. The culture from the abdomen wound showed Mucormycosis. His CT chest had shown mediastinitis and he had multiple lesions in the kidneys suggestive of septic emboli.

Discussion and Conclusion: Mucormycosis is usually fatal disease when it rarely infects immunocompetent host due to delay in the diagnosis. We describe the first case in Saudi Arabia of Mucormycosis mediastinitis and discuss the clinical and radiological findings and review the literature regarding Mucormycosis mediastinitis and Mucormycosis in the immunocompetent.

P-N-052

ASSOCIATION OF INTERLEUKIN-10 SERUM LEVEL AND PORT SCORE WITH MORTALITY STATUS IN MODERATE-SEVERE COMMUNITY ACQUIRED PNEUMONIA WITH COPD AND HEART FAILURE

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Background: Community-acquired pneumonia (CAP) is the 6th most common cause of death in development country with mortality 10–15%. Overexpression of anti-inflammatory cytokine impaired infection resolution. Usually CAP came with comorbidity such as COPD and heart failure. Divergent data regarding harmful roles of IL-10 have been reported but study about relationship between IL-10 and PORT score in CAP with COPD and heart failure was infrequent.

Method: A cohort study on 15 moderate-severe CAP with population B-C COPD and heart failure functional class 2–3. PORT score was measured on admission day. IL-10 serum was measured with ELISA Biologend on day 1 and day 7. Mortality was observed in 30 days.

Result: Overall mortality was 20%. There was no significant association between PORT score and mortality ($p=0.999$) but all survivors was on risk class IV. All nonsurvivors had a very high level of IL-10 serum on day 1 and didn't decreased until day 7 (mean $268,33 \pm 37,25$ pg/ml and $268,39 \pm 30,29$ pg/ml, respectively). In all survivors IL-10 serum level was decreased significantly from day 1 to day 7 (mean $164,13 \pm 35,38$ pg/ml and $26,57 \pm 30,29$ pg/ml, respectively).

Conclusion: Decreased of IL-10 serum level was potentially as predictor for mortality status in moderate-severe CAP with COPD and heart failure.

P-N-055

AN UNUSUAL CAUSE FOR BILATERAL SPONTANEOUS PNEUMOTHORAX

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Septic embolism is a rare disease characterized by circulating infective thrombi traversing the pulmonary circulation. It is usually associated with history of intravenous drug abuse, tricuspid regurgitation, infected thrombophlebitis, indwelling catheter or an immunocompromised state. Complications such as hydropneumothorax and pneumothorax are rarer. We report a middle aged immunocompetent female presenting with right sided spontaneous pneumothorax. Her pneumothorax responded to conservative management, but she later developed a hydropneumothorax on her left side for which a chest tube was placed. Xray imaging showed nodular infiltrates bilaterally. CT scan of the thorax revealed bilateral multiple ill-defined nodules with central cavitation and effusion which was suggestive of septic embolism. A septic source was searched for and an abscess was noted over her right calf. A correlation was seen between pus culture of *E.coli* and a similar bacteremia. There was no evidence of endocarditis or thrombophlebitis. Patient responded on surgical management of the abscess and appropriate antibiotic therapy. A diagnosis of bilateral spontaneous pneumothorax secondary to septic embolism from right calf abscess was made based on the clinical, radiological and culture reports. Septic embolism is usually missed due to its nonspecific presentation, pneumothorax being one of them. The diagnosis rests on strong suspicion based on history and clinical characteristics along with radiological findings coupled with evidence of a septic focus elsewhere in the body. This case is important because of the rare presentation of bilateral pneumothorax, absence of endocarditis and a hidden and unusual source for septic embolism.

P-N-056

HYPERINFECTION SYNDROME

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The first case is a 31 year old, male, a chronic alcoholic and fond of eating raw fresh river fish and wading in the river. He initially presented with progressive weight loss, bipedal oedema, abdominal pain and vomiting. He was later diagnosed to have nephrotic syndrome and underwent pulse therapy using 500 milligrams methylprednisolone intravenously once a day for three days. He had subsequent hospitalizations due to inguinal and abdominal wall abscesses and later developed nosocomial pneumonia. The patient was cachectic, tachycardic, dyspneic and febrile. There was crackles and diffuse wheezing in all lung fields. A grade 1 bipedal pitting oedema with petechial and purpuric rashes were noted. Human immunodeficiency virus and lupus erythematosus panel were unremarkable. He had anaemia, leukocytosis, eosinopenia and hypoalbuminemia. Chest roentgenograms and arterial blood gases were consistent with acute respiratory distress syndrome. Routine fecalysis revealed 170 *Strongyloides stercoralis* larvae per smear. Sputum examination showed larvae. Patient eventually expired. The second case was a 64 year old, male, farmer, who worked and lived beside a creek and fond of eating half cooked fish. He initially presented with facial and bipedal oedema and elevated lipid profile levels. A kidney biopsy was done which revealed focal proliferative glomerulonephritis. He was started on prednisone. Two months later, he complained of cough, fever and dyspnea and was subsequently admitted in a hospital due to septic shock secondary to community acquired pneumonia high risk. He also had diarrheic stools, which the fecalysis later showed larvae of *Strongyloides stercoralis*. Chest roentgenograms showed diffuse fanning interstitial infiltrates with scattered ill-defined densities on the left lung. He was started with broad spectrum antibiotics for gram negative sepsis and albendazole. Repeat chest imaging showed resolution of the previous infiltrates leaving a granuloma on the left lung. He later complained of abdominal pain, thus upper gastrointestinal endoscopy with multiple gastric and duodenal biopsies were done. Duodenal biopsies showed mucosae with mild chronic, moderate active inflammation, increased eosinophilic infiltrates and reactive epithelial change, no dysplasia, helminth present. He was started on Ivermectin and presently under close follow-up. In both cases, the diagnosis of hyperinfection syndrome was considered and relatively straightforward, due to prior immunosuppression by steroids, exacerbation of pulmonary symptoms and given the high numbers of larvae that exist in the stool and sputum and who were been highly exposed to *strongyloides*. A simple routine fecalysis should be a requisite before any immunosuppression. Screening by culture techniques and serologic examination should be suggested for high risk population. Ivermectin, the drug of choice, should be available in endemic areas. Clinicians should be familiar with the common and unusual presentations of this rare but fatal condition, as well as the various underlying predisposing diseases.

POSTER PRESENTATION – RESPIRATORY NEUROBIOLOGY AND SLEEP

P-O-001

THE EFFECT OF CHRONIC INTERMITTENT HYPOXIA ON HEPATIC INJURY AND MECHANISM IN LEAN MICE AND MICE WITH DIET-INDUCED OBESITY

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Background: Obstructive sleep apnea (OSA) causes chronic intermittent hypoxia (CIH) during sleep. OSA is related with nonalcoholic fatty liver disease in obese individuals. The purpose of this study was to investigate the effects of CIH on the liver in lean mice and mice with diet-induced obesity (DIO).

Methods: Eight-week-old C57BL/6J mice were divided into two groups and then exposed to control conditions (room air, n = 16) or CIH (n = 16) for 4 weeks. Each group was divided into two groups again, and then was fed a regular diet or high-fat, high-cholesterol diet for 4 weeks. At the end of the exposure, several genes including hypoxia inducible factor (HIF-1 α), vascular endothelial growth factor (VEGF), nuclear factor kappa B (NF- κ B), Toll-like receptor 4 (TLR4) in liver were examined.

Results: There was a significant reduction in body weight in mice exposed to CIH steadily through 4 weeks compared with the control group (P < 0.05). In mice with DIO under CIH, lipid peroxidation of liver tissue was significantly increased compared with control mice. In DIO mice, CIH led to increase the activation of NF- κ B in the nuclear fraction of hepatocytes and levels of TLR4 in both mRNA and protein expression, which was not observed in lean mice. The expression of VEGF was shown to be significantly increased in livers and serum in the CIH with DIO group respectively, while the level of HIF-1 α was observed a slight increase but not significantly.

Conclusions: CIH is associated with enhanced expression and signalling events downstream of TLR4 in livers of DIO mice. Our data indicates that CIH causes significant inflammation and liver injury in DIO mice, via TLR4-mediated NF- κ B activation. These results suggest that TLR4 may play a critical role in CIH-induced hepatic inflammation.

P-O-002

DIFFERENT HYPOXIA PATTERNS INDUCE DIFFERENT EXPRESSION OF NA⁺/H⁺ EXCHANGER ISOFORM 3 IN ADULT RAT MEDULLA OBLONGATA

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The present experiments were carried out to investigate the expression of Na⁺/H⁺ exchanger isoform 3 (NHE3) in medulla oblongata of rats and effects of different hypoxia patterns (intermittent hypoxia, IH and continuing hypoxia, CH) on its expression. Wistar adult rats were randomly divided into three groups, including control (Con) group, IH group and CH group. Each group was divided into three subgroups by days (1 day, 3 days, 7 days). NHE3 mRNA and protein expression were analyzed by real-time RT-PCR and Western blotting, respectively, and the expression of NHE3 in nucleus tractus solitarius (NTS) in medulla oblongata of rats was investigated with immunohistochemical technique. The real-time RT-PCR and Western blotting analyses showed that NHE3 mRNA and protein were expressed in the medulla oblongata of rats and hypoxia (IH and CH) decreased the expression of NHE3 in rat medulla oblongata (P < 0.05) and IH decreased the expression of NHE3 more significantly than CH (P < 0.05), the expression of NHE3 was positive correlation with time in IH but negative correlation in CH. Immunohistochemical staining indicated the same results in NTS. In conclusion, NHE3 exists in the NTS of medullary respiratory nuclei and its mRNA and protein expression can be decreased by hypoxia in adult rat medulla oblongata, and different hypoxia patterns induce different expression of NHE3, hypoxia is the independent factor that decreases expression of NHE3 in adult rat medulla oblongata.

P-O-003

ASSOCIATION OF CHEMERIN WITH HIGH SENSITIVE C-REACTIVE PROTEIN IN OBSTRUCTIVE SLEEP APNEOA HYPOPNEA SYNDROME WITH HYPERLIPIDEMIA

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Objectives: To probe the pathogenesis of fat metabolism disorders by investigate serum levels of chemerin and high sensitive C-reactive protein in patients with obstructive sleep apnea hypopnea syndrome with hyperlipidemia.

Methods: 71 patients were classified into four groups according to Lipid composition and polysomnograph (PSG), control group, OSAHS group, hyperlipidemia group, OSAHS combined hyperlipidemia group, the results were statistically analyzed.

Results: The levels of serum chemerin and hs-CRP of patients with OSAHS and hyperlipidemia were significantly higher than patients with single OSAHS, single hyperlipidemia or control group ($P < 0.01$), the difference was statistical significance. OSAHS and hyperlipidemia had interactions effects on the levels of serum chemerin. The chemerin and hs-CRP of obesity group were higher than that of non obesity group in all these groups ($P < 0.05$). The levels of serum chemerin and hs-CRP in the obese group has significant differences among patients with OSAHS and hyperlipidemia, patients with single OSAHS or single hyperlipidemia. In linear correlation analysis, chemerin was positively correlated with triglyceride, cholesterol, body mass index (BMI) and hs-CRP ($P < 0.05$), negatively correlated with HDL-C, LSAO2 ($P < 0.05$). In multiple linear regression analysis, triglyceride, AHI, hs-CRP, were the positively risk factors of chemerin ($P < 0.05$), LSAO2 was the negatively risk factors of chemerin ($P < 0.05$).

Conclusion: The patients with OSAHS and hyperlipidemia tend to have higher serum chemerin and hs-CRP. The levels of serum chemerin and hs-CRP in patients of OSAHS with obesity were significantly higher than those in OSAHS with non obese patients. The level of serum chemerin was associated with hs-CRP.

P-O-004

A NEW APPROACH IN THE DIAGNOSIS OF UPPER AIRWAY RESISTANCE SYNDROME (UARS): PAP METHOD

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Aim: Upper Airway Resistance Syndrome (UARS) is characterized by repeated number of arousals at night, and excessive daytime sleepiness or somnolence (EDS). In UARS, upper respiratory tract resistance increases the intra-thoracic negative pressure without causing apneas and hypopneas. The syndrome is often missed in classical polysomnographic diagnostic approaches and misdiagnosed as simple snoring or idiopathic hypersomnia, thereby is often left untreated. In this manuscript, we propose that Positive Airway Pressure (PAP), which has shown to be effective against UARS, can be used as a diagnostic tool as well. The study designed to test whether patients with high titration pressures can be diagnosed for UARS, and whether this pressure can be used as the treatment pressure in UARS.

Materials and Methods: This study is a retrospective cohort study. The patients with the following selection criteria: Apnea Hypopnea Index (AHI) < 5 , Respiratory Effort Related Arousal (RERA) index > 20 , Excessive daytime sleepiness or somnolence (EDS) without nocturnal oxygen desaturation levels were included to the study. After diagnostic polysomnography (PSG), PAP titration was applied to diagnose and treatment.

Results: Fourteen (%46.7) of the patients were male, 16 (%53.3) were female, with a mean age of 46.4 ± 9.9 and mean body mass index (BMI) of 26 ± 3.3 . The patients had a mean Epworth Sleepiness Scale 15.3 ± 3.9 , mean AHI: 2.3 ± 1.4 and average RERA: 26.1 ± 4.9 . The mean CPAP titration pressure was 7.1 ± 1.1 cm H₂O.

Discussion: In the light of current findings, during PAP titration patients required high pressures is the evidence of increased upper airway resistance in UARS. The patients who did not require pressures higher than 4 cm H₂O excluded from UARS diagnosis. It is believed that this method is important in evidence-based medicine to ascertain the diagnosis of UARS. Using the from therapy to diagnosis protocol, the PAP protocol determines the individual therapeutic pressures needed by patients. Following up the clinical outcomes of these patients under the PAP treatment, and including a larger cohort will contribute greatly to treating this syndrome, defined as one of the "unresolved problems in years".

P-O-005

SERUM LEVELS OF SOLUBLE FORM OF RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEOA

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Aim: Obstructive sleep apnea (OSA) has been proved to be independently a risk of cardiovascular events. Patients with OSA also have the multiple risks such as obesity, hypertension, dyslipidemia and diabetes mellitus. Recently it has been demonstrated advanced glycation end-products (AGEs) is one of biomarkers of vascular dysfunction with impaired glucose tolerance. Soluble form of receptor for AGE (sRAGE) is considered to act as a decoy receptor for AGE, while decline of sRAGE was reported to contribute to coronary disease, atherosclerosis and stroke. In these context, we investigated sRAGE and relations to the various parameters in patients with OSA.

Methods: Thirty-three patients received full standard diagnostic polysomnography (PSG) at Nara Medical University Hospital (Nara, Japan) were enrolled this study. Patients with the following underlying diseases were excluded: stroke, coronary artery disease, asthma, chronic obstructive pulmonary disease, autoimmune disease, rhinitis, and malignant diseases. Serum samples were collected from OSA patients at 6:00 h under monitoring of the PSG. We measured fasting plasma glucose (FPG), HbA1c, insulin and sRAGE. sRAGE were measured by using human sRAGE ELISA kit (CyclLex Co., Ltd.).

Results: All patients were male, and mean age was 45.8 ± 10 years. The mean apnea-hypopnea index (AHI) was 49.7 ± 22 . The mean HbA1c was $5.8 \pm 0.6\%$ and mean HOMA-R was 2.91 ± 3.4 . Nine patients showed mild or moderate (AHI 5 or more and less than 30) OSA and 24 patients showed severe (AHI 30 and more) OSA. There was no significant difference in FPG, HbA1c, insulin, HOMA-R and sRAGE in patients with mild or moderate OSA compared with severe OSA. In the analysis of all the patients, sRAGE showed inversed correlation to age, AHI, 3%ODI, HbA1c.

Conclusion: Decline of sRAGE may be associated with increased risk for cardiovascular disease in patients with OSA.

P-O-006

INTERMITTENT HYPOXIA INDUCED PANCREATIC BETA-CELL PROLIFERATION VIA UP-REGULATION OF REG FAMILY GENES AND HGF GENE

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Background and Aims: Sleep apnea syndrome (SAS) is a highly prevalent sleep disorder characterized by intermittent hypoxia (IH). Accumulating evidence suggests that SAS is associated with glucose intolerance and insulin resistance. In addition to glucose intolerance and insulin resistance, the progression to type 2 diabetes depends on both the impairment of glucose-induced insulin secretion from pancreatic beta cells and the presence of insulin resistance. On the other hand, hyperglycemia is known to increase the replication rate of beta cells, which provide much more insulin to combat the insulin resistance. Yokoe et al. reported that IH causes beta-cell replication without hyperglycemia in mice, suggesting a possibility that IH directly stimulates beta-cell replication. Thus, in the present study we investigated direct effects of IH on beta-cell replication and the changes of gene expression by IH.

Materials and Methods: Rat islets, hamster HIT-T15, rat RINm5F, and human 1.1B4 beta cells were exposed either to 64 cycles/24 h of IH mimicking SAS patient beta-cells, i.e. 5 min hypoxia (1% O₂)/10 min normoxia (21%O₂), or to normoxia of 21% O₂, or to sustained hypoxia (SH) of 1% O₂ for 24 hours. After the treatment, cellular proliferation and apoptosis were measured by WST-8 assay and TUNEL method, respectively. Gene expression was measured by real-time RT-PCR.

Results: The cell proliferation was significantly increased by IH. On the other hand, apoptosis of the cells were unchanged by IH. The mRNA levels of Reg family genes, which encode autocrine beta-cell growth factors, except for PAP I/Reg 2, were significantly increased in RINm5F and that REG I α mRNA was specifically increased in 1.1B4 by IH. siRNAs for Reg I, PAP II/Reg III, PAP III and Reg IV resulted in reduced IH-induced cell proliferation. In addition, IH significantly increased the mRNA of IL-6, which was reported to increase Reg family gene expression, in RINm5F and 1.1B4 cells. siRNAs for Reg family genes resulted in reduced IH-induced cell proliferation. The mRNA level of hepatocyte growth factor (HGF) which is a well-known anti-apoptotic factor, was increased in IH-treated RINm5F and 1.1B4 cells.

Conclusion: These results indicate that IH stimulates beta cell proliferation. It is quite possible that the cyclic change of hypoxia-reoxygenation, which occurs in SAS patients, induces beta cell proliferation, resulting in glucose intolerance and type 2 diabetes.

P-O-007

RELATIONSHIP BETWEEN NOCTURNAL OXYGEN SATURATION AND FUNCTION OF DIAPHRAGM ASSESSED BY ULTRASONOGRAPHY IN COPD

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Aim: Nocturnal oxygen desaturation often occurs and affects the function of the diaphragm in chronic obstructive pulmonary disease (COPD). However, very few studies have been reported in regard to the effect of nocturnal oxygen saturation on the action of the diaphragm in COPD. The purpose of this study was to investigate the relationship between nocturnal oxygenation and the function of the diaphragm assessed by ultrasonography in COPD.

Methods: Thirteen outpatients with stable COPD (Age: 72.0 \pm 6.2 yr, FEV₁: 48.0 \pm 11.2% of predicted) were recruited in this study. A pulmonary function test, blood gas analysis for PaO₂ and PaCO₂ at rest and breathing room air were performed. Changes in the thickness of the diaphragm during breathing was evaluated using high-resolution ultrasonography (Aloka Noblus, Tokyo, Japan). We measured the thickness of the diaphragm (Tdi) in the zone of apposition using B-mode ultrasonographic imaging. In the supine position, a transducer was placed on the chest wall in the 8th or 9th right intercostal space at the middle axillary line. The change of Tdi (% Δ Tdi) was calculated as the difference between the thicknesses at the end of inspiration and at the end of expiration divided by the thickness at the end of expiration. Oxygen saturation (SpO₂) and the total time with saturation below 90% (%Time<90%) were measured throughout the night using a pulse oximeter (Teijin PULSOX-Me300i, Tokyo, Japan). Pearson's correlation was used to assess the relationship among nocturnal oxygen saturation, blood gas, pulmonary function and % Δ Tdi.

Results: There was a significant positive correlation between % Δ Tdi and mean SpO₂ ($r = 0.719$, $p = 0.003$), mean SpO₂ and PaO₂ ($r = 0.785$, $p = 0.001$), %Time<90% and PaO₂ ($r = 0.704$, $p = 0.003$) and also a significant negative correlation between % Δ Tdi and %Time<90% ($r = -0.517$, $p = 0.048$). There was not correlation between pulmonary function and % Δ Tdi, and SpO₂.

Conclusions: Our study indicated the existence of a close relationship between nocturnal oxygen desaturation and the thickness of the diaphragm, suggesting that nocturnal hypoxia might deteriorate the function of the diaphragm in COPD patients. Ultrasonography was also has shown to be a useful assessment tool for examining the function of the diaphragm.

P-O-008

THE DOSE-RESPONSE RELATIONSHIP BETWEEN CPAP ADHERENCE AND EXCESSIVE DAYTIME SLEEPINESS IN SUBJECTS WITH OBSTRUCTIVE SLEEP APNEOA

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Introduction: Subjects with obstructive sleep apnea (OSA) often present with excessive daytime sleepiness, and continuous positive airway pressure (CPAP) is the standard and effective treatment for these sleepy subjects. This study investigated the relationship between CPAP usage and symptomatic relief.

Methods: Subjects with newly diagnosed OSA were recruited. CPAP titration was individually done at an optimal pressure. Subjects were advised to keep CPAP treatment for 3 months, they filled in Epworth sleepiness scale (ESS) questionnaire at baseline and 3 months post treatment. CPAP compliance data were downloaded from the built-in memory card in the machine.

Results: 100 subjects with OSA were recruited, with a mean age of 52.0 \pm 9.6 years, mean body mass index of 29.0 \pm 5.5 kg/m², mean ESS of 9.2 \pm 5.4, and average CPAP usage of 3.4 \pm 2.3 hours/night. 28 subjects had ESS < 10 and 72 with ESS \geq 10. In those with ESS \geq 10, when we put them into 3 groups according to the CPAP compliance data, group 1 ($n = 23$): using CPAP < 3 hours / night, group 2 ($n = 24$): using CPAP \geq 3 to < 5 hours / night, group 3 ($n = 25$): using CPAP \geq 5 hours /night, there was increasing percentage of subjects becoming non-sleepy, 57.5%, 77.4% and 86.2% respectively ($p = 0.023$).

Discussion: In subjects with OSA, good CPAP adherence gives them symptomatic relief in a dose-response dependent manner.

P-O-009

5-HT_{1A} RECEPTOR IN RAPHE MAGNUS NUCLEUS SUPPRESSES GENIOGLOSSUS CORTICOMOTOR ACTIVITY DURING INTERMITTENT HYPOXIA IN RATS

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Objective: Raphe magnus (RMg) 5-HT neurons play an important role in the facilitation of genioglossus corticomotor activity induced by intermittent hypoxia (IH). It has been suggested that RMg contains a large amount of 5-HT_{1A} receptor, while the role of 5-HT_{1A} receptor in RMg in genioglossus corticomotor activity during IH was still unknown. In the present study, we evaluated the effect of 5-HT_{1A} receptor in RMg on the transcranial magnetic stimulation (TMS) response of genioglossus corticomotor area during IH.

Methods: The rats were divided into 4 group: normoxia group, IH group, IH-artificial cerebrospinal fluid (IH-ACSF) group, IH-8-OH-DPAT group. In IH-8-OH-DPAT group, the rats were injected 5-HT_{1A} agonist (8-OH-DPAT, 100 nL, 0.1 mM) into RMg followed by 8-hour IH. The rats in IH-ACSF group were microinjected equivalent dose of ACSF in parallel. TMS were measured before and on the 1st day, 3rd day, 7th day, 14th day and 21st day of IH after central injections in all rats.

Results: Compared with the normoxia group, shorter latencies of genioglossus TMS responses were observed on the day of 7, 14 and 21 of IH in IH group ($P < 0.05$). Compared with the corresponding ACSF-injected groups, the longer TMS latencies were observed in the IH-8-OH-DPAT group on the 1st, 3rd, 7th and 14th day of IH ($P < 0.05$).

Conclusions: The results indicate that RMg 5-HT_{1A} receptor play an important role in attenuating the corticomotor activity of genioglossus during IH.

P-O-010

NASAL POSITIVE END EXPIRATORY PRESSURE VALVE TREATMENT FOR OSA

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Background: Continuous positive airway pressure (CPAP) is very effective in treatment of obstructive sleep apnoea (OSA). However CPAP compliance is suboptimal at around 50%. Less cumbersome form of treatments like oral appliances result in better patient acceptance yet clinical efficacy is usually suboptimal.

Aim: Explore the clinical usefulness of a nasal positive end expiratory pressure (nPEEP) valve in patients declined of CPAP. The nPEEP valve was predominately an one way valve with no resistance during inspiration but keeping a resistance during expiration so a PEEP was built up to splint the airway.

Methods: A case control study recruiting symptomatic patients with OSA (AHI > 5 /hr by PSG or > 10 by type III devices) who refused or could not tolerate CPAP. A subgroup of patients using dental device were also recruited. Patients with successful acclimatization for one week were continued with the valves for 4 weeks. Each nPEEP valve was applied to each nostril with the attached self-adhesive tape before bed. PSG with tailor made cannula was performed after 4 weeks to assess efficacy.

Results: A total of 196 subjects were recruited during July 2012 to July 2013. 46(23%) failed acclimatization, 14(7%) withdrew from the study. For the 120 patients with PSG data, 72(60%) and 75(63%) had $> 50\%$ reduction in mean overall AHI 26.3 to 17.8 (SEM: 1.6) and mean supine AHI 30.6 to 11 (SEM 2.8-2.1) respectively, $p < 0.001$. There were no significant changes in non-supine AHI, oxygen desaturation index or arousal index with nPEEP. Compared to others, patients with $< 50\%$ reduction in AHI had higher mean overall AHI (30 vs 23, $p = 0.03$), higher mean supine AHI (34.6 vs 25.8, $p = 0.04$), more severe mean oxygen desaturation nadir (76.7 vs 82.7, $p < 0.01$) and longer mean period of desaturation $< 90\%$ SaO₂ (7.7 vs 2.4, $p = 0.02$). There were no significant differences in baseline BMI, age and daytime sleepiness between the two groups. Mean Epworth Sleepiness Scales were marginally improved from 8.9 to 9.8, $p = 0.04$. Feeling of difficulty to breath was the major reason for withdrawal. Dry mouth was the commonest side effect. Compared to oral appliance, there was a larger mean reduction in supine AHI (29 vs 16, SEM 5.2 vs 6.3) and oxygen desaturation index (1.3 vs 0.9, both SEM 0.4) respectively, $p < 0.001$.

Conclusion: nPEEP valves might be useful in selected group of patients with milder or positional related OSA.

P-O-011

SLEEP-DISORDERED BREATHING FOR JAPANESE EXPATRIATES LIVED IN CHINA AND INDONESIA

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Aim: Japanese expatriates living overseas tend to become obese and suffered from sleep disorder breathing (SDB). Providing appropriate diagnostic and treatment system for SDB and running it in these country may contribute to improve clinical symptoms, work efficiency, depression, lifestyle diseases and death cases.

Method: 1. We performed lecture to increase the awareness of SDB and the importance of appropriate diagnosis as well as treatment among Japanese expatriates, Japanese physicians, and local doctors in Shanghai (SNH, China) and Jakarta (JKT, Indonesia). 2. We performed 'sleep apnoea survey' by questionnaire for SDB related complaints, work situation, and SF-36, and respiratory polygraph (PMP-300E: Pacific Medico) examination among adult Japanese male. Medical information and downloaded respiratory polygraph data are sent by internet from these area to Japan. If the subject was diagnosed as "treatment required", visiting the physician for appropriate diagnosis and treatment will be highly recommended. Criteria for introducing CPAP are that respiratory disturbance index (RDI) is greater than or equal to 15 events per hour or RDI is greater than or equal to 5 and less than or equal to 14 events per hour and documentation of excessive daytime sleepiness, impaired cognition, mood disorders, or insomnia, hypertension, ischemic heart disease, or history of stroke.

Result: There were 19 subjects in Shanghai and 16 in Jakarta. RDI ≥ 15 is 11 (58%) SNH, 6 (38%) in JKT. Major complaints were loud snore (71%), sleep apnoea (43%), polyuria (31%), and dry mouth (34%). General health (GH) and vitality (VT) score of SF-36 decrease in both of area, role emotional (RE) and mental health (MH) were decreased in SNH and elevated in JKT.

Conclusion: There are big SDB burden among Japanese expatriates who lived in Asia. Further research and construction of public support system for SDB are required. These study were supported by grand of overseas development support of Japanese medical technologies and services of ministry of economic, trading and economy in Japan.

Cooperated Company: Pacific Medico, Japan Total Sleep Health Check Association, Magnet.

P-O-012

PREVALENCE OF OBSTRUCTIVE SLEEP APNOEA AND POSSIBLE FACTORS RELATED TO TRAFFIC POLICE IN EAST JAKARTA

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Background: Traffic police is a distinctive profession because of the huge responsibility, overnight shifts, long hours of working time and fractured sleep. These conditions interfere the working performance because of the sleepiness. Sleepiness might be caused by obstructive sleep apnoea (OSA) which causes dangerous pauses in breathing during sleep. Sleep apnoea, common in the obese, is tightly linked to hypertension and heart disease.

Method: This study was conducted with cross sectional design. The data was collected in June 2014 at the police office in East Jakarta. Data collection used Berlin's Questionnaire and Physical examinations (blood pressure, weight, height, neck circumference) to 60 police officers.

Result: This research showed that there are 10%, it means 6 respondents from 60 respondents have suspected OSA. Prevalence of suspected OSA among police officers is caused by several factors. The factors are snoring historical in family (adjusted OR 11.88, $p < 0.001$, 95% CI 1.28–109.89), neck circumference > 40 cm (adjusted OR 6.31, $p 0.002$, 95% CI 1.03–38.48).

Conclusion: This research has founded that there are 10%, it means 6 respondents from 60 respondents have suspected OSA. Prevalence of suspected OSA among police officers correlate with snoring historical in family and neck circumference > 40 cm.

P-O-013

CLINICAL CHARACTERISTICS OF REM-RELATED OSA: EXPERIENCE IN A TERTIARY MEDICAL CENTRE OF TAIWAN

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Background: Obstructive sleep apnoea syndrome (OSAS) is characterized by recurrent episodes of upper airway collapse with intermittent hypoxaemia and arousals. Apnoea tends to be pronounced with greater de-oxygenation during rapid eye movement (REM) sleep. The aim of this study is to investigate the clinical features of REM-related sleep-disordered breathing.

Methods: All patients diagnosed with OSAS (apnea-hypopnea index, AHI ≥ 5 /h) using conventional overnight polysomnography (PSG) in the Sleep Center of Taipei Veterans General Hospital from September to December 2013 were analyzed retrospectively. Those with a ratio of AHI during REM (REM-AHI) to AHI during non-REM (NREM-AHI) >2 and NREM-AHI <15 were classified as REM-related OSA (REM-OSA) group. Those with REM-AHI/NREM-AHI <2 were classified as NREM-OSA group and those with REM-AHI/NREM-AHI >2 but NREM AHI ≥ 15 were classified as mixed group. The following data were recorded: clinical demographics and symptoms related to OSAS, PSG results, and associated medical co-morbidities.

Results: A total of 318 patients were analyzed, of whom 237 (74.5%) were diagnosed with OSAS during this period. The severity of total AHI increased in proportion to body mass index (BMI). Female patients had significantly lower total AHI compared to males, and increased total AHI in proportion to age. 63 (26.6%) had exclusively REM-related OSA, 163 (68.6%) were the NREM-OSA group, and 11 (4.6%) were the mixed group. The REM-OSA group had more females and lower BMI compared to the NREM-OSA group. The mean age of REM-OSA group was younger compared to the NREM-OSA group, but did not reach significance. However, the mean age and AHI during REM of mixed group were oldest and highest compared to the other groups. The AHI during NREM and severity of total AHI were highest in NREM-OSA group compared to the other groups, although the symptom of daytime hypersomnolence was most severe in the mixed group and the prevalence in REM-OSA group was higher compared to NREM-OSA group. There was a trend for REM-OSA group to have more rhinitis symptoms compared to the other groups. The mixed group had more associated cardiovascular diseases history or events compared to the other groups.

Conclusions: OSAS may be differentiated to different clinical phenotypes according to the ratio of REM-AHI to NREM-AHI with or without concurrent increased NREM-AHI. Although the total AHI and severity of OSAS were lower in REM-OSA group, this specific phenotype should be critically evaluated the necessity of positive pressure ventilation therapy because of troublesome daytime symptoms.

P-O-016

OBSTRUCTIVE SLEEP APNOEA: INDEPENDENT RISK FACTOR FOR INSULIN RESISTANCE

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Introduction: Epidemiological studies have implicated obstructive sleep apnoea (OSA) as an independent comorbid factor in cardiovascular and cerebrovascular diseases. It is postulated that recurrent episodes of occlusion of upper airways during sleep result in pathophysiological changes that may predispose to vascular diseases. Insulin resistance is a known risk factor for atherosclerosis, and we postulate that OSA represents a stress that promotes insulin resistance.

Objectives: Through this study it is desired to study the association between insulin resistance and OSA and thereby development of DM in OSA. This study investigated the relationship between sleep disordered breathing and insulin resistance, indicated by fasting serum insulin level.

Place Of Study: Department of Tuberculosis and Respiratory Diseases, SS Hospital, IMS, BHU, Varanasi.

Methods: 20 patients after full night polysomnography and having AHI >15 and same number of normal subjects (both groups did not have diabetes mellitus) were chosen for this study and. After receiving the consent and fully explaining about the study and required procedures, the patients underwent biochemical analysis for FASTING INSULIN LEVELS in the serum.

Results: All the patients with OSA had more insulin resistance as indicated by higher fasting insulin levels in the serum. Conversely the normal subjects were having normal fasting insulin levels.

Conclusion: This association between OSA and insulin resistance was seen in both obese and nonobese subjects. Each additional apnoea or hypopnea per sleep hour increased the fasting insulin level by about 0.5%. Our findings suggest that OSA is independently associated with insulin resistance, thereby increasing the atherogenic potential.

P-O-017

CLINICAL ANALYSIS OF SLEEP-DISORDERED BREATHING IN END-STAGE RENAL DISEASE WITH HAEMODIALYSIS

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Background and Aim of Study: Sleep-disordered breathing (SDB) is common in patients with end-stage renal disease (ESRD) receiving haemodialysis (HD). It was hypothesized that this is related to obstructive collapse of upper airway due to pharyngeal oedema mixed with central apnoea due to congestive heart failure. We investigate the clinical characteristics of SDB in HD patients.

Methods: We studied 25 patients with ESRD on thrice weekly maintenance HD who had excessive daytime sleepiness in dialysis centre of Ookubo hospital. They had undergone diagnostic nocturnal polygraphy (Using a categorization of sleep monitoring procedure Type 3) at next day of HD. Gender (M/F:13/12), age 76.5 \pm 7.8(62–87), BMI 20.4 \pm 3.5(14–26.8), interval (month) from induction of HD 93.4 M(17–298). Ultrafiltration volume of the day before 1376 \pm 679 mL(0–2700). Etiology of ESRD (Diabetes/polycystic kidney /Glomerulonephritis/ others=12/2/4/7), complicate (cardiovascular disease/cerebrovascular disease = 3/12). 11 pts. were dead until now.

Results: Overall mean OSA-index was 14.8 \pm 13.5(0.8–45.5). Obstructive sleep apnoea (>5) was found in 19 pts. Mean CSA-index was 2.0 \pm 3.28(0–14.3). Central sleep apnoea (>5) was found in 4 pts. Mean Mixed apnoea index was 2.8 \pm 3.2(0–9.1). Mixed sleep apnoea (>5) was found in 6 pts. 3%ODI was 23.2 \pm 19.0(0.4–70.2). RDI was 26.1 \pm 18.9(1.9–65.9). RDI (>15) found in 13 pts (52%) and RDI (>30) in 8 pts (32%). We performed therapeutic intervention (NCPAP or ASV) to 9 pts. Therapeutic continuation was possible four pts. Furthermore serum CRP, albumin, ferritin, Hb, whole PTH, hANP were monitored.

Conclusion: Japanese Elderly patients with ESRD receiving maintenance HD have SDB in high frequency. They have OSA in particular. We will publish details of the study results at the 19th Congress of the Asian Pacific Society of Respirology (APSR).

P-O-018

FACTORS AFFECTING COMPLIANCE OF PATIENTS WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) UTILIZATION IN CASES OF OBSTRUCTIVE SLEEP APNEOA SYNDROME (OSAS)

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Objective of Study: To study compliance for CPAP in patient with Obstructive Sleep Apnoea Syndrome and the factors associated with the non-compliance.

Methods: Study Area: Study was carried out in the Chest and TB department of Lilavati Hospital and Research Centre (LHRC), Mumbai, a multispecialty tertiary care hospital.

Study Population and Sample Size: Study included 65 patients who were diagnosed as obstructive sleep apnoea and was prescribed positive airway pressure therapy. The patients attending Chest OPD of LHRC and indoor patients who were referred to our sleep laboratory for sleep study and/or CPAP titration study within July 2012 to December 2012.

Data Collection and Sample Collection Tools: It was an observational study in which all patients coming to OPD/sleep laboratory/indoor, meeting the inclusion criteria were interviewed, Epworth Sleepiness Scale (ESS) scoring was also done. Follow up after three month was done regarding CPAP compliance either in front or telephonically.

Result: Approximately 55.38% (36 out of 65) of our patients were using CPAP at follow up which was minimum of three month or more. If we exclude the patient who has never started the therapy then the compliance increases up to 81 % (36 out of 44). About 43% (29 patients) were not using CPAP. Most of individuals among non-users i.e. 32.3% (21 patients) had never started. Eight patients out of 65 have left using after initiating the treatment i.e. 12.3% has stopped CPAP after using it.

Conclusion: Compliance of the CPAP is 55.38% in our study population. Machine size and facemask causing discomfort to the patient is an important factor for non-compliance. Cost and ritual issues are also there in India which is responsible for the non-compliance.

P-O-019

MENAGE A TROIS: A CASE OF SEVERE OBESITY, SEVERE KYPHOSCOLIOSIS AND OBSTRUCTIVE SLEEP APNEOA

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Introduction: In an Obese patient with OSA, presenting with chronic respiratory acidosis a diagnosis of Obesity Hypoventilation syndrome (OHS) is straight forward when certain diseases like chestwall deformities, hypothyroid, severe interstitial lung disease and severe COPD are ruled out. But what happens when a young patient with severe Obesity and is complicated with Severe Kyphoscoliosis and Severe OSA. The association between obesity and hypersomnolence has long been recognized. Did Quasimodo, have serious sleep disturbances that could explain certain aspects of his personality? Victor Hugo never resolved the question. It was not until 1981 that this was answered – when Guilleminault described how severe kyphoscoliosis resulted in alterations in sleep states, coining the term Quasimodo syndrome. Fast forward to present, we have a new face nobody has seen before, obesity, kyphoscoliosis and obstructive sleep apnoea all occurring in a single patient. We have a ménage a trois.

Case: PD is a 29 year-old, male, and hypertensive, diabetic, morbidly obese, with kyphoscoliosis. He had an eight year history of gradual weight gain, with an increased appetite and decreased physical activity, increased sleeping time, loud snoring, witnessed apneic episodes, increased daytime sleepiness. Other associated symptoms were morning headaches, constant irritability, mood swings and memory lapses. He has a short neck with neck circumference of 48 centimeters, Mallampati IV. Polysomnography done showed RDI of 59.8/hr of sleep. Therapeutic Study revealed optimum pressure of 17 cm H2O. An xray of the thoracolumbar spine showed a Cobb angle of 100 degrees. Arterial Blood Gas showed Chronic Respiratory Acidosis with Moderate Hypoxaemia. Pulmonary Function test showed a Moderately severe restrictive ventilatory defect. Diffusion study is moderately reduced. With our patient presenting with severe kyphoscoliosis at 100 degrees, and the presence of his comorbidities, he is not a good candidate for spinal surgery. Obesity and OSA are best approached in tandem. CPAP was initiated in our patient.

Conclusion: We have unfolded a ménage a trois of kyphoscoliosis, obesity, and obstructive sleep apnoea. In time, the fateful mix will carry a much worse prognosis than any of the three entities alone. We can only hope that our interventions for this young man will carry him through.

POSTER PRESENTATION – RESPIRATORY STRUCTURE AND FUNCTION

P-P-001

INFERIOR TRIBUNATE REDUCTION BY RADIOFREQUENCY ABLATION IMPROVES PULMONARY FUNCTION

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Background: Inferior Tibunate reduction by radiofrequency ablation improves pulmonary function.

Methods: The study was conducted on 19 patients with symptoms of nasal obstruction associated with inferior tribunate hypertrophy bilaterally for 6 months, and who failed to respond to a 3-month therapy of steroids and systemic decongestants. Additional exclusion criteria included systemic corticosteroid, teophyllin, anticholinergic, antileukotriene, nedokromil and anticoagulant use. The patients with pathologies found by anterior rhinoscopy and nasal endoscopy inspections (septal deviation, nasal polyposis, obstruction in nasal valve, alar collapse, middle tribunate hypertrophy, and the patients had nasal surgery or septal perforation) are also exempted. Subjective symptoms including severity of nasal obstruction were measured by a standard, 10 cm visual analog scale (VAS). A score of 0 for no obstruction and a score of 10 indicated severe nasal obstruction. Data obtained for each nasal cavity by acoustic rhinometry (AR) before and 6 weeks after IT RF. Post-op evaluations were made in week 6. The RF equipment used was CelonLabENT (Celon AG). All patients were checked at postop week 1 and 6. Pulmonary function tests (PFT), including FVC, EV1, PEF and FEV1/FVC values were evaluated according to American Thoracic Society criteria. For statistical evaluation of data; standard deviation, mean (average), min, max and median values were used. Paired-samples "t", Kolmogorov Smirnow and Wilcoxon tests were used for repeated measurements. Analysis were computed by SSPS 21.0 S/W.

Results: 38 L&R IT analyzed after RF applied, VAS values retrieved by t-test. Post-op week 6 VAS values compared with Pre-op, significant improvement ($p < 0.05$) obtained. Mean cross-section area of 1&2 (MCA1, MCA2) and R, L volumes and totVOL were evaluated. Significant ($p < 0.05$) increase observed in post-op values of L/R, 1/2 and total volumes. Pre-op and Post-op comparison of PFT results of FVC and FEV1 values showed significant increase ($p < 0.05$), unlikely FEV1/FVC and PERF increases were not significant ($p > 0.05$).

Conclusion: Evaluation of RF tribunate ablation with AR measurements showed a significant increase in nasal flow and significant decrease in decongestion effects. Small scale changes in the tribunate provided improvement in the symptoms through increasing of airflow in the nasal valve and resulted in positive PFT changes. Correction of the obstruction of the IT caused by hypertrophy by RF ablation, individually eased breathing resulting in improving pulmonary functions.

P-P-002

MAXIMUM VOLUNTARY VENTILATION IN AUTO RICKSHAW DRIVERS

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Background: Drivers of non air conditioned vehicles are affected more than air conditioned vehicle drivers. Several studies have shown a deterioration of Ventilatory lung function in people who are constantly exposed to air pollution. Professional drivers e.g. auto rickshaw drivers, taxi drivers etc, who spend a lot of time in the traffic are at higher risk to respiratory and cardiovascular diseases. Maximum voluntary ventilation (MVV) provides an estimate of the ventilatory reserves available.

Objective: To determine Maximum voluntary ventilation (MVV) using computerized automated flow Spirometry in Auto Rickshaw Drivers.

Methods: The subjects selected were 100 auto rickshaw drivers who had been driving auto rickshaws of open cabin type for more than 5 years and for more than 8 hours daily in Pune city; control group were non smokers not suffering from any cardio respiratory ailments and between the age group of 25–45 years. MVV was recorded on a Computerized portable "Schiller SP-1" lung function unit, the automated flow Spirometer. The volunteers were instructed to breathe as deeply and as rapidly as one can for minimum of 15 seconds. The volume of air exhaled in 15 seconds during repetitive maximal respiratory effort was recorded and expressed in L/ minute a the MVV. Statistical analysis was done by using SPSS software for statistical analysis.

Results: MVV was found not significant association between Study group and Control group.

Conclusion: The lungs have large functional reserve and the person will become symptomatic only when the lung functions are diminished markedly. A large sample and longitudinal study in this field will definitely be of a greater value in predicting the relationship between traffic pollution and ventilator lung function.

P-P-004

FACTORS INFLUENCING LUNG FUNCTION OF ELDERLY IN SURABAYA

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Background: Lung function testing with spirometry can be used to detect pulmonary diseases in early stage before any clinical symptom found. Elderly often have comorbidities, history of smoking and other factors influencing spirometry result. The aim of this study was to observe the influence of age, sex, smoking, nutritional status, comorbidities and exercise to lung function of elderly in Surabaya.

Method: A cross-sectional research design was used. Seventy two subjects aged 60 years and older, who did not have respiratory disease, enrolled in this study. The data taken from respondents by survey method using questionnaire and spirometry to measure lung capacity, were analyzed with linear regression analysis.

Result: Mean spirometry results of elderly in Surabaya were normal. It was found that age has negative correlation with FVC ($r = -0,268$), hypertension has negative correlation with MBC ($r = -0,266$), and stroke has negative correlation with FEV1 ($r = -0,252$). Sex, nutritional status, smoking, diabetes mellitus and heart failure were not associated with lung function of elderly in Surabaya.

Conclusion: Age, hypertension and stroke were factors negatively correlated to lung function of elderly in Surabaya.

P-P-003

ASSOCIATION BETWEEN SMOKING BEHAVIOUR WITH PULMONARY FUNCTION IN INDONESIA SMOKERS PILGRIMS

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Background: There are many of Indonesian pilgrims who have smoking habits. Smoking can cause pulmonary function disorder. Pulmonary function could be normal, obstructive, restrictive, or mixed. Previous studies had showed a close association between smoking behaviour and respiratory tract diseases. There is no research about pulmonary function on smoking Indonesian pilgrims.

Aims: To obtain characteristics of pulmonary function and the association between smoking behaviour with pulmonary function on smoking Indonesian pilgrims at Jakarta-Pondok Gede embarkation in 2012.

Methodology: This was a cross-sectional study on smoking Indonesian pilgrims during Hajj health checkup at the health centre and embarkation District of Jakarta-Pondok Gede. Assessment of smoking behaviour based on Brinkman index and pulmonary function assessment based on spirometry screening using spirometry. Bivariate analysis using Kolmogorov-Smirnov.

Result: This study got 209 subjects of smoker pilgrims. Subjects are generally male (99.5%), < 60 years (78.0%), overweight (63.2%), no comorbidity (68.9%), high education level (75.1%), medium Brinkman index (53.1%). Pulmonary functions are generally categorized as restrictive (51.2%). This study showed no significant association between smoking behaviour with pulmonary function in the medium-heavy Brinkman index group than the light Brinkman Index group ($p = 0.925$).

Conclusion: Subjects are generally male, < 60 years, overweight, no comorbidity, high education level, medium Brinkman index. Pulmonary functions are generally categorized as restrictive. This study showed no significant association between smoking behaviour with pulmonary function in the medium-heavy Brinkman index group than the light Brinkman Index group.

P-P-005

PULMONARY CONGENITAL CYSTIC ADENOMATOID MALFORMATION STOCKER CLASS TYPE 1 IN A 26 YEAR OLD FEMALE: A CASE REPORT

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Congenital Cystic Adenomatoid Malformation (CCAM) of the lung is an uncommon fetal developmental anomaly of the terminal respiratory structures. Almost all cases are diagnosed during the first two years of life in 80–87% of cases. Its presentation in adulthood is extremely rare, with the oldest presentation in a 34 year old caucasian female presenting with recurrent pneumonia and haemoptysis. Due to its rarity, it is seldom suspected in an adult patient. This case is the first reported case of CCAM in the Philippines. We report a case of CCAM Stocker Class Type 1 in a 26 year old female presenting as recurrent flight-related dyspnoea which spontaneously resolved immediately after landing. In one of her routine check-up, chest X-ray showed a large cystic mass with air-fluid level in the right upper lobe. Patient remained asymptomatic but advised further work-up. Chest CT scan revealed a 8.7 x 7.9 x 13.6 cm pneumatocele in the apical and posterior segments of the right upper lobe with areas of septation and air-fluid level suggestive of an infected cyst/pneumatocele. Patient underwent lobectomy by open thoracotomy. Intraoperatively, a huge bullae occupying 95% of the right upper lobe approximately 15 cm in its widest diameter was seen. There were loculations inside the cavity filled with brownish fluid. Pathology of the cyst revealed multiple cystic masses lined by ciliated pseudostratified columnar epithelium consistent with CCAM Type 1. Repeat chest xray on the first post-operative day showed disappearance of the large cystic mass with air-fluid level. Patient had an unremarkable post-operative course and was discharged improved. Patient followed-up one month after surgery and had been asymptomatic with a repeat chest X-ray showed complete disappearance of the previously noted huge cystic mass occupying the right upper lobe.

P-P-006

P-P-008

A CASE REPORT ON MDMA – INDUCED PNEUMOTHORAX, PNEUMOMEDIASTINUM, PNEUMORACHIS AND SUBCUTANEOUS EMPHYSEMA

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Background: MDMA, is a popular illicit recreational or party drug amongst young adults, illegally distributed worldwide since the 1980s and is popularly known as “Ecstasy”, “XTC” or “E”. Major clinical effects are reported including fatalities.

Objective: To present a case of MDMA induced pneumothorax, pneumomediastinum, pneumorachis and subcutaneous emphysema who was managed conservatively with observation and oxygen supplementation.

Case: A case is reported of a 20 year old male who presented with chest tightness and limited range of motion in the head and neck area. Neck and chest CT scan showed subcutaneous emphysema in the head and neck region, thorax and upper arms, including pneumomediastinum, pneumopericardium and pneumorachis. The patient was initially managed as a possible case of mandibular dislocation and retromandibular abscess. He was given oxygen support and was eventually discharged stable after 5 days.

Conclusion: In conclusion, a thorough history and physical examination is indeed very essential to the management of any patient. Expanding our differentials to any case has salvaged our patient from continued antibiotic therapy which eventually he did not require. And although believed to be a “safe” drug by most users, significant mortality and morbidity may occur with MDMA use. Awareness of the complications of MDMA needs to be emphasized in order to prevent its use and to decrease its potential morbidity and mortality.

A RARE CONGENITAL ANOMALY – MOURNIER KUHN SYNDROME

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Introduction: Mounier Kuhn syndrome is rare condition characterized by marked dilation of the trachea and main bronchi along with bilateral bronchiectasis and recurrent lower respiratory tract infection. Less than 100 cases have been reported till date. We report a case of Mounier Kuhn syndrome diagnosed in a 44 year old male.

Case Report: A 44 year old male patient presented with complaints of recurrent cough with purulent expectoration since childhood, Dyspnoea grade 2 and wheezing. Past history of recurrent childhood respiratory infections. On examination, clubbing and coarse crepitations over bilateral lung bases. Chest x-ray PA view showed bilateral multiple cystic shadows in both mid-lower zones. HRCT Thorax showed dilatation of trachea and main bronchi with extensive cystic bronchiectatic changes mid-lower lobes. Spirometry showed moderate obstruction. Bronchoscopy showed dilated trachea and main bronchial tree with thick, purulent secretions. Anatomy of distal airways was altered so that differentiation of various bronchial segments could not be done. With these findings, diagnosis of Mounier Kuhn Syndrome was made. Patient was treated with conservative measures. After 2 months, on follow up patient was symptomatically better.

Discussion: Congenital form of tracheobronchomalacia is known as Mounier Kuhn Syndrome and is due to atrophy of muscular and elastic tissues of trachea and main bronchi. It has 3 subtypes. Our case was unique which was type 3 disease with trachea diverticuli. It is more common men and diagnosed in 3rd or 4th decade of life. Diagnosis is made using CT. The diagnostic criteria are diameters of trachea >30 mm; of the right main bronchus >20 mm; and of the left main bronchus >18 mm and bronchoscopy findings of tracheomalacia. In our case the diameters of trachea, right main bronchi, and left main bronchi were 30 mm, 22 mm, 21 mm respectively. Bronchoscopy showed not only dilatation of trachea and main bronchi but also dilatation of distal segmental bronchi with significant anatomical distortion. Therapy is usually supportive and conservative. Symptomatic patients with airway collapse may require endobronchial stenting.

P-P-007

A RARE CAUSE OF CHYLURIA AND RECURRENT CHYLOTHORAX – LYMPHATIC DYSPLASIA SYNDROME

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This is a case report of one of the rarest cause of recurrent left sided pleural effusion which was basically recurrent chylothorax. The patient reported is case of lymphatic duct dysplasia which has led to said problem. He also had history of chyluria in 2005 for which he was operated. He had post operative complication of shrunken kidney. Patient after being asymptomatic for such long period has presented to us with recurrent chylothorax. We investigated with computed tomography, PET-CT, magnetic resonance imaging and finally with lymphoscintigraphy and came to the conclusion that it was the lymphatic duct abnormality which has initially presented with chyluria and after being operated for that has presented with chylothorax. We ultimately did pleurodesis and thoracic duct ligation through VATS (videoscopic assisted thoracic surgery).

POSTER PRESENTATION – TUBERCULOSIS

P-Q-003

P-Q-001

TUBERCULOUS PLEURISY: ULTRASOUND GUIDED BEDSIDE ABRAM'S BIOPSY VERSUS PLEUROSCOPY

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Background: Tuberculous (TB) pleurisy is a common cause of pleural effusion in high TB incidence areas. Biopsy of the parietal pleura for histology (granulomas) is helpful in the diagnosis of TB pleurisy. Biopsy can be obtained with an Abram's needle at the bedside or during pleuroscopy. However, the preferred mode is not well defined.

Methods: A retrospective study done in Changi general Hospital revealed that 94 patients received treatment for TB pleurisy from July 2010 to June 2013. Sixty-one patients (64.9%) underwent pleural biopsy. Of these patients, 49 (80.3%) had pleural biopsy performed by Respiratory Physicians. From these 49 patients, the diagnostic yields of ultrasound guided bedside Abram's needle and pleuroscopy. Complications and the cost of hospitalization for these two procedures were also looked at.

Results: A total of 52 biopsies were done by Respiratory physicians. These consisted of 36 bedside Abram's needle biopsies performed under ultrasound guidance and 16 pleuroscopic biopsies. Three patients had to undergo both procedures as the initial Abram's biopsies were negative. Among 36 ultrasound guided bedside Abram's biopsies, granulomas were seen in thirty-one (86.1%) biopsy specimens. Among 16 pleuroscopic biopsies, granulomas were seen in fifteen (93.8%) biopsy specimens. There was no statistical significance between these two methods of biopsy ($p = 0.426$). Complication rates were similar in both procedures: three in bedside Abram's biopsy (8.3%) and two in pleuroscopy (12.5%) ($p = 0.638$). Based on the cost of hospitalization and average daily cost, bedside Abram's needle biopsy was shown to be more cost effective. The cost for hospitalization for ultrasound guided Abram's biopsy was S\$5266.39 \pm SD 2355.36, with an average daily cost of S\$624.06 \pm SD 169.89. The cost of hospitalization for pleuroscopy was S\$7152.96 \pm SD 2390.70, with an average daily cost of S\$819.29 \pm SD 187.00. The differences in the cost of hospitalization and average daily cost were statistically significant, with p values of ($p = 0.19$) and ($p = 0.01$) respectively.

Conclusions: In the diagnosis of TB pleurisy, ultrasound guided bedside Abram's needle biopsy is an effective, safe and cost effective method of biopsy. As a result of our findings, this method could be considered as the main method of pleural biopsy in areas of high TB incidence.

P-Q-002

DIAGNOSTIC TEST OF SERUM TNF-A IN SUSPECT TUBERCULOSIS PATIENTS IN MOHAMMAD HOESIN GENERAL HOSPITAL, PALEMBANG INDONESIA

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Background: Early and accurate diagnosis of pulmonary tuberculosis is essential in effort against it. The most common method used to diagnose tuberculosis are with microscopic acid fast bacilli sputum and culture. These methods need considerable time with low sensitivity and specificity value. Tumour necrosis factor- α serum level has been accepted in many countries as a new method to diagnose tuberculosis. But study shows various validity values.

Method: During a six-month period, TNF- α serum level was measured with ELISA. Using a standard cut-off point of 4.29 pg/ml, analysis with 2 x 2 table was conducted to determine diagnostic value of TNF- α . Clinical symptoms, acid fast bacilli sputum and radiology were used as reference standard to diagnose pulmonary tuberculosis. This study was performed in referral hospital type A of Dr Moehammad Hoesin, Palembang.

Result: Study subjects involving 77 patients with suspected pulmonary tuberculosis. Forty patients diagnosed as pulmonary tuberculosis (prev pulmonary TB among suspected, 51.59%) with TNF- α serum level (med 5.20 pg/ml (1.35–38.19 pg/ml), $p < 0.05$) significantly higher than non-tuberculosis patients (med 3.91 pg/ml (1.87–25.90 pg/ml), $p < 0.05$).

Conclusion: Tumour necrosis factor- α serum level is not valid (sensitivity, 60%; specificity, 64%) and has a weak diagnostic value (AUC 60.2%) as a seromarker to diagnose pulmonary TB. The best cut-off point in this study was 4.29 pg/ml, with sensitivity of 60% and specificity of 64%. Although this value was lower than expected, TNF- α shows diagnostic value equal to acid fast bacilli sputum so it can be considered as alternative method when acid fast bacilli sputum is not possible.

EFFECTS ON THE KNOWLEDGE, ATTITUDES AND PRACTICES (KAP) OF THIRD YEAR FILIPINO HIGH SCHOOL STUDENTS IN METRO MANILA REGARDING TUBERCULOSIS AFTER USING AN EDUCATIONAL INTERVENTION

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Background: A KAP survey is a representative survey of a specific population to collect information on what is known, believed and done in relation to a particular topic, in this case, tuberculosis (TB). Several studies in Asia showed limited or deficient knowledge on TB. A local study showed significant improvement in this aspect after an educational intervention.

Objective: To determine if an educational intervention would affect the KAP of third year Filipino high school students from selected schools in Metro Manila regarding TB.

Methodology: A quasi-experimental study was conducted on third year high school students from 2 schools. The sample size was computed based on the population at hand. A TB module prepared by the Committee on Childhood TB of the Philippine Academy of Pediatric Pulmonologists in was used. A pre-tested questionnaire was given on the day of intervention with follow-up studies conducted at 1 month and 3 months interval. Tabulation of the responses was done. Categorical data was analyzed using chi-square test and the Friedman's test to show changes in answers.

Results: Two hundred seventy five respondents were obtained. One hundred and fifty two (152) came from PNHS, without intervention, of which 121 were included in the evaluation of changes in scores over a period of time and 123 came from MBAHS, with educational intervention, of which 111 were included in the evaluation of changes in responses. Knowledge questions were subdivided as to transmissibility, nature and cause, effects on physical health and prevention. Results showed significant improvement in the mean scores on transmissibility (2.11, 2.67, 2.61, 2.61), nature and cause (2.22, 2.67, 2.55, 2.55), and prevention (2.34, 2.52, 2.57, 2.57); the group with intervention, however, showed a decline in the aspect of effects on physical health (2.54, 2.54, 2.46, 2.46). Significant improvement on the aspect of transmissibility (1.78, 2.11, 2.11) and nature and cause (1.77, 2.12, 2.12) was noted for the group without intervention. As to the attitudes, despite having significant changes ($p = .040$, with intervention; $p < .001$, without intervention), a decline in the mean rank was noted for the group with intervention. The same goes true for the practices of the group, however not significant. Conversely, significant improvement regarding practices was noted for the group without intervention.

Conclusion: The PAPP TB educational intervention improved the level of awareness of students, greatly influenced their attitudes and practices along with their beliefs and socio-economic perspectives. However, a single exposure to the module is not adequate to change all these.

P-Q-004

P-Q-007

PROFILE OF SEVERE TUBERCULOSIS HOSPITALIZED PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL

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Background: Bacillary load, extent of disease and anatomical site are factors that determine the severity of TB disease and consequently, its appropriate treatment. A case of pulmonary TB is classified as severe if parenchymal involvement is extensive. The following forms of extra-pulmonary TB are classified as severe: meningeal, pericardial, peritoneal, bilateral or extensive pleural effusion, spinal, intestinal and genitourinary. Severe TB patients have higher risk of death. The aim of this study is to determine the profile of severe tuberculosis hospitalized patients in Cipto Mangunkusumo Hospital in Jakarta, Indonesia.

Methods: A descriptive cross-sectional study was conducted among severe tuberculosis patients hospitalized in Cipto Mangunkusumo hospital from January 2008–September 2013. Data were collected at initiation of inpatients period and in hospital mortality status.

Results: A total of 78 patients were enrolled in the study. In-hospital mortality rate was 34.6%. There were 52 (66.7%) male and median age of the sample was 30 (range, 18–80) years old. Miliary TB were found in 40 (51.3%), whereas meningeal TB was found in 38 (48.7%) subjects. Patients were mostly malnourished, with BMI <18.5 (65.8%). Fifty percent of the subjects were HIV-positive. Chronic liver disease was the most common comorbidity found (20.5%).

Conclusion: Severe TB patients hospitalized were male, age range 18–80 years old. Most of the patients had miliary TB. Most of the patients were in malnutrition state with low BMI. Chronic liver disease were the most common comorbidity found. In-hospital mortality rate was high.

PREVALENCE AND DRUG RESISTANCE PATTERNS OF ANTI-TUBERCULOSIS DRUGS (ATDS) AMONG NEWLY DIAGNOSED AND PREVIOUSLY TREATED SPUTUM-POSITIVE PATIENTS OF BANGLADESH

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Background: Anti-TB drug resistance is emerging as a new health problem. Presently, Bangladesh ranks 10th among 27 high MDR-TB burden countries and 6th among 22 high TB burden countries. National TB drug resistance survey reflects the magnitude of the problem and guides the programme to address it. The extent of TB drug resistance in Bangladesh is not known as there is no national survey. WHO estimated MDR-TB rates of 3.5% and 20% among new and previously treated cases, respectively. Different limited surveys show variable data of MDR-TB at different locations. Due to high prevalence of TB, MDR-TB burden of the country will be higher.

Objectives: To determine the prevalence and drug resistance patterns of first-line and second-line ATDs among newly diagnosed and previously treated sputum-positive cases.

Material and Method: This cross-sectional study was carried out among 1,340 patients. They were selected by weighted cluster sampling methods having clinical and/or radiological features of tuberculosis attending 40 Upozila Health Complex (UHC) as clusters and 26 Chest Disease Clinic (CDC) covering 34 districts were enrolled in this study during 2008 to 2009. Two sputum samples were collected and processed for culture by digestion, decontamination and concentration following modified Petroff's methods and were inoculated on two slopes of Lowenstein-Jensen (L-J) media for six weeks. The identity of the isolates was made by growth rate, colony morphology, P-nitrobenzoic acid (PNB) susceptibility, catalase and nitrate reduction tests. Ultimately, drug susceptibility testing (DST) was performed. All samples were sent to NTRL (National Reference Laboratory for TB).

Results: Among 1,340 patients, 1,049 (87.7%) were new cases and 291 (56.8%) were previously treated cases. 12.3% of new cases and 43.2% of previously treated cases were resistant to any drugs, respectively. 8.4% of new cases and 10% of previously treated cases were mono drug resistant. 1.4% of new cases and 28.5% of previously treated cases have multi-drug resistance, respectively. Drug susceptibility testing for isoniazid (INH), rifampicin (RIF), ethambutol (EMB), streptomycin (SM), ofloxacin and kanamycin was done.

Conclusion: Pattern of anti-TB drug resistance was identified in this study. More surveillance and immediate therapeutic interventions should be performed in order to combat the threat of MDR-TB to the general population. Early diagnosis and immediate therapeutic interventions should be performed to prevent the dissemination of MDR-TB to the general population.

P-Q-008

RAPID IDENTIFICATION OF MYCOBACTERIA BY MATRIX-ASSISTED LASER DESORPTION IONIZATION TIME OF FLIGHT MASS SPECTROMETRY

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Background: A matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) system may represent alternative apparatus for clinical laboratories in future because of its possibility of early diagnosis and low running cost. Mycobacterial identification using MALDI-TOF MS system is possible; however the risk of infection and rapidly remain a problem.

Materials and Methods: Bacterial strains. Eight different species of mycobacteria were identified by molecular techniques such as a polymerase chain reaction method (TaqMan PCR method), DNA probes (DNA-DNA hybridization) and/or 16S rRNA/hsp 65 sequencing. 6 reference strains and 221 strains (183 isolates of *Mycobacterium tuberculosis* complex (MTC) and 38 isolates of non tuberculous mycobacteria (NTM)) previously isolated from patients submitted to Aizu Medical Center were used. All strains were further cultured in a mycobacterium growth indicator tube (MGIT). When the MGIT was detected as positive, the liquid was harvested, and was centrifuged. The supernatant was discarded, then the pellet was resuspended and heat-inactivated for 30 minutes at 110°C. We next added 100% ethanol to the suspension. The tubes were centrifuged again and all residual liquid was completely removed with a pellet. The pellet was suspended in acetonitrile, and glass beads were added to the pellet. The tubes were vortexed for 10 minutes, and 70% formic acid was added. The supernatant was used for analysis by MALDI-TOF MS.

Results: Analysis time for a specimen was about 60 minutes by the MALDI-TOF system. Examination of 183 strains of clinically isolated MTC revealed an identification coincidence rate of 99.5% in the genus level in a matching pattern; when the species level was induced, 95.6%. As for the 38 NTM strains, the identification rate in the genus level was 94.6%. *Mycobacterium bovis* (Tokyo strain) in the reference strain was judged by the matching pattern to be MTC.

Discussion: The MALDI-TOF MS system could not distinguish between *Mycobacterium tuberculosis* and *Mycobacterium bovis*. Some species are only distinguishable at the complex level because of high similarities between their spectra. Although this method may not be able to distinguish between affinity species with high DNA homology, it is rapid, low-cost and safe for the identification and characterization of mycobacterium species.

P-Q-009

EVALUATION OF GENEXPERT MTB/RIF ASSAY AS A TB DIAGNOSTIC TOOL IN TAIWAN

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Introduction: The existing tuberculosis diagnostic tests are not ideal. The acid-fast bacillus staining has low sensitivity and specificity whereas the mycobacterium cultures fail to provide instant results for clinical use. The GeneXpert MTB/RIF test, by contrast, is able to detect Mycobacterium tuberculosis complex (MTBC) and rifampicin resistance simultaneously within 2 hours. It provides a rapid and accurate diagnosis of tuberculosis. However, very few data is available on the implementation of this test in Taiwan. Our study aims to compare the accuracy and time required for the standard tuberculosis diagnosis and the new GeneXpert MTB/RIF test.

Methods: From 1st July 2013 to 31st October 2013, all patients with abnormal chest X-Ray and were suspected of tuberculosis, were required to have their sputum examined in the Changhua hospital out-patient department, and were included in the study. A total of 102 specimens were collected and processed via the standard smear and culture as well as for the GeneXpert MTB/RIF test.

Results: The standard routine test yielded a high proportion of nontuberculous mycobacterium (NTM) (50%, 13/26). The time required for the specimen to be transferred, smeared, and cultured for diagnosis averaged 43.1 days. The GeneXpert MTB/RIF, by contrast, provided results within 2 hours and accurately distinguished NTM from MTBC. As a PCR device, however, the GeneXpert MTB/RIF detected both the dead and live bacteria, leading to a false-positive result. Overall, the sensitivity for confirmed MTBC was 76.9% (10/13), specificity was 96.6% (86/89); the positive predictive value was 76.9% and the negative predictive value was 96.6%.

Conclusion: GeneXpert MTB/RIF test provides a rapid and accurate result for the diagnosis of tuberculosis, however, from our results the sensitive rate is only 76.9% and it could be due to the small study size.

P-Q-010

PREVALENCE OF VITAMIN D INSUFFICIENCY IN ACTIVE PULMONARY TUBERCULOSIS PATIENTS IN THAILAND

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Background: Vitamin D has been found to play an important role in host immune defense against tuberculosis (TB). However, the association between vitamin D insufficiency and active TB is different among regions of the world. Our study aims to determine prevalence of vitamin D insufficiency among active pulmonary TB patients, compared to control subjects in Thailand.

Methods: A prospective study was conducted on 120 TB patients and 83 control subjects. Serum 25-hydroxyvitamin D (25-OHD) levels were measured and compared in both groups. Vitamin D insufficiency and vitamin D deficiency were defined when serum levels of 25-OHD were lower than 30 and 20 ng/ml, respectively.

Results: Baseline demographic data were comparable in both groups. The mean 25-OHD level was not different in TB patients (27.1 + 9.3 ng/ml) compared with control subjects (28.2 + 8.6 ng/ml) (p = 0.39). There were no significant differences in the prevalence of vitamin D insufficiency and vitamin D deficiency between TB patients (43.3% and 21.7%) and controls (45.8% and 15.7%) (p = 0.56). In TB patients, the levels of 25-OHD were not associated with extent of radiographic diseases (minimal, 27.3 + 9.3 ng/ml; moderately advanced, 27.7 + 9.9 ng/ml; and far advanced, 25.8 + 9.0 ng/ml, p = 0.68).

Conclusion: In Thailand, vitamin D levels are not associated with the presence of pulmonary TB. Furthermore, vitamin D levels do not impact on the extent of pulmonary TB lesions.

P-Q-011

DIAGNOSTIC VALUE OF PLEURAL FLUID ADENOSINE DEAMINASE IN TUBERCULOUS PLEURITIS AT THAMMASAT UNIVERSITY HOSPITAL

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Introduction: Pleural fluid adenosine deaminase (ADAPF) is a diagnostic test for the early diagnosing tuberculous pleuritis (TBP). The cutoff value is various levels in many studies. The study aims to determine the diagnostic value of ADAPF for diagnosis of TBP.

Methods: A prospective study was performed between August 2012 and April 2014. A total of 158 patients with pleural effusions; 26 TBPs, 55 malignant pleural effusions (MPEs), 38 parapneumonic effusions, 15 transudates, 5 empyemas, 15 other exudative causes, and 4 unknown causes were investigated.

Results: The mean \pm SD of ADAPF were 62.0 ± 26.2 U/L with TBPs, 16.5 ± 11.9 U/L with MPEs, 16.3 ± 9.9 U/L with parapneumonic effusions, 6.1 ± 5.7 U/L with transudates, 13.8 ± 7.7 U/L with empyemas, 15.5 ± 8.1 U/L with other exudative causes, and 17.8 ± 4.6 U/L with unknown causes. The best cutoff value for diagnosing TBP were 32.0 U/L, with a sensitivity of 96.2% (95% CI: 78.4–99.8%), and specificity of 91.5% (95% CI: 84.9–95.5%). The positive predictive value was 69.4% (95%CI: 51.7–83.1%) and the negative predictive value (NPV) was 99.2% (95%CI: 94.7–99.9%). The positive likelihood ratio was 11.3 and the negative likelihood ratio was 0.04. ADAPF value < 30.5 U/L suggests that a tuberculous pleuritis is highly unlikely (100% sensitive with 100% NPV and negative likelihood ratio was 0 for a pleural fluid ADA level ≥ 30.5 U/L). In addition, the area under the ROC curve was 0.982 (S.E. = 0.009, 95% CI: 0.965–0.998).

Conclusion: Pleural fluid ADA assay is a helpful diagnostic tool with high sensitive and specific test for rapid diagnosis of TB pleuritis.

P-Q-012

DIFFERENCES IN CLINICAL MANIFESTATIONS AND PLEURAL FLUID CHARACTERISTICS OF TUBERCULOUS AND MALIGNANT PLEURAL EFFUSIONS

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Background: Distinguishing tuberculous pleural effusions (TBPEs) from malignant pleural effusions (MPEs) is challenging because both share similar clinical and radiographic findings and both may produce lymphocytic-predominant, exudative effusions.

Objective: To determine the differences in clinical manifestations, pleural fluid characteristics and radiographic findings between TBPEs and MPEs.

Material and Methods: A retrospective study was performed at Thammasat University Hospital between January 2007 and December 2012. Demographic data included sex, age, smoking status, co-morbid diseases, clinical features, pleural fluid characteristics, and radiographic findings were collected and analyzed.

Results: 47 TBPEs and 73 MPEs were included; 69 (57.5%) were males. Mean [\pm SD (range)] age was 60.2 [\pm 16.9 (19–94)] years. Clinical features were presented with history of contact TB (2.5%), previous anti-TB treatment (1.7%), current smoking (37.5%), presence of underlying diseases (52.5%), HIV infection (4.2%), and mean \pm SD duration of symptoms 31.6 \pm 51.6 days. Univariate analysis found differences in TBPE groups when compared with MPE groups: mean age (51.1 vs 66.0 years, $p < 0.001$), mean duration of symptoms (17.0 vs 41.0 days, $p = 0.004$), HIV infection (8.5 vs 1.4%, $p < 0.001$), dyspnoea (46.8 vs 91.8%, $p < 0.001$), fever (78.7 vs 12.3%, $p < 0.001$), chest pain (57.4 vs 24.7%, $p < 0.001$), small effusion (40.4 vs 15.1%, $p = 0.002$), massive effusion (4.3 vs 28.8%, $p = 0.001$), mediastinal lymphadenopathy (6.4 vs 38.4%, $p < 0.001$), lung mass (2.1 vs 27.4%, $p < 0.001$), pleural nodules (0 vs 28.8%, $p < 0.001$), serosanguinous effusion (5.0 vs 31.7%, $p < 0.001$), yellowish effusion (34.0 vs 8.2%, $p < 0.001$), pleural fluid RBC count (8,731 vs 74,100 cells/uL, $p = 0.004$), WBC count (2,467 vs 1,359 cells/uL, $p < 0.001$), % neutrophil (16.8 vs 26.7%, $p = 0.002$), % lymphocyte (82.8 vs 73.2%, $p = 0.002$), mean pleural fluid protein concentration (5.1 vs 4.5%, $p = 0.001$), and adenosine deaminase (ADA) level (51.0 ± 21.7 vs 12.2 ± 8.4 U/L, $p < 0.001$). Multivariate logistic regression analysis found fever (odds ratio [OR], 8.2; 95% confidence interval [CI], 1.9–35.9, $p = 0.005$), non-serosanguinous effusions (OR, 6.1; 95% CI 1.1–33.6, $p = 0.038$), and ADA level > 30 U/L (OR, 86.7; 95%CI 4.3–1735, $p = 0.004$) were independent predictors for TBPE.

Conclusion: Compared with MPE, the strong predictors for TBPE were fever, non-serosanguinous pleural effusions and high ADA level. These parameters should be required to verify the predictive models for the suggesting diagnosis of TBPEs.

P-Q-013

COMMON CAUSES OF LOSS TO FOLLOW UP OF MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS IN MOEWARDI HOSPITAL SURAKARTA 2011–2013

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Introduction: Treatment of Multidrug Resistance Tuberculosis (MDR TB) is challenging. Loss to follow up is a matter of particular concern in the evaluation of treatment outcomes of MDR TB in the world, including in Indonesia, but so far there has never been published research on loss to follow up of MDR TB in Indonesia. The purpose of this study was to determine the causes of loss to follow up MDR TB in Moewardi Hospital 1st January 2011–31st December 2013.
Methods: A retrospective descriptive design study conducted in loss to follow up MDR TB patients based on inclusion and exclusion criterias at the Moewardi Hospital Surakarta from 1st January 2011 –31st December 2013. Data were collected from medical records and interviews using questionnaires.
Results: From total of 25 loss to follow up MDR TB patients, we found 19 patients who met the inclusion and exclusion criterias for this study. Subjects were mostly male (63.2%), aged 51–60 years (42.1%), primary school and lower (73.7%), household income of less than one million rupiah per month (84.2%), residing settled (100%), and all patients are non-users of alcohol and drugs, but 63.2% were smokers. During the treatment most of them (63.2%) were delivered by the husband/wife when visiting MDR TB clinic. MDR TB criteria in patients with loss to follow up was mostly failed category II (42.1%) and relapse cases (42.1%). Duration of treatment of MDR TB before loss to follow up was (52.6%) 1–3 months. Most patients had a history of previous treatment of anti tuberculosis drug category II (63.2%) and no history of loss to follow up (89.5%), only 2 (10.5%) patients who had a history of loss to follow up. All patients experienced side effects from the treatment of MDR TB. The most disturbing complaint is weakness (57.7%), 5 (26.3%) patients experienced severe side effects, and most patients (63.1%) experienced more than two side effects during treatment. Distance to go to MDR TB clinic for treatment in most of patients (78.9%) was less than 10 miles, but there were 3 (15.8%) patients who travelled more than 15 kilometers. The travel time on the 12 (63.1%) patients to MDR clinic was less than 30 minutes. However, most of MDR TB patients (52.6%) cost at least 15 thousand rupiah a day to go to MDR TB clinic. The cause of loss to follow up MDR TB are adverse effects (73.7%), transportation cost (21.1%), no escort (15.8%), bored (15.8%), and unable to work (5.3%). Each patient may have more than one cause.
Conclusion: Adverse effects is the most common cause of loss to follow up MDR TB patients.

P-Q-015

ROLE OF MALNUTRITION SCREENING TOOL FOR PREDICTING HOSPITAL MORTALITY IN PULMONARY TUBERCULOSIS AND HIV CO-INFECTION PATIENTS

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Background and Aims: Mycobacterium tuberculosis and human immunodeficiency virus (HIV) co-infection has become a public health issue worldwide. Pulmonary tuberculosis (TB) and HIV co-infection patients who are hospitalized have varying nutritional conditions. A simple nutrition screening method is needed to predict a poor prognosis, especially mortality. Malnutrition Screening Tool (MST) is a simple, rapid and valid nutrition screening method for identifying patients with malnutrition. This study was aimed to know the role of MST for predicting hospital mortality in pulmonary TB and HIV co-infection patients.
Methods: This was a retrospective cohort study of 115 HIV-positive and 140 HIV-negative pulmonary TB patients who were hospitalized in Cipto Mangunkusumo Hospital between January 2011 and September 2013. MST scores were obtained at admission, then subjects were observed to evaluate their hospital mortality.
Results and Discussion: The hospital mortality rate in HIV-positive pulmonary TB patients was 31.3%, and in HIV-negative pulmonary TB patients was 20.7%. ROC analysis got MST score ≥ 3 as the best cut-off for predicting hospital mortality in both HIV-positive and HIV-negative pulmonary TB patients (AUC 0.594; 95% CI 0.486–0.702, and AUC 0.685; 95% CI 0.586–0.785, respectively). MST score ≥ 3 increased the risk of hospital mortality in both HIV-positive and HIV-negative pulmonary TB patients (RR 1.770; 95% CI 0.983–3.188; $p = 0.048$, and RR 3.815; 95% CI 1.545–9.422; $p = 0.001$, respectively).
Conclusion: MST score ≥ 3 associated with higher risk of hospital mortality in both HIV-positive and HIV-negative pulmonary TB patients. MST appears to be a reliable tool to identify hospitalized pulmonary TB and HIV co-infection patients who have risk of malnutrition and mortality.

P-Q-016

THE USEFULNESS OF SERUM PROCALCITONIN IN PATIENTS WITH TUBERCULOUS PLEURISY

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Background: Serum procalcitonin (PCT) has known to be a prognostic marker for pulmonary tuberculosis (PTB). However, few assessed the relationship between PCT level and clinical characteristics of tuberculous pleurisy (TP) patients.
Methods: We retrospectively analyzed 73 TP patients to investigate the relationship between serum PCT level and clinical characteristics, from January 2010 to December 2012.
Results: There were 46 males and 27 females with a median age of 46 years. Serum PCT was normal in 40 patients (54.8%). Radiographic active signs for tuberculosis were found in 38 patients (52.1%). Additionally, mycobacterium was identified in 4 patients with radiographic inactivity. Consequently, 42 patients (57.5%) had pleuro-pulmonary tuberculosis. The others had isolated TP. The protein ($P = 0.016$) and LDH ($P < 0.001$) in pleural fluid were significantly associated with serum PCT level. The frequency of positive culture in pleural fluid ($P = 0.004$), pleuro-pulmonary tuberculosis ($P = 0.005$) and cavity on CT ($P = 0.013$) were also more common in patients with serum PCT level above normal. In a multiple logistic regression analysis, patients with a PCT above normal had more likely to have pleuro-pulmonary tuberculosis (OR, 64.179; 95% CI, 1.945–2117.439, $P = 0.020$) and positive effusion cultures (OR, 27.703; 95% CI, 1.392–551.348, $P = 0.030$).
Conclusions: Serum PCT levels above normal suggest the possibility of pleuro-pulmonary tuberculosis and positive pleural fluid culture in TP patients. Thus, serum PCT may be able to aid physicians in selecting patients that require early isolation and multiple evaluations to obtain the specimen for confirmatory diagnosis and drug sensitivity testing.

P-Q-017

MORTALITY PREDICTION MODEL FOR HOSPITALIZED TUBERCULOSIS PATIENTS

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Aim: To develop a model that predicts the risk of death for hospitalized tuberculosis patients.

Methods: A retrospective cohort study was conducted among hospitalized tuberculosis patients (aged 18 years and older) in Cipto Mangunkusumo Hospital from January 2008 until September 2013. Data were collected at initiation of inpatients period and the main outcome was all-cause mortality during hospitalization. We analyzed 13 prognostic factors in bivariate analysis using Chi-square test. Multivariate logistic regression analysis was performed to identify independent predictors of mortality and each independent predictor was quantified to develop mortality prediction model. The calibration performance of the model was tested by Hosmer-lameshow test and its discrimination ability was determined by calculating area under the receiver operating characteristic curve (AUC).

Results: Subject consist of 470 patient, predominantly male (72.1%). Median age of the population was 34 (range 18 to 86) years old and median length of stay was 10 (range 1 to 97) days. In-hospital mortality rate was 25.1%. Four independent predictors for mortality were identified, including: hypoalbuminemia (OR 5,12; 95% CI 1,80–14,57), cavitory lesion (OR 3,91; 95% CI 1,53- 9,97), sepsis (OR 23,31; 95% CI 8,95–60,68), and respiratory failure (OR 177,39 ; 95% CI 27,09- 1161,55). Mortality prediction model was developed using the final model of multivariate analysis. It has good discrimination ability (AUC 0,962) and good precision ($p = 0.973$). Patient with score ≥ 3 classify as high mortality risk.

Conclusion: Respiratory failure, sepsis, hypoalbuminemia, and cavitory lesion were independent predictors of in-hospital mortality among hospitalized tuberculosis patients. A model has been developed to predict and classify mortality risk. It is accurate enough to be used to describe the risk of mortality in hospitalized tuberculosis patients.

P-Q-018

PREDICTORS OF MORTALITY AMONG HOSPITALIZED TUBERCULOSIS PATIENTS

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Background: Indonesia is the world's fourth highest tuberculosis burden in the world. Tuberculosis is the second leading cause of death for all age in the country, according to the Health Ministry. Mortality remains high among tuberculosis hospitalized patients compare to the non-TB patients. The prediction of patients outcome is important in decision-making process and in the effort reducing mortality rate. Studies exploring predictors of mortality in patients with pulmonary tuberculosis produced conflicting results and there are no comprehensive reports in Indonesia.

Objective: To determine predictors of mortality among hospitalized tuberculosis patients.

Methods: We performed a retrospective cohort study among hospitalized tuberculosis patients in Cipto Mangunkusumo Hospital between January 2008 – September 2013. Data were collected at initiation of inpatients period and the main outcome was all-cause mortality during hospitalization. We analyzed age, sex, history of previous anti-tuberculosis treatment, tuberculosis severity, sputum smear positivity, hypoalbuminemia, BMI, HIV status, concomitant pneumonia, sepsis, respiratory failure, pulmonary radiographic lesion, comorbidity (CCI score) in bivariate analysis using Chi-square test. Missing data were handled using multiple imputation methods. Multivariate logistic regression analysis was performed to identify independent predictors of mortality.

Results: A total of 470 patients were evaluated in this study. In-hospital mortality rate was 25.1%. There were 339 (72.1%) male and 131 (27.9%) female patients. Median age of the population was 34 (range 18 to 86) years old and median length of stay was 10 (range 1 to 97) days. The independent predictors of mortality in multivariate analysis were hypoalbuminemia (OR 5,12; 95% CI 1,80–14,57), cavitory lesion (OR 3,91; 95%CI 1,53–9,97), sepsis (OR 23,31; 95%CI 8,95–60,68), and respiratory failure (OR 177,39; 95%CI27,09–1161,55).

Conclusion: Respiratory failure, sepsis, hypoalbuminemia, and cavitory lesion were independent predictors of in-hospital mortality among hospitalized tuberculosis patients.

P-Q-019

PLASMA SUPAR LEVEL AND CLINICAL CHARACTERISTICS AS PREDICTING FACTORS FOR THE RESULT OF MYCOBACTERIAL CULTURE IN SUSPECTED MDR-TB PATIENTS

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Background: Mycobacterial culture are not always positive in suspected multidrug-resistant tuberculosis (MDR-TB) patients who AFB smear still positive or positive again after OAT treatment. Most of them have negative cultures, so their management need to be modified. Previously studies showed the use of certain clinical characteristics to predict the result of mycobacterial culture. Besides that, it was noted that level of suPAR, as a biomarker, relates with mycobacterial load in sputum of lung tuberculosis patients. This study aimed to evaluate the use of plasma suPAR level and some clinical characteristics as predicting factors for the result of mycobacterial culture in suspected MDR-TB patients.

Methods: By cross sectional study, this study included 30 subjects of suspected MDR-TB which fulfilled criteria of treatment failure after first category OAT treatment, AFB smear still positive after three months first category OAT treatment, and relaps cases. We examined plasma suPAR levels and sputum mycobacterial cultures. The data were analyzed by ANOVA and correlation test.

Results: We found mycobacterial cultures were positives in 15 (50%) subjects, negatives in 14 (46.67%) subjects, and MOTT in 1 (3.33%) subject. There were 5 subjects MDR-TB, 2 subjects monoresistant, and 8 subjects sensitive to all of first line OAT among positive culture subjects. We found five factors which can be used as predicting factors of positive mycobacterial culture, i.e. plasma suPAR level > 8 ng/mL (Odds Ratio = 8.7, $p = 0.064$), age < 50 years old (Odds Ratio = 14.00, $p = 0.023$), relaps case (Odds Ratio = 6.86, $p = 0.037$), AFB smears +2 or +3 (Odds Ratio = 35.7, $p = 0.003$), and erythrocyte sedimentation rate > 70 mm/hour (Odds Ratio = 6.86, $p = 0.037$). If the suspected MDR-TB patient has three factors or more of the above five predicting factors, it more likely has positive mycobacterial culture (PPV 100%, NPV 82.3%, sensitivity 80%, specificity 100%).

Conclusion: Plasma suPAR level > 8 ng/mL and other four clinical factors can be used as predicting factors for the result of mycobacterial culture in MDR-TB suspects.

P-Q-020

MYCOBACTERIUM TUBERCULOSIS 38 KDA RECOMBINANT PROTEIN CAN INDUCE CD3+ T LYMPHOCYTES TO EXPRESS INTERLEUKIN-2 AND INTERLEUKIN-4 IN PBMC CULTURES

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Background: Controlling the epidemic of tuberculosis (TB) is a global health priority, and one of the way is vaccination. The only available TB vaccine *Mycobacterium bovis* BCG's efficacy range vary widely from 0 until 80 percent protection so the development of new vaccination is needed. The new protein as candidates vaccine should be assessed of their immunogenicity. The purpose of this study is to examine whether *Mycobacterium tuberculosis* 38 kDa recombinant protein can stimulate a cellular immune response especially CD3+ T lymphocytes to express IL-2 and IL-4 in Peripheral Blood Mononuclear Cell (PBMC) cultures.

Method: This study is an experimental research laboratory design. There are 3 groups of PBMC cultures, consisting of TB patients, contacts of TB positive and healthy subjects, which contain 8 subjects in each group. All PBMC cultures induced by *Mycobacterium tuberculosis* 38 kDa recombinant protein, and without antigen as a comparison. Expression of IL-2 and IL-4 CD3+ T lymphocytes were measured with flowcytometry.

Results: In healthy subject, *Mycobacterium tuberculosis* 38 kDa recombinant protein can significantly induce expression of IL-2 ($p < 0.000$) and IL-4 ($p < 0.09$) CD3+ T lymphocytes compared to without antigen. In TB contact, there is significantly expression of IL-2 ($p < 0.04$) and IL-4 ($p < 0.01$) CD3+ T lymphocytes compared to without antigen. The highest IL-2 expression is in healthy subject (8.13 ± 0.622) and the highest expression of IL-4 is in TB patients (6.436 ± 4.586).

Conclusion: *Mycobacterium tuberculosis* 38 kDa recombinant protein can stimulate CD3+ T lymphocytes to express IL-2 and IL-4 in healthy subjects and contact with TB.

P-Q-021

NUTRITIONAL STATUS AND MORTALITY AMONG HOSPITALIZED PULMONARY TUBERCULOSIS PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL, JAKARTA, INDONESIA

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Background: Tuberculosis (TB) remains a major global public health problem, responsible for more than 1 million deaths each year. The association between TB and malnutrition is well recognized. Malnutrition is common in pulmonary TB patients, especially who are hospitalized. Malnutrition can adversely affect treatment outcomes and also closely related to mortality. However, data from Indonesia are sparse, despite the high burden of TB. Therefore, nutritional status assessment and nutritional management of hospitalized pulmonary TB patients play a central role in every day practice.

Methods: This was a retrospective cohort study with secondary data of 345 hospitalized pulmonary TB patients in Cipto Mangunkusumo Hospital between January 2011 and September 2013. We assessed the nutritional status at the time of hospital admission, such as Body Mass Index (BMI), Malnutrition Screening Tool (MST) assessments and serum albumin level examinations, then subjects were observed to evaluate their hospital mortality.

Result and Discussion: At the time of hospital admission, 66.4% of subjects had BMI < 18.5 kg/m², 50.7% of subjects had serum albumin level < 3.0 g/dL, and 83.8% of subjects had MST score ≥ 2 . BMI < 18.5 kg/m², serum albumin level < 3.0 g/dL, and MST score ≥ 2 increased the risk of hospital mortality in pulmonary tuberculosis patients (RR 1.589, 95% CI 1.020–2.473, $p = 0.033$; RR 4.588, 95% CI 2.649–7.945, $p < 0.001$; RR 3.255, 95% CI 1.384–7.660, $p = 0.002$; respectively).

Conclusion: More than half of hospitalized pulmonary TB patients were malnourished at admission. Malnutrition associated with higher risk of hospital mortality in hospitalized pulmonary TB patients. The findings can be used to advance the argument in support for initiation of nutritional status assessment and nutritional management among hospitalized pulmonary TB patients in Indonesia.

P-Q-022

38K DA MYCOBACTERIUM TUBERCULOSIS PROTEIN RECOMBINANT MODULATES THE EXPRESSION OF IFN- γ CD3+ T LYMPHOCYTES IN PBMC CULTURES AND RECOGNIZED BY SERUM IMMUNOGLOBULIN G

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Background: Tuberculosis remains a worldwide health problem. One way in controlling TB is by performing BCG vaccination that provides protection against severe TB in children, but its effectiveness varies in adults (20–80%). In the process of vaccine developing immunogenicity test is required to determine the antigenicity. The purpose of this study is to assess whether 38k Da *Mycobacterium tuberculosis* protein recombinant modulates the expression of IFN- γ CD3+ T lymphocytes in PBMC cultures and recognize serum immunoglobulin G.

Method: Experimental laboratory study design. There were 3 groups consist of healthy, TB contact, and TB patient groups, 8 subjects in each group. Recognizing of serum IgG to 38 kDa *Mycobacterium tuberculosis* protein recombinant was obtained by using dot blot. Expression of IFN- γ CD3+ T lymphocyte in PBMC cultures that induced by 38 kDa *Mycobacterium tuberculosis* protein recombinant was determined by flowcytometry.

Result: Serum Ig G in all groups can recognize 38 kDa *Mycobacterium tuberculosis* protein recombinant. There are no significant difference ($p = 0.502$) in 3 groups for recognizing serum Ig G to 38 kDa *Mycobacterium tuberculosis* protein recombinant. In healthy group, after induced by 38 kDa *Mycobacterium tuberculosis* protein recombinant, IFN- γ CD3+ T lymphocyte presentage (12.19 ± 0.34) was significantly higher ($p = 0.001$ and $p = 0.000$) compared to either TB contacts (8.81 ± 0.34 ;) and TB patients (6.39 ± 2.72).

Conclusion: 38 kDa *Mycobacterium tuberculosis* protein recombinant could be recognized by serum Ig G and induced higher expression of IFN- γ CD3+ T lymphocyte in healthy group.

P-Q-024

P-Q-026

REVISITING MANTOUX TESTING IN HEALTH CARE WORKERS AND INTERPRETATION OF LATE READING OF THE MANTOUX TEST

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Objective: Mantoux positive rates among health care workers and interpreting results of late reading.

Methodology: Healthcare workers in respiratory clinic, medical and respiratory ward were enrolled and an interviewer administered questionnaire was used. The Mantoux test (PPD RD23(2 TU/0.1 ml)) was performed and induration was read at 24, 48, 72, 96, 120 and 144 hrs. It was interpreted as positive if the induration was >9 mm at 72 hrs as per national guideline and positive subjects were investigated.

Results: Of the 79 (54 female) subjects, 35, 29 and 15 were working in clinic, medical wards and respiratory ward respectively. There were 35 (44%) positive, 23 (29%) with induration >15 mm. There were 12 (41%), 6 (40%) and 17(48%) positives in the general medical ward, respiratory ward and clinic respectively; when investigated, none of them had active TB. The chance of being positive did not increase significantly with duration of work in general medical wards {Pearson correlation coefficient(PCC) 0.083} and respiratory clinic (PCC 0.046) but there was correlation between duration of work and mantoux positivity in the respiratory ward (PCC 0.33). None of the negative subjects developed an induration of >9 mm after 72 hrs. The induration reduced in size with time after 72 hrs in 69%. Out of the positives, 93% had an induration >9 mm at 48 hrs. None who had an induration of >9 mm at 48 hrs were negative. There was no significant difference between 48 hr and 72 hr readings ($p = 0.885$). All positives at 72 hrs had a persisting induration at 144 hrs. Linear equation to predict the induration at 72 hrs by measuring the induration 24 hrs apart correctly predicted that both would have been positive at 72 hrs.

Discussion: This cohort had a higher positivity rate in compared to the global latent TB rate. There was no clear relationship of reactivity to duration of work. The induration reduced in size after 72 hrs in the majority. Positivity or an induration >15 mm did not indicate active TB in our cohort. Reading at 48 hrs or 72 hrs would only make a change of the result only in a minority. If positive at 48 hrs, it is likely to be positive at 72 hrs and therefore warrant earlier action. If presented for late reading and induration is >10 mm, it is more likely to have been positive. If induration is <10 mm on a late reading, it is possible to have been positive. By applying a linear equation to calculate the result at 72 hrs correctly gave the correct result, but larger sample has to be studied in order to validate this. If there was no induration, it is likely to have been negative at 72 hrs.

P-Q-025

P-Q-027

RELAPSE RATE AND RISK FACTORS FOR PATIENTS WITH SUCCESSFULLY TREATED MAC LUNG DISEASE

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Background: We aimed to identify the relapse rate and risk factors for patients with successfully treated Mycobacterium Avium Complex (MAC) lung disease.

Methods: Between March 2000 and December 2012, 158 patients who had MAC lung disease were successfully treated with a standard regimen at a tertiary referral centre in South Korea, and these patients' medical records were retrospectively analyzed.

Results: The mean age was 60.7 ± 11.1 years and females were predominant among the subjects (52.5%, 83/158). The aetiological agent was Mycobacterium avium in 77 patients (48.7%) and Mycobacterium intracellulare in 81 patients (51.3%). A total of 95 patients (60.1%) had the nodular bronchiectatic form of the disease. Almost all patients had been previously treated with a macrolide-containing regimen and 68 patients (43.0%) had received aminoglycoside. During the median of 43.8 months of follow-up period, 50 (31.6%) cases relapsed after a median of 21.9 months after treatment completion. Relapse rate was higher in patients with old age (> 65 years, $p = 0.028$) and nodular bronchiectatic form of disease ($p = 0.001$). In multivariate analysis, only nodular bronchiectatic form of disease (OR = 3.16, 95% CI 1.40–7.13) was independently associated with increased risk of relapse.

Conclusions: A substantial portion of patients with MAC lung disease may suffer from a relapse after treatment success. The relapse rate was significantly higher in patients with the nodular bronchiectatic form of the disease.

A RETROSPECTIVE ANALYSIS OF PATIENT DATA FOR THE MANAGEMENT OF TUBERCULOSIS IN HANOI

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Viet Nam is one of the high TB-burden countries and the estimated prevalence of tuberculosis (TB) is declining slowly. Although National Tuberculosis Control Program (NTP) has been working effectively in recent years, the prevalence of isoniazid- and streptomycin-resistant TB without previous treatment is considerably high. In Hanoi, the capital of Viet Nam, large-scale computerized data of the patient population have not been available for the regional TB management. In this retrospective study, we analyzed clinical information about individual TB patients filed as paper-based records for NTP registration in all district TB units inside the city and medical records from Hanoi Lung Hospital. We obtained clinical information about TB from January 2005 to December 2006 in Hanoi. Different types of paper-based records were provided: One of them was about notification and treatment information registered for NTP from all of the 14 districts in Hanoi, and others we used were about sputum smear examination and inpatient information from Hanoi Lung Hospital. Each of all the records was input into two computer systems independently. Sets of the data in two systems were checked for consistency, and the records were confirmed after errors were corrected. By the scoring method using name, sex, and year of birth, each of the records was numbered to link all records for one patient. The records were processed and analyzed using the R programme. There were 13,609 records about sputum smear examination, 4,527 records about notification and treatment registered for the NTP, and 1,096 records about inpatient information. Of the 13,609 records, 12,671 were about sputum smear examination for the purpose of TB detection, and smear-positive results were observed in 2,016 records (15.9%). In the notification and treatment database, 2,155 (47.6%) were registered as new smear positive patients. Of the 2,155 cases, 1,695 (78.7%) were treated with the regimen of 2HRZS/6HE used during the study period. Treatment success rate of new smear positive patients was 91.4%. Rates of death, failure, and default were 4.1%, 1.0%, and 0.3%, respectively. In the inpatient database, 72.8% of the patients had no previous history of TB. Most of the new smear positive patients registered in Hanoi during the period were treated successfully, similar to the Vietnamese nationwide TB profile published by World Health Organization. Furthermore, results of the data analysis after merging different types of records will be presented.

DISTRIBUTION OF MYCOBACTERIUM TUBERCULOSIS GENOTYPE AND TUBERCULOSIS TRANSMISSION IN JAYAPURA CITY, PAPUA PROVINCE INDONESIA

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Background: Papua is one of the provinces in Indonesia with the highest Tuberculosis (TB) prevalence. Many factors contribute to TB transmission, including environment, socioeconomic condition, and factors relating to Mycobacterium tuberculosis as a pathogen.

Aim: The aim of the study to identified the genotype of Mycobacterium tuberculosis in pulmonary TB patients, and its transmission in household contacts.

Methods: This study was conducted in May–November 2013. Sputum samples from 40 pulmonary TB patients were collected, cultured, tested with Drug Susceptibility Test (DST) and examined with spoligotyping to identify the genotype. In other hand, home visit was arranged to assess the household contacts by questionnaire, physical examination, and chest x ray in contacts with symptoms.

Results: The spoligotyping results were: 4 (10%) Beijing, 31 (77.5%) Non Beijing and 5 (12.5%) Orphan. DST result: 28 (70%) isolates were sensitive with anti tuberculosis. From 331 household contacts we found 67 (20.2%) with TB symptoms and 7 (2.1%) with chest x ray positive, no sputum sample could be collected.

Conclusions: In this study Beijing was not a dominant TB strain and there was no significant relationship between Beijing strain and drug resistant or TB transmission.

P-Q-028

THE Rs5743708 GENE POLYMORPHISM IN THE TLR2 GENE CONTRIBUTES TO THE RISK OF TUBERCULOSIS DISEASE INVOLVING NINETEEN STUDIES

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Background: It has been reported that one single nucleotide polymorphisms (SNPs) rs5743708 in TLR2 gene might be associated with the susceptibility to tuberculosis disease. Owing to mixed and inconclusive results, we conducted a meta-analysis to systematically summarize and clarify the association between the rs5743708 gene polymorphism in the TLR2 gene and the risk of tuberculosis disease.

Methods: A systematic search of studies on the association of the rs5743708 gene polymorphism in the TLR2 gene with susceptibility to tuberculosis disease was conducted in PubMed. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were used to pool the effect size.

Results: A total of nineteen case-control studies from 12 articles on rs2910164 and 3 studies on the rs5743708 gene polymorphism in the TLR2 gene and the risk of tuberculosis disease were included. A significant relationship between the rs5743708 gene polymorphism in the TLR2 gene and tuberculosis disease was discovered in an allelic genetic model (OR: 2.545, 95% CI: 1.875–3.453, $P=0.000$), a homozygote model (OR: 5.795, 95% CI: 1.982–16.941, $P=0.001$), a heterozygote model (OR: 2.297, 95% CI: 1.577–3.3431, $P=0.000$), a recessive genetic model OR: (5.568, 95% CI: 1.907–16.255, $P=0.002$) and a dominant genetic model (OR: 2.525, 95% CI: 1.784–3.576, $P=0.002$). In sub-group analysis base on ethnicity, significance was observed between the Caucasian group and the Asian group.

Conclusions: The rs5743708 gene polymorphism in the TLR2 gene contributes to the risk of tuberculosis disease. Individuals with the rs5743708 gene polymorphism in the TLR2 gene polymorphism in the CXCL12 gene are under a higher risk for tuberculosis disease.

P-Q-029

NEGATIVE INTERFERON-GAMMA RESPONSE WITH AND WITHOUT POSITIVE CONVERSION DURING TREATMENT IN PATIENTS WITH ACTIVE TUBERCULOSIS

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Background: Interferon-gamma release assay (IGRA) is used to detect tuberculosis (TB) infection. Its sensitivity is no more than 90%, which causes difficulties in excluding TB infection when the prevalence of TB infection is high. We characterized host and pathogenic background and immune status of the patients with false-negative results of IGRA during anti-TB treatment.

Methods: The study was approved by the relevant ethical committees. In our previous study, 24 of 504 patients with culture-confirmed active pulmonary TB showed IGRA-negative results before treatment (Month 0). We followed up 20 of these IGRA-negative patients with two more times of blood collection at 2 (Month 2) and 7 (Month 7) months after starting anti-TB treatment. Concentrations of immunological parameters were measured at the above time points in the supernatants of plasma that remained after performing the IGRA with or without TB-specific antigen stimulation. Clinical data before and during the treatment period were also collected.

Results: Pulmonary cavitory lesions remained in one of the six zones on chest radiography in the transiently IGRA-negative group with positive conversion on average, whereas no cavitory lesions remained in the continuously IGRA-negative group with no positive conversion at Month 7. Out of 27 immune analytes measured, the concentrations of IL-1RA with no stimulation, and those of IL-1RA and IL-2 stimulated with TB-specific antigens were significantly higher in the IGRA-negative group with positive conversion than in the group with no positive conversion at Month 7. IP-10 also tended to be elevated in the IGRA-negative group with positive conversion.

Conclusion: Our clinical and experimental data suggest that false-negative results of IGRA in active pulmonary TB can be divided into two types in response to IGRA antigens; a group with continuous unresponsiveness and the other group with initially-suppressed but gradually restoring responsiveness during the treatment. Recognition of these two patterns will help understanding the unfavourable mechanism for reducing the IGRA sensitivity.

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P-Q-030

ASSOCIATION OF UNDERNUTRITION AND TUBERCULOSIS PREVALENCE IN TYPE 2 DIABETES MELLITUS PATIENTS

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Background: Diabetes mellitus and undernutrition separately were proved as risk factors of tuberculosis incidence. This analytical cross sectional study aimed to measure the prevalence of lung tuberculosis (TB) among type 2 diabetes mellitus (DM) patients and its association with undernutrition.

Methods: Retrospective cross sectional study using medical records from Cipto Mangunkusumo hospital since January 2013 to December 2013.

Results: A total of 462 DM patients were analyzed and the results showed that 125 patients (27.1%) had TB and 125 patients (27.1%) were undernourished. Within DM patients who had TB, there were 78 undernourished patients (62.4%), while the other 47 patients (37.6%) are not undernourished. We found out there is a significant statistical association between undernutrition and prevalence of TB among DM patients ($p < 0.001$, CI 95% range 4.269 to 4.679).

Conclusion: Undernourished type 2 diabetes mellitus patients are highly associated with tuberculosis. Therefore, nutritional interventions for diabetic patients are indispensable in overall holistic approach to reduce the incidence of lung tuberculosis.

P-Q-031

P-Q-033

CHARACTERISTICS OF TUBERCULOUS PLEURAL EFFUSIONS

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Background: Tuberculous pleural effusion is one of the most common forms of extrapulmonary tuberculosis (TB), accounting for up to 25% of TB cases. The incidence of TB in Singapore is on the rise over the last few years, with an associated increase in TB effusions. Tuberculous effusions are classically described as lymphocytic exudates, however there has been variable inconsistencies in previous studies. We embark on a retrospective study to investigate the occurrence of tuberculous pleural effusions in our local setting, as well as study the clinical and biochemical characteristics of these effusions.

Aim: This study aims to shed light on the incidence of pleural tuberculosis in a local setting as well as the characteristics of tuberculous pleural effusions. These will allow us to compare the characteristics with those typically mentioned in literature.

Methods: Retrospective analysis of patients admitted to Changi General Hospital over a three year period from 1 July 2010 to 30 June 2013, with a diagnosis of tuberculous pleural effusion. Pleural fluid characteristics, tissue histology and patient outcomes were analyzed. Final diagnoses were determined using either clinical, histological criteria or microbiological culture.

Results: A total of 94 patients with tuberculous pleurisy were identified. Mean age of patients was 50.4 years (SD +/- 19.72). 85.1% of pleural effusions were small to moderate-sized. Associated pulmonary lesions were seen in 38% of patients, with 34% exhibiting consolidation and 2% cavitation. Only 4.3% of patients were asymptomatic; with chest pain, dyspnoea and anorexia being the most common presentations. The median percentage of lymphocytosis identified in pleural fluid was 90%, and less than 10% of cases had a lymphocyte percentage of less than 50%. Fluid adenosine deaminase (ADA) was elevated, with a median value of 86.5 units/litre. Pleural fluid cultures were positive in 35.1% of patients. 91% of patients (n = 61) with pleural biopsies had positive histology and 52.4% of biopsy cultures were positive. There was no significant correlation between pleural fluid cultures and tissue histology. Majority of patients (83.6%) had negative sputum smears for acid-fast bacilli (AFB).

Conclusion: Our findings are similar to previous studies. Tuberculous pleural effusions are still predominantly smear-negative lymphocyte-rich exudates; usually affecting two-thirds of hemi-thorax or less. Histological examination of pleural specimens still provides the best diagnostic yields in the diagnosis of pleural TB. ADA can be considered as a test modality for TB effusions.

PREDICTORS OF SUCCESS FACTORS OF EXTRAPULMONARY TUBERCULOSIS TREATMENT USING DOTS STRATEGY IN RSUPN DR. CIPTO MANGUNKUSUMO JAKARTA

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Background: Extrapulmonary tuberculosis (EPTB) is common presentation found in Indonesia, besides Tuberculosis (TB). We found that no more research about EPTB in Indonesia, especially EPTB success treatment using the DOTS strategy and its predictor factors.

Aims: To determine predictors of TB treatment success factors such as age, sex, diabetes mellitus, HIV and anti-tuberculosis records. To acknowledge the success rate of EPTB treatment using DOTS strategy, when administered for a minimum of 9 months.

Result: A retrospective cohort study was conducted from 1 January 2008 through 31 December 2012. A total of 542 patients of EPTB were identified, 193 patients were pure EPTB while 279 were mixed ones and 70 were incomplete data. The majority of patients were female (52.3%). Generally young age (18–60 years old (95.9%)), mean $31,34 \pm 11,64$ years old. The most common type of EPTB were lymph node. Success treatment rate of EPTB among age of 18–60 years was 49.7% (OR 2.968, 95% CI 0.584 to 15.087, p 0.313). Success treatment rate of EPTB among female sex was 55.4% (OR 1.768, 95% CI 0.999 to 3.131, p 0.05). Success treatment rate using DOTS strategy among diabetes mellitus was 33,3% (OR 1.957, 95% CI 0.475–8.062, p 0.546) and the one that had tuberculosis record previously was 55,6% (OR 0.738, 95% CI 0.278–1.959, p 0.717) Success treatment rate in extrapulmonary patient among HIV-seropositive was 32,1% (OR 2.588, 95% CI 1.330–5.038, p 0.007). In multivariate analysis, the success rate for EPTB with HIV co-infection factor, had OR 2.588, CI 95% 1.330–5.038, p 0.005. EPTB among HIV-seropositive patients had lower therapy success rate using DOTS strategy and were associated with unsuccessful therapy and poor prognosis. The success rate of EPTB treatment using DOTS strategy for <9 months was 20.2%. There were 94.6% EPTB patients successfully treated with the DOTS strategy for >9 months.

Conclusion: HIV was a predictor factor that may decrease therapy success rate of EPTB using DOTS strategy. Success rate of extrapulmonary TB treatment using DOTS strategy for minimum 9 months was good (94.6%).

P-Q-032

THE ASSOCIATION OF EXPOSURE TO SECOND HAND SMOKE AND OTHER SOCIAL FACTORS TO TUBERCULOSIS IN FILIPINO CHILDREN

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Background: Exposure to second hand smoke is a major health concern worldwide. It predisposes the exposed child to a gamut of respiratory infections, including tuberculosis.

Methods: This is a cross-sectional analytic study done in three schools in the Philippines from October 2013-March 2014. Second hand smoke exposure, socioeconomic class and overcrowding status were asked. Tuberculin skin testing and chest xray was done on all patients. They were classified based on the Philippine Pediatric Society TB consensus to have TB exposure, TB infection or TB disease.

Results: A total of 130 students qualified for inclusion in the study. Fifty seven out of the 130 subjects (44%) reported exposure to second hand smoke. Males, middle socioeconomic class, overcrowding and public school students had more report of second hand smoke exposure. TB exposure and TB disease were seen with a higher prevalence among students exposed to second hand smoke but did not reach statistical significance. Belonging to the middle socioeconomic class was statistically significant ($p = 0.034$) to predict TB infection. Overcrowding is a factor for all outcomes of tuberculosis.

Conclusion: There is a proportional percentage of Filipino children who are exposed to second hand smoking (44%). TB exposure and disease were more prevalent among those with second hand smoke exposure. Belonging to the middle socioeconomic class was considered significant ($p = 0.034$) in acquiring a TB infection. Overcrowding is a strong variable predisposing to tuberculosis.

P-Q-034

ASSOCIATION BETWEEN SERUM VITAMIN D LEVEL AND PULMONARY TUBERCULOSIS IN MEDAN INDONESIA

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Background: Vitamin D is known to have an important role in macrophage activation and the subsequent restriction of *Mycobacterium tuberculosis* growth, and it has been implicated as a risk factor for TB. Vitamin D also induced the expression of cathelicidin, which is involved in the first line of defense in TB patients. An association between 25(OH) vitamin D (25[OH]D) levels and TB has been described in several studies.

Objective: To compare serum vitamin D level in subjects with and without TB, to find out association of serum vitamin D level with TB and association of serum vitamin D level with extent of lesion in chest X-ray.

Methods: A cross sectional study was conducted in Adam Malik Hospital Medan, Indonesia from Januari to Juni 2013. New TB cases was diagnosed by the presence of acid-fast bacilli on sputum smears and chest x ray. We excluded TB patients with DM, HIV, malignancy, immunosupresan treatment and immunocompromized patients. Non TB subjects were selected randomly from health care staff, who didn't have TB from anamnesis and chest X ray. The serum concentrations of 25(OH)D were determined by an CLIA methode. Vitamin D deficiency, vitamin D insufficiency, vitamin D sufficiency, vitamin D optimal defined as serum 25(OH)D concentrations of ≤ 10 ng/ml, 10–20 ng/ml, 20–30 ng/ml and >30 ng/ml respectively.

Results: Thirty one subjects with TB and 31 subjects without TB were enrolled. Mean serum vitamin D level of subjects with and without TB were 25,21 (SD $\pm 7,93$)ng/ml and 21,50 (SD $\pm 9,37$)ng/ml, respectively ($p = 0,098$). Vitamin D deficiency was not found in all subjects. Mean serum vitamin D level in far advanced and minimal lesion in TB patients ($21,61 \pm 5,50$ ng/ml versus $29,58 \pm 8,39$ ng/ml, $p = 0,04$), respectively. Regression test was performed to assess the influence of vitamin D in extent of lesion of TB patients ($R = 0,000$ and p model = 0,897).

Conclusion: There was no significant association between serum vitamin D level and TB. There was a significant difference in vitamin D level between far advance lesion and minimal lesion in TB patients. However statistically extent of lesion was not influenced by serum vitamin D level significantly. Serum vitamin D level of subjects without TB was lower than with TB. It remain to be established other factors that influences serum vitamin D level.

P-Q-035

FACTORS RELATED TO DEFAULT PATIENTS WITH PULMONARY TUBERCULOSIS IN MEDAN, INDONESIA

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Background: Pulmonary tuberculosis (PTB) patient often discontinue their treatment prematurely. This problem causes an increase in morbidity and mortality risk, and also the risk of infecting others. Many factors can cause patients to discontinue their treatment for pulmonary tuberculosis.

Objective: The aim of this study was to determine the cause of treatment discontinuation in PTB patients in Medan, Indonesia.

Methods: This study was conducted in some of PTB centres in Medan, Indonesia, from August 2013 to January 2014. This was an analytical cross-sectional study. The subjects were 63 PTB patients who discontinued their treatment (default patient), while 63 PTB patients who never discontinued their treatment and has been declared cured was used as a comparison group. Data were collected through questionnaire and interviews.

Results: In this study, there was no significant differences between the patients who never discontinued their treatment (non-default patient) and the patients who discontinued their treatment (default patient) in gender, age group, and education level ($p > 0.05$). In the default group we found more males than females (63,50% vs. 36.50%), the larger age group was 46–55 years (31,70%), junior-high school education level (77,80%). Factors those were not significantly different ($p > 0.05$) in discontinued their treatment in default PTB patients compared with non-default PTB patients are the presence of co-morbid, and the cost of treatment. While the significant factors in discontinuing their treatment are the distance to the healthcare, medication side effect, feeling better, the knowledge of TB treatment duration, not knowing the risk of discontinuing the treatment, and worsening of the disease ($p < 0.05$).

Conclusions: Significant factors that cause PTB patients to discontinue their treatment were distance to the healthcare, medication side effect, feeling better, the knowledge of TB treatment duration, not knowing the risk of discontinuing the treatment, and worsening of the disease. These factors should be considered in addressing care and policy actions in tuberculosis control.

P-Q-036

P-Q-038

GENDER DIFFERENCES AND TB TREATMENT OUTCOME AMONG ANTI TUBERCULOSIS DRUG INDUCED HEPATITIS PATIENTS

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Background: Anti-tubercle drug-induced hepatotoxicity (ATDH) causes substantial morbidity and mortality and diminishes treatment effectiveness.

Aims And Objective: The aim of current study was to note the association between gender differences among anti-tuberculosis drug induced hepatotoxicity patients and to evaluate TB treatment outcomes.

Method: A retrospective cohort study was conducted at Hospital Pulau Pinang Malaysia. All TB patients presented between January 2007 and September 2013 were included for the current study. Patients with inadequate medical records and patients receiving concurrent potential hepatotoxic medications along with anti-TB treatment were excluded from current study. A valid data collection form was used for collecting patient demographic and clinical data. Data was analyzed by using SPSS version 20.

Results: A total of 3093 TB patients were included for the final analysis. One hundred and ninety patients suffered from drug induced hepatitis, of which 146 (76.8%) were male and 44 (23.3%) were female patients. The mean age of male patients suffering from drug induced hepatitis was 47.49 (SD ± 14.28) years whereas the mean age for female patients was 45.0 (SD ± 14.96). Area of residence ($p < 0.001$), smoking habit ($p < 0.001$), alcohol consumption ($p < 0.001$) and intravenous drug users ($p < 0.001$) had statistical significant association with drug induced hepatitis patient gender. Anti-tuberculosis induced drug hepatitis patients with diabetes mellitus ($p < 0.046$) and HIV/AIDS 107 ($p < 0.014$) also had statistical significant association with gender. A total of 82 (72.6%) male and 31 (27.4%) female patients treatment outcome were successful, 21 (87.5%) male and 3 (12.5%) female patients were defaulter, 12 (85.7%) male and 2 (14.3%) female patients were transferred out, 22 (81.5%) male and 5 (18.5%) female patients expired whereas 9 (75%) male and 3 (25%) female patients treatment was continued.

Conclusion: Multiple factors are associated with patient gender in the development of anti-tubercle drug induced hepatitis. Therefore careful monitoring and regular patient assessment can optimize TB treatment outcomes in such patients.

P-Q-037

CHARACTERISTIC FEATURES OF MDR TB PATIENTS WHO WERE TREATED IN HAJI ADAM MALIK GENERAL HOSPITAL MEDAN

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Background: TB drug resistance is a problem for TB prevention and eradication programme of the world. Over the years, more cases of Multidrug Resistance (MDR) TB had arose and becoming a new threat to eradicate TB. Therefore, the needs to investigate characteristics of patients with MDR TB became important.

Objective: The purpose of this study is to determine the characteristics of patients with MDR TB.

Method: This research is a descriptive study. Data were collected between September 2013 and December 2013. Data was retrieved directly from the medical records of subjects who came to the pulmonology clinic or were staying at the Haji Adam Malik General Hospital. A total of forty subject had undergone the experiment. Subjects were patient diagnosed with MDR TB, who have undergone a sputum direct smear examination, acid fast culture, GeneXpert, and sensitivity test for anti-tuberculosis drugs.

Result: From the 40 subjects that had participated in this research, we found that most of the subjects were male (72.5%). Most had graduated from senior high school (65.0%), and most were married (90.0%). All of the subjects' chief complaint was cough (100%) and their radiologic chest X-ray data showed some cloudy appearance (100%). Most of the subjects had history of first line anti-tuberculosis drug. The Regimens are kanamisin, levofloxacin, sikloserin, etionmid, and piranizamid.

Conclusions: The MDR TB patients in H. Adam Malik General Hospital were due to secondary drug resistance. We used standard regimen for these patients.

CAUSES AND IMAGING PATTERNS OF TREE-IN-BUD OPACITIES ON COMPUTER TOMOGRAPHY OF THE THORAX IN AN ASIAN POPULATION – A RETROSPECTIVE REVIEW

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Background: There are numerous aetiologies for tree-in-bud (TIB) opacities in Computer Tomography (CT) scans of the thorax. Our aims are to evaluate the clinical characteristics and CT patterns which aid in determining the aetiology of TIB in our Asian population.

Methods: We evaluated radiological records with TIB opacities, from the period of January 1, 2010, to December 31, 2010 and performed a retrospective review of the patients' clinical, biochemical, microbiological and radiological examination for the causes of TIB opacities. Patterns of disease on CT were reviewed and analyzed.

Results: 71 out of 1621 (4.38%) CT thorax studies were reported as having TIB appearance, of which 40.8% had a confirmed aetiology. 93.1% were confirmed cases of infection. 65.5% of these cases were attributed to Mycobacterium Tuberculosis infection, while 10.4% had nontuberculous mycobacterial infection. Of the remaining infections, 13.8% were of bacterial aetiology and 3.45% were of fungal aetiology. 2.81% were found to have underlying malignancy. 15.5% of patients had underlying oropharyngeal dysphagia, with 88.9% of this subgroup having confirmed bacterial infections. 44.4% were found and treated for Mycobacterium Tuberculosis infection. There was no significant correlation with other clinical or biochemical indicators to suggest a particular aetiology for TIB. Imaging patterns were broad. The evaluation of TIB in a single lobe distribution versus widespread involvement did not contribute to specific diagnosis. There was no significant relation found between the presence of pure TIB versus that of TIB associated with ground-glass opacities, bronchiectasis, or nodules.

Conclusion: Multiple causes of TIB patterns on CT thorax have been reported. In contrast to studies of Western populations, ours show that Mycobacterium Tuberculosis infection was the main cause in the Asian population, as opposed to non-tuberculous mycobacteria, fungal and viral infections. Mycobacterium Tuberculosis is the predominant cause of infection in all patient subgroups, inclusive of patients with oropharyngeal dysphagia and concomitant aspiration. No patients with connective tissue disorders or immunologic disorders were found in our study, which is consistent with an Asian population. No additional information was obtained from analyzing other CT patterns and features. In summary, the TIB sign is most often a manifestation of infection and aspiration, with Mycobacterium Tuberculosis as the commonest cause. This will impact and guide future management decisions.

P-Q-039

PULMONARY TUBERCULOSIS AFTER ANTI-TNF- α TREATMENT

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Anti-Tumour necrosis alpha factor (anti-TNF- α) immunotherapy has revolutionized the treatment of inflammatory diseases, such as ankylosing spondylitis and rheumatoid arthritis. A major concern is that patients receiving anti-TNF- α agents have an increased risk of infection, particularly of tuberculosis (TB). Current guidelines recommend investigating latent tuberculosis infection (LTBI) prior to commencing use of these medications, such that individuals may receive chemoprophylaxis, if they are tested positive with Tuberculin Skin Test (TST) and or interferon gamma releasing assay (INGRA). Individuals with a negative test may then be started on the therapy. The rheumatologist and general practitioner then follow those patients but there is no review of the TB immune status during the treatment. We present the case of Mr. TL, a 23-year-old male who presented to our hospital at the end of December 2013 with malaise, fever, moist cough and weight loss for four weeks. He had returned from a trip to Asia where he had felt unwell since the beginning, but opted to continue. Mr. T.L. is Australian born student of information technology, he has severe ankylosing spondylitis, and at the time of his presentation he was receiving adalimumab 40 mg sci fortnightly for 5 years. Prior to commencing his treatment a protocol that included checking for TB exposure, TST or INGRA and chest radiograph had been performed and were negative. He had never smoked or drank alcohol. Initially he was diagnosed with right upper lobe community-acquired pneumonia. His sputum samples were AFB negative. As he continued to have fevers and malaise, INGRA was repeated. A CT chest and bronchoscopy with washing and bronchial biopsies were performed. After the bronchoscopy he was admitted in to an isolation ward. INGRA was positive and Mycobacterium tuberculosis was recovered from his pulmonary samples. Daily doses of isoniazid, ethambutol, pyrazinamide, rifampicin and pyridoxine were started in hospital. After 10 days, he was discharged to continue treatment in the chest clinic, with 3 times a week direct observed therapy. In patients on immunosuppression with anti-TNF- α medications, one needs to be cognizant and vigilant to the development of pulmonary tuberculosis, at any stage of treatment. We plan to review our protocols in screening and managing such patients, prior to and whilst on treatment, including when considering going to endemic tuberculosis areas.

P-Q-040

LUNG FUNCTION IMPAIRMENT ACCORDING TO PRIOR PULMONARY TUBERCULOSIS

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Background: Tuberculosis (TB) can affect lung function, but a few data exist on long-term follow-up.

Objective: This study was conducted to evaluate whether prior pulmonary TB was related with lung function impairment in Korean adult population and risk factors of decreased lung function in subjects with prior pulmonary TB.

Methods: We used data from the fifth annual South Korean National Health and Nutrition Examination Survey (Korean NHANES V) conducted in 2012. From a total of 8,058 subjects, 3,325 adult subjects who were at least 40 years of age were included in the study population. The correlation between prior pulmonary TB and chest x-ray abnormality and impaired lung function using questionnaires about diagnosis of pulmonary tuberculosis, chest x-ray and pulmonary lung function were analyzed. All estimates were calculated on the basis of sampling weight.

Results: Mean age was 56.1 years and males were 48.0%. Subjects with diagnosed pulmonary TB were 5.1%. Chest PA with sequale of pulmonary tuberculosis was 10.2%. FEV1%, FVC%, FEV1/FVC in subjects with prior pulmonary TB were significantly low compared with those without TB (83.17 \pm 1.75 vs. 92.42 \pm 0.34, $P < 0.001$, 89.51 \pm 1.42 vs. 93.01 \pm 0.33, $P = 0.008$, and 71.92 \pm 0.01 vs. 77.87 \pm 0.00, $P < 0.001$, respectively). In subject with prior pulmonary TB, age and male sex were risk factors to lung function with obstruction pattern (OR = 1.053, 95% CI: 1.005–1.103, OR = 5.028, 95% CI: 1.329–19.020, respectively) after multivaiaated analysis with age, sex, smoking status, age, sex, BMI and age of diagnosis.

Conclusion: In the current study, pulmonary TB morbidity was significantly related with decreased lung function in Korean adults. In patients with pulmonary TB, age and male sex may be risk factor for obstructive lung disease.

P-Q-041

RELATIONSHIP BETWEEN LEVEL OF INTERLEUKIN-10 AND MULTI-DRUG RESISTANT TUBERCULOSIS

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Background: Protection against Mycobacterium tuberculosis is dependent on Th1 cell CD4+ that produced pro-inflammatory cytokines such as IFN- γ and TNF- α . Tregs produced IL-10 as anti-inflammatory cytokine is against the function of those pro-inflammatory cytokines. Immune suppression is responsible for MDR-TB. The previous study showed impaired Th1 responses and enhanced Tregs levels in circulatory blood of MDR-TB patients. The study of IL-10 represented anti-inflammation cytokine as immune suppression never been conducted in Indonesia.

Objective: To analyze relationship between level of interleukin-10 and Multi-drug resistant tuberculosis.

Methods: The study was conducted at the outpatient department of MDR-TB and DOTS of Dr. Soetomo hospital in Surabaya. Total sample was 38 of TB patients that consist of 19 MDR-TB patients (secondary resistant) and 19 non-MDR TB patients as control.

Results: In this study we found that the median level of IL-10 as 5,7 \pm 3,3 pg/mL in the group of MDR-TB patients with minimum level was 1,3 pg/mL and maximum level was 14,0 pg/mL while median level of IL-10 in non-MDR TB patients was 7,0 \pm 3,4 pg/mL with 3,2 pg/mL and 16,5 pg/mL, respectively. To analyze correlation between time to first of having TB until became MDR-TB and level of IL-10 by using Pearson's correlation, we showed that no statistical correlation ($p > 0,05$). According to statistical classification, we found that no statistical correlation between level of IL-10 and the history of treatment in MDR-TB patients ($p > 0,05$). Data showed that all the history of treatment classification dominated by MDR-TB patients with the low level of IL-10. We also found that no statistical difference with the level of IL-10 in MDR-TB and non-MDR TB patients ($p > 0,05$) although in descriptive state we found the level of IL-10 was higher in non-MDR TB patients. And also there was no relationship between level of IL-10 and MDR-TB ($p > 0,05$). It could be explained that the host factor was not involved and in the other side we still not known the factor of agents, yet. The low level of IL-10 that was observed in this study could be interfering by the strain of M.tb which not assessed in this study.

Conclusion: In this study we found that level of IL-10 is not increase in MDR-TB patients and there was no relationship between level of IL-10 and MDR-TB ($p > 0,05$).

P-Q-042

P-Q-043

TUBERCULOSIS INFECTION WITH THE MANIFESTATION OF ACUTE RESPIRATORY DISTRESS SYNDROME

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Background: Tuberculosis (TB) is still a global issue throughout the world and remains to be the primary cause of morbidity and mortality, particularly in developing countries. Indonesia is at the 4th rank of countries with the highest TB incidence in 2012, with 0.4–0.5 million new cases annually. TB is recently considered as one of the aetiologies of acute respiratory distress syndrome (ARDS). ARDS is a life threatening condition that is caused by several factors, including infection and lung trauma. From serial case reports of 109 patients with TB, only 7 cases were manifested as ARDS. Patients with miliary or disseminated type of TB are those with the higher risk of developing ARDS.

Case: A 27-year-old woman was admitted to Dr Soetomo Hospital with shortness of breath since 1 week ago, that progressed 1 day before admission. She has been coughing for 1 week without sputum. Chest examination reveals increase in fremitus on both lungs, and rhonchi was found in 2/3 lower part of the lungs. Blood gas analysis result showed a severe hypoxaemia with PaO₂/FiO₂ ratio of 107. Radiologic finding suggest the appearance of reticulogranular pattern on both lungs. Patient was having moderate ARDS based on Berlin criteria. Based on clinical judgement, patient was treated with anti tuberculosis drugs (ATD) regimen of rifampicin, isoniazid, ethambutol, pyrazinamide, and streptomycin. Acid-fast bacilli was found from the sputum microscopic examination after the treatment started. After 7 days of receiving ATD, patient's symptoms improved.

Conclusion: Tuberculosis is a condition that can act as the primary cause of ARDS, although the incidence of this case is rare. The diagnosis of TB involves clinical symptoms, sputum microscopic examination, radiology, and laboratory data. The diagnosis and treatment of tuberculosis in such cases can be delayed. The main point of management of ARDS is to ensure optimal supportive care while treating the underlying cause. Therefore tuberculosis should always be kept a possibility of ARDS particularly in the developing world.

ALL FAILURE CASES ON DOTS THERAPY ARE NOT DRUG RESISTANT IN PROGRAMME CONDITION

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Introduction: DOTS treatment under Revised National Tuberculosis Control Programme (RNTCP) in India has covered whole country. Failure (showing persistent sputum +ve) is a major challenge, which means no clinical response with the treatment, in all category, I, II & III under DOTS. It gives a wrong impression of drug resistance. In this study sensitivity pattern of repamficin isonilised, ethambutol and streptomycin was done in all failure cases of category I, II, III and the resistance pattern were observed.

Material Method: The study was conducted in Department of Tuberculosis and Respiratory Diseases Institute of Medical Science, Banaras Hindu University, Varanasi, India. During the period of Jan 2011 to June 2012. Total 50 failure patients, who were receiving category I, II and III and show ed sputum +ve at the end of 5th month were included. The sensitivity pattern of MTB were done by the proportion method in L J media. The tested drug were RHES.

Observation: Sensitivity pattern of DOTS failure cases (total cases 50).

Drugs	MTB Strain showing sensitive to drugs					Resistance to H & R
	H	R	E	S	HRES	MDR
CAT I failure 16 cases	62.5% (10/16)	75% (12/16)	81.25% (13/16)	68.7% (11/16)	31.7% (5/6)	43.7% (7/16)
CAT II failure 26 cases	53.8% (14/26)	61.5% (16/26)	69.23% (18/26)	57.69% (15/26)	30.7% (8/26)	61.5% (16/26)
CAT III failure 8 cases	62.5% (5/8)	75% (6/8)	87.5% (7/8)	62.5% (5/8)	37.5% (3/8)	37.5% (3/8)
Total 50 cases	58% (29/50)	68% (34/50)	76% (38/50)	62% (31/50)	32% (16/50)	52% (26/50)

Conclusion: In any programme condition the treatment failure is very usual. The general practitioners takes it as drug resistant or MDR. But in this study the resistant pattern with single drug or multiple drugs or MDR was not high. Only 43.7% MDR in category I, 61.5% MDR in category II and 37.5% MDR in category III were observed. Overall MDR was 52%. That is still 48% were sensitive to other drug among failure cases. The other social reasons like irregular treatment, ignorance, alcohol, drug side effect etc. may be the reason of treatment failure and not the drug resistance. So it is recommended that all failure case examine for sensitivity test for MTB and then only they should be labeled as drug resistance case and should be put on DOTS Plus or second line treatment.

P-Q-044

IMPACT OF CO-MORBID CONDITIONS ON TREATMENT OUTCOME AMONG TUBERCULOSIS PATIENTS IN MALAYSIA

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Background: The threat of tuberculosis (TB) seems to become increasingly ominous along with its fatal co-morbidities.

Objective: The aim of the present study was to obtain comprehensive data pertaining to the epidemiology and effect of different co-morbid conditions on clinical outcomes of tuberculosis in Malaysia.

Methodology: A multi-centre retrospective study design was adopted from January 2006 to March 2009 in four states of Malaysia (Penang, Sabah, Sarawak and Selangor) in order to collect data of TB patients. All adult patients diagnosed with TB were included, whereas patients with missing records were excluded. A validated data collection form was used to note patient demographic and clinical data. All the data was analyzed by using SPSS version 20.0. All relevant ethical considerations were obtained.

Results: A total of 9337 TB patients were included, out of which 6442 (69%) were males; 2504 (26.8%) were Malay; 6706 (71.8%) were unmarried; 4313 (46.2%) were smokers; and 3632 (38.9%) lies in the age group 26 to 45 years. The mean age and weight of patients was 41.61 ± 16.57 years and 41.75 ± 10.11 kg respectively. Co-morbidities were noted in 3414 (36.5%) patients. The most common were diabetes mellitus (56%) and HIV/AIDS (31%). Male gender (OR = 0.56, 95% CI 0.51–0.62, $p < 0.001$), Malay race (OR = 0.89, 95% CI 0.80–0.99, $p < 0.001$), unmarried individuals (OR = 1.30, 95% CI 1.18–1.43, $p < 0.001$) and smokers (OR = 0.54, 95% CI 0.49–0.58, $p < 0.001$) had significant difference with co-morbid condition. A total of 7240 (77.5%) patients were successfully treated. When TB-alone, TB-DM, TB-HIV/AIDS and TB-Hepatitis cases were assessed, a treatment success rate of 80.3%, 71.7%, 71.4%, and 71.2% was noted respectively. Therefore, treatment failure was 1.5 times (95% CI 1.41–1.72, $p < 0.001$) high in patients having co-morbidities.

Conclusion: The treatment success rate was highest among TB patients without any co-morbidity. Therefore, threat of TB seems to have become increasingly ominous due to its lethal combination with other co-morbid conditions such as HIV/AIDS, DM and hepatitis, as well as drug resistance.

P-Q-046

GASTRECTOMY AND THE RISK OF TUBERCULOSIS

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Background: Patients who had undergone gastrectomy are considered to be high risk of developing tuberculosis. But there are insufficient data regarding gastrectomy and risk of tuberculosis in patients with gastric cancer. Our objective were to examine the incidence of TB in gastrectomy patients and to investigate risk factors leading to tuberculosis after gastrectomy.

Methods: A retrospective cohort study of gastrectomy patients with gastric cancer was performed at the university-affiliated hospital, Seoul, South Korea between January 2007 and December 2009. Standardized incidence ratios (SIRs) of TB were calculated to compare the incidence of TB in gastrectomy patients with that in the general Korean population and risk factors of TB after gastrectomy were analyzed.

Results: Among the 1776 gastrectomy patients, 0.9% (16/1097) developed post-gastrectomy TB, with an incidence of 223.7 cases per 100 000 patients per year. The overall incidence of TB in gastrectomy patients, adjusted by sex and age, was significantly higher than in the general population (SIR 2.00, 95% CI 1.14–3.25). Lower post BMI (per 1 kg/m²; OR 1.37, $P = 0.019$) and previously healed TB on CXR (OR 6.99, $P = 0.009$) were significant risk factors for TB after gastrectomy on multivariate analysis.

Conclusions: The incidence of TB in gastrectomy patients was higher than in the general population. Those with Low BMI or previously healed TB on CXR have a high risk of TB after gastrectomy.

P-Q-047

PREVALENCE AND MANAGEMENT OF ADVERSE DRUG REACTIONS AMONG MULTI DRUG RESISTANT-TUBERCULOSIS PATIENTS IN PAKISTAN

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Background: Multi drug-resistant tuberculosis (MDR-TB) requires prolonged and complicated treatment with second line anti-tubercle drugs that are associated with adverse drug reactions (ADRs).

Objective: The aim of the present study was to evaluate the prevalence and management ADRs among MDR-TB patients.

Methodology: A prospective observational study was conducted at Gulab Devi Chest Hospital from June 2013 till the end of treatment. All adults with confirmed MDR-TB cases were included. An informed consent form was filled by each patient and validated data collection form was used to collect patient's demographics and clinical data. Ethical approval was taken from the relevant authorities. All statistical analysis was carried out on SPSS version 20.0.

Results: Of the total 50 pulmonary MDR-TB patients, 39 (78%) were males and 11 (22%) were females. The mean age and weight of patients was about 35.94 ± 12.37 years and 46.10 ± 6.64 kg respectively. Most of the patients 43 (86%) were being treated with Am+Z+Eto+Cs+Lfx therapy. ADRs were reported in 26 (52%) patients. Male gender (OR = 3.11, 95% CI 0.71–13.51, $p = 0.13$), urban residents (OR = 1.88, 95% CI 0.60–5.88, $p = 0.27$), employers (OR = 1.20, 95% CI 0.39–3.67, $p = 0.75$), unmarried individuals (OR = 2.0, 95% CI 0.58–6.84, $p = 0.27$) and smokers (OR = 1.15, 95% CI 0.37–3.52, $p = 0.80$) had no significant difference when compared to ADRs. The total mean of ADRs was 1.38 ± 1.51 . The common observed ADRs includes nausea/vomiting ($n = 19$), arthralgia ($n = 11$), gastritis ($n = 13$), abdominal pain ($n = 8$), anorexia and anxiety ($n = 6$). Ototoxicity and diarrhea were also observed ($n = 3$). All ADRs were managed by administering curative or symptomatic therapy while discontinuation of causative agent was seen in 3 cases only.

Conclusion: The prevalence of ADRs among MDR-TB patients was quite high and seems to be a contributing factor towards poor outcomes. Therefore, proper management of ADRs can improve the treatment outcome and patient compliance.

P-Q-045

SEVERE ADVERSE DRUG REACTION TO FIRST-LINE ANTITUBERCULOSE IN SINGLE CENTRE

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Introduction: Tuberculosis is one of the major diseases that reflects the health and social status of a country. Treating tuberculosis is a challenge in tuberculosis management, as anti-tuberculosis medication may produce side effects varying from unimportant to life-threatening condition.

Objectives: To assess the rate of Adverse Drug Reactions (ADRs) induced by Anti-TB drugs in Institut Perubatan Respiratori (IPR) for a period of one year and to determine factors associated with anti-tuberculosis adverse drug reactions.

Methodology: Retrospective observational study of patients in Institut Perubatan Respiratori who were diagnosed with pulmonary tuberculosis from 1 Jan 2012 to 31 Dec 2012. Patients were identified from pharmacist records of adverse drug reaction for the year 2012 and data collections were done based on individual patients medical record.

Results: During the study period, 1520 patients received Anti-TB drugs; of them 21 developed at least one ADR (71.5%). Majority of them is Malaysian (95.2%) and newly diagnosed with tuberculosis (81%). ADR more commonly develop in males (71.4%). The most common side effect was rash (71.4%) followed by haematology abnormality (19%), hepatitis (14%), and acute kidney injury (9%). In most of the cases, we manage to rechallenge with anti TB, with the exception of one death due to septicemia.

Conclusions: Anti-TB drugs may cause significant adverse effects both in quantity and severity. These reactions may lead to hospitalization, prolonged hospital stay and even death.

P-Q-048

P-Q-049

EVALUATION OF ISONIAZID PREVENTIVE THERAPY 300 MG PER DAY FOR 6 MONTHS AFTER ONE YEAR MONITORING IN HIV-INFECTED PATIENTS IN PERSAHABATAN HOSPITAL JAKARTA, INDONESIA

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Background: Human Immunodeficiency Virus (HIV) infection has been known to be one of the cause of mortality in the world. Tuberculosis (TB) is a common opportunistic infection and leading cause of morbidity and mortality in HIV infection. The development of the HIV epidemic in Indonesia is one of the fastest in Asia, incidens rates of TB in Indonesia still in the fifth largest TB problem in the world. As a result of HIV, incidence rates of TB is increasing > 15 per cent per year. HIV infection increases the risk of subsequent episodes of TB 30–50% compared to in HIV-negative adult patients. The World Health Organization (WHO) recommended in 1998 that isoniazid preventive therapy (IPT) be offered to HIV-infected patients. Preventive therapy for tuberculosis with isoniazid in HIV-infected patients has been known to lowers incidence by 70–90%, but is not widely used in Indonesia.

Objective: To know the effectiveness of isoniazid prophylaxis in tuberculosis and patient compliance with the treatment in HIV-infected patients in Persahabatan Hospital Jakarta, Indonesia.

Method: Longitudinal-study from December 2012-June 2014. HIV-infected patients screened for TB based on symptoms, physical examination, chest radiograph, sputum microscopy and sputum GeneXpert. Given isoniazid 300 mg daily for 6 moths and monitored for 1 year.

Results: Of 32 individulas were male (59,4%) with median aged 29 years (min 22,max 46 years),among patients have highest education from high school (75,8%) and unemployed (31,3%). Mean CD4 among patients 286,06 ± 155,01 cell/mm³, mean time of ART(antiretroviral therapy) consumption 4 years (min 1,max 12 years). Among patients are smoker (56,3%) and has history of previous TB treatment (71,9%). Incidens TB after 1 year monitoring 2 patients (6,25%), died because of TB 1 patient (3,1%). Complianc of IPT among patients with complete treatment 68,8%. Relations of incidence TB between age ($p = 0,145$), sex ($p = 0,502$), education ($p = 1,00$), income ($p = 1,00$), CD4 ($p = 0,819$), time of ART consumption ($p = 0,734$), smoking habit ($p = 1,00$), previous TB treatment ($p = 0,49$) and complianc IPT ($p = 0,534$).

Conclusion: After 1 year monitoring there are 2 patients out of 32 patients(6,25%) gain TB. There are no significance relations between age, sex, education, income, CD4, time of ART consumption, smoking, previous TB treatment and complianc of IPT with incidence of TB.

HAEMATOLOGY PROFILE OF NEW PULMONARY TUBERCULOSIS PATIENTS WITH POSITIVE AFB BEFORE AND AFTER ANTITUBERCULOSIS DRUGS DURING INTENSIVE PHASE

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Background and Aim of the Study: Tuberculosis (TB) remains a major global health problems. Study in Indonesia, England, India and Japan showed that nutritional status of patients with pulmonary Tb was significantly lower than healthy. Tuberculosis also produced abnormalities in peripheral blood and several studies showed that Tb was associated with haematology and protein disorders. Our objective to evaluate haematology profile (haemoglobine, leucocyte, differentiation count, erythrocyte sediment rate/ESR) and nutritional status (albumin and body mass index/BMI) in new pulmonary TB cases with positive AFB before and after anti-TB drugs during intensive phase related with sputum conversion.

Methods: We performed pre-eliminatory, pre-post study among 75 patients with new pulmonary TB who came to outpatient lung clinic, Persahabatan Hospital. New TB cases with smear positive were treated with standard regimen. During intensive phase of treatment, we assessed 1) haematology profile by measured haemoglobin (HB), leucocyte (L), erythrocyte sediment rate (ESR) and 2) nutritional status by measured albumine and body mass index (BMI), before and after intensive phase.

Results: Seventy five of new cases TB with smear positive were participated this study from Januari to June 2014. Fifty males (66.67%) and 25 females (33.33%) with average 37,83 years old (range 16–71) participated. We determined nutritional status during intensive phase with increased albumin level from 3,56 g/dL (SD 0.49) to 4.11 g/dL (SD 0.42) ($p < 0.05$) and BMI increased from 19.13 kg/m² (SD 3.19) to 20.19 kg/m² (SD 3.10) ($p < 0.05$). After perfoming intensive phase treatment, sputum conversion was 67 part of 75 (10.66%). Haematology profile of 67 patients that found some changes in several haematology parameters during intensive phase, for example Hb increased from 12.21 g/dL (SD 1.65) to 12.90 g/dL (SD1.55), L decreased from 11.383/mm³ (SD 3695) to 9.747/ mm³ (SD 3384), lymphocyte from 16.97% to 21.73%, monocyte from 8.04% to 7.39%, neutrophile from 73.10% to 66.08%, basophile from 0.67% to 1.29%, eosinophile from 1.82% to 3.04%, and ESR decreased from 91.22 mm/hrs (SD 27.49) to 63.39 mm/hrs (SD 34.91) ($p < 0.05$).

Conclusions: The resolution of abnormalities laboratory caused by infection TB, such as increased Hb, decreased ESR, increased albumin level and BMI, were prognostic factors of treatment success from the various studies. Our data showed that patients with sputum conversion during intensive phase have already established significant changes in haematological variables and nutritional status.

P-Q-050

LUNG RESECTIONS IN CHILDHOOD PULMONARY TUBERCULOSIS; REPORT OF TWO CASES

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Introduction: The facts of childhood Tuberculosis (TB) are that half of million children become ill with TB each year, and 70–80% of them had the disease in the lung (pulmonary TB). Childhood pulmonary TB sometimes poses clinical manifestations that mandate surgical treatment despite the adequate anti-tuberculosis drugs. It can be found in severe forms such as complex empyema with persistent bronchopleural fistula or destroyed lung with marked signs of infections. In this report the considerations and the result of the lung resections in destroyed lobe or lung due to childhood pulmonary TB will be presented.

Methods: We collect childhood pulmonary TB that underwent lung resections between the year 2011–2013. The first case was a 6 years old boy, with destroyed left lung and empyema with bronchopleural fistula. A left pneumonectomy was carried out. The second case was a 5 years old boy with prolonged high fever and destroyed middle and lower lobe. The anti-tuberculosis drugs and appropriate antibiotics were given but the 2 months prolonged high fever mandates surgical treatment. He underwent middle lobectomy.

Results: The postoperative course of the 6 years old boy was uneventful. He continued the anti-tuberculosis drugs. Six months after surgery, he returned with empyema and fistula of the bronchial stump. A re-do thoracotomy was performed, and the result was good afterwards. The 5 years old boy only had middle lobectomy, as it was impossible to do lower lobectomy due to very dense adhesions. His fever is gone after the surgery, and the overall performance status is excellent. On the follow up, he got a small wound dehiscence and air leak through it. We are now still planning to do a bronchoscopic evaluation to differ that the air leak is due to bronchial stump fistula, or from the surface of the lower lobe. Next, we will do a re-do thoracotomy to manage the airleak and repair the wound.

Conclusions: Integrated multidisciplinary approach is very important in managing the childhood pulmonary TB to reach the goal of zero death among children with TB. The surgical treatment should be performed when necessary with careful considerations of the indications, timing of surgery, surgical techniques, and complications management.

P-Q-051

COMPARISON ACID FAST BACILLI SMEAR MICROSCOPY EXAMINATION AND XPERT MTB/RIF IN DIABETES MELLITUS PATIENTS WHO SUSPECTED PULMONARY TUBERCULOSIS

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Background: The relationship between tuberculosis (TB) and Diabetes Mellitus (DM) has long been known. People with DM have 2–3 times the risk of developing TB. The prevalence of TB-DM based from cross sectional study by Wijayanto in Endocrine clinic in Persahabatan Hospital in DM type 2 patients in 2013 was 28.2%. Pablos-Mendez et al. found that only DM poorly controlled or uncontrolled associated with an increased risk of TB.

Objectives: The main objective of this study was to determine the sensitivity and specificity of Acid Fast Bacilli (AFB) smear and Xpert MTB/RIF for diagnosis of TB in DM.

Methods: This study was a cross-sectional descriptive analytic study in patients with DM group were still underwent treatment at Persahabatan Hospital from May 2014. The study was conducted in Pulmonary clinic and Internal Medicine clinic. Patients with DM who have TB complaints that have not been taken either TB drug or with a history of treatment and supported from chest X-ray shows the suspicion of TB will require the microbiological diagnosis of AFB smear and Xpert MTB/RIF.

Result: Samples were collected in 57 patients with 2 samples excluded due to proven AFB smear (+)ve and not checked Xpert MTB/RIF. Among 55 samples, there were 32 males (58.2%) and 23 females (41.8). Age between 25–72 years old. There were less weight 11(20%), normal weight 31 (56.4%) and over weight 13 (23.6%). The blood sugar between 110–481 g/dl with a SD of 244.8 ± 98.5 g/dl. The length of time DM <5 years were 40 (72.7%), 5–10 years were 7 (12.7%), 10–15 years were 6 (10.9%) and >15 years were 2 (3.6%). HbA1c values between 5.3–17.7 with a mean of 9.83 ± 3.00. The controlled HbA1c 11 (20%) and uncontrolled 44 (80%). By history TB has never suffered 41 (74.5%), treatment cured 9 (16.4%) and failure or withdrawal 5 (9.1%). Controlled HbA1c levels obtained 2 (3.6%) are not TB, clinical pulmonary TB 3 (5.5%) and pulmonary TB with AFB smear/Xpert (+)ve 6 (10.9%). Uncontrolled HbA1c levels obtained 13 (23.6%) instead of TB, clinical pulmonary TB 2 (3.6%) and pulmonary TB with AFB smear/Xpert (+)ve 29 (52.7%). Samples with AFB smear (+)ve and Xpert (+)ve 28 (50.9%), AFB smear (+)ve and Xpert (-)ve 1 (1.6%), AFB smear (-)ve with Xpert (+)ve 8 (14.4%) and AFB smear (-)ve with Xpert (-)ve 18 (32.7%). Sensitivity and specificity by using both were 96.5% and 69.3%.

Conclusion: There is no difference in the sensitivity and specificity of AFB smear and Xpert MTB/RIF for TB diagnosis in patients with DM.

P-Q-052

POLYMORPHISM OF INTERLEUKIN-4 AND INTERLEUKIN-10 GENES AS UNDERLYING FACTOR IN THE PRODUCTION OF CYTOKINES AND RATE OF PULMONARY TUBERCULOSIS

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Background and Objective: To study the polymorphism of interleukin (IL)-4 and IL-10 genes in relation to serum levels of cytokines and prevalence of pulmonary tuberculosis (PTB).

Methods: The study comprised 80 individuals in Kharkiv region of Ukraine including 59 patients PTB (group 1) and 21 healthy donors (group 2). Serum levels of cytokines IL-4 and IL-10 were evaluated by ELISA. Investigations of gene polymorphisms of these cytokines were performed using restriction analysis of the amplification products of specific regions of the genome. Two polymorphic variants were examined: C-589T region of IL-4 gene and promoter region G-1082A of IL-10. Statistical evaluation: the obtained data were evaluated by standard Student t-test and probability relative frequency deviation from a constant probability of independent trials. The difference was considered to be significant at $p < 0.05$.

Results: In the 1st group the levels of IL-4 and IL-10 were 9.55 ± 0.24 pg/L and 40.04 ± 0.74 pg/L, while in 2nd group these values were 29.99 ± 1.27 pg/L and 50.25 ± 1.26 pg/L respectively ($p < 0.05$). Among patients with PTB the heterozygous genotype was most prevalent; 67.79 % (N = 40) for IL-10 and 59.32 % 35 (N = 35) for IL-4. The homozygous genotype was accordingly less common: 32.21 % (N = 19) and 40.68% (N = 24), of which 11.86 % (N = 7) and 15.25 % (N = 9) of patients had mutation and remaining had normal homozygote genotype, i.e., 20.35 % (N = 12) and 25.43 % (N = 15) for IL-10 and IL-4 respectively. In contrast, most of healthy donors had normal homozygous genotype with 61.9 % (N = 13) and 71.43 % (N = 15) with low frequency of mutations; 14.30 % (N = 3) and 9.53 % (N = 2) and heterozygous genotype 23.8 % (N = 5) and 19.04 % (N = 4) for IL-10 and IL-4 genes respectively.

Conclusion: Compared to healthy controls patients with PTB had significantly lower levels of serum IL-4 and IL-10. This coincided with greater frequency of heterozygous polymorphism C-589T and G-1082A genes of IL-4 and IL-10. Further studies are warranted whether higher rate of pulmonary TB has a causal immunogenetic relationship to polymorphism of genes encoding for IL-10 and IL-4.

P-Q-053

DIAGNOSTIC VALUE OF SAME DAY TWO SPUTUM SMEARS IN DIAGNOSING PULMONARY TUBERCULOSIS (PTB) INSTEAD OF THREE STANDARD SAMPLES

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Background: Sri Lanka is a country with intermediate burden of tuberculosis with an incidence of 66/100,000 in 2010. Examining three direct sputum smears for acid fast bacilli is the standard method for diagnosis of PTB. The estimated economic burden in Sri Lanka for each slide examined is \$6. The estimated financial loss for a patient to attend a microscopic centre to submit sputum on two days is \$16.

Objective: The aim was to evaluate the diagnostic value of two same day sputum smears in diagnosis of PTB instead of three standard samples.

Method: The study sample included all consecutive tuberculosis suspects admitted to respiratory unit 2, Teaching Hospital Kandy from October to December 2013. Two early morning sputum samples were examined using Ziehl-Neelsen method by a trained microscopist on Day 1 and one early morning sample each on day 2 and 3 in all patients. Sputum collection was performed with the standard technique. Smear positive pulmonary tuberculosis was diagnosed with 2 positive smears. The two methods were compared statistically.

Results: Out of the sample of 147, 12 patients were diagnosed as smear positive. Day1 Sample1 was positive in 10 patients and negative in 2, Day1 Sample2 positive in 11 patients and negative in 1, Day2 positive in 10 patients and negative in 2 and Day3 positive in 11 and negative in 1. Collectively, same day two sputum samples picked up 11 patients out of the smear positive 12. Only one patient was missed by Day1 sputum examination. Sensitivity of the new method was 91.6% and specificity 100%. Positive predictive value of 100% and a negative predictive value 99.2% were obtained. The economic burden reduction per patient using the new method will be \$6 to the government and \$8 for each patient.

Conclusion: The new method revealed good sensitivity and specificity for diagnosis. When the sputum examination is reduced from three to two there will be significant saving on material, manpower and expenses and is valuable in a resource poor setting such as ours. Treatment can be commenced earlier and may aid in control as well. Following analysis of a larger sample we may propose same Day 2 sputum sample examination to be accepted as standard.

P-Q-054

FIRST LINE ANTI-TUBERCULOSIS DRUG RESISTANCE PATTERN IN MYCOBACTERIUM TUBERCULOSIS ISOLATES AT THE UNIVERSITY OF SANTO TOMAS HOSPITAL, MANILA, PHILIPPINES FROM 2003–2013: A TEN YEAR EXPERIENCE

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Background: Development of drug resistance is one of the most important barriers in achieving global control of tuberculosis. Continuous surveillance, such as observation of susceptibility and resistance patterns to anti-TB drugs, together with nationwide programs aimed at TB case identification, treatment and control, physician and patient education, is a valuable tool in the goal towards reducing TB prevalence and mortality.

Objective: It is the aim of this study to determine the prevalence rate and resistance pattern of first line anti-tuberculosis drugs in a tertiary hospital in Manila, Philippines.

Methodology: Records of specimens submitted for TB culture and sensitivity, using BACTEC MGIT 960 SIRE Kit and PZA Kit, at the Section of Clinical Pathology, University of Santo Tomas Hospital, were reviewed. Isolates cultured for Mycobacterium tuberculosis were subjected to sensitivity studies to Rifampicin (R), Isoniazid (I), Ethambutol (E), Pyrazinamide (P) and Streptomycin (S).

Results: A total of 546 specimens were cultured for Mycobacterium tuberculosis and sent for sensitivity studies. Majority of the specimens were from pulmonary sources (77%). Overall resistance rate was 52.38% (n = 286). One-drug resistance was 23.26% (n = 127; highest with R followed by I); two-drug resistance was 15.38% (n = 84; highest with H-R); three-drug resistance was 8.61% (n = 47; highest with H-R-E and H-R-S); four-drug resistance was 4.58% (n = 25; highest with H-R-E-S) and five-drug resistance (HRES) rate was 0.55% (n = 3).

Conclusion: The University of Santo Tomas Hospital as a referral facility, is encountering an increasing number of drug-resistant tuberculosis from 2003 to 2013.

P-Q-055

THE ASSOCIATION BETWEEN CD4 CELL COUNTS IN HIV/AIDS PATIENTS WITH PULMONARY TUBERCULOSIS

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Background: Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) infection lead to decreased immune system, especially cellulare immunity, cause oportunistic infection, eg. pulmonary tuberculosis (TB). Tuberculosis is an infectious diseases, caused by Mycobacterium tuberculosis (Mtb). HIV infection required specific receptor in host cell, call as clustering differentiation-4 (CD4) molecule. CD4 cells may also likely to be important in the protective response against Mtb.

Objectives: To evaluated the association between CD4 cell counts in HIV/AIDS patients with pulmonary tuberculosis.

Methods: This is an observational study with cross-sectional approach, conducted on HIV/AIDS patients aged 15 to 50 tahun years old in teaching hospital Makassar on April 2010 to December 2010. All patients examined to CD4 cell counts, sputum smears for acid-fast bacilli (AFB) and culture for AFB. Pulmonary TB was defined by positive sputum smears for AFB and positive culture for AFB.

Results: Fifty one subjects were included and we founds that average CD4 cell counts in HIV/AIDS patients with positive sputum smears for AFB was 21,8 cell/mm3 and negative sputum smears for AFB was 41,8 cell/mm3. The average CD4 cell counts in HIV/AIDS patients with positive culture for AFB was 19,0 cell/mm3 and negative culture for AFB was 48,4 cell/mm3.

Conclusions: There is an association between CD4 cell counts in HIV/AIDS patients with pulmonary tuberculosis based on sputum smears for AFB and culture for AFB.

P-Q-056

ASSOCIATION BETWEEN THE INTERLEUKIN-27 POLYMORPHISMS AND PULMONARY TUBERCULOSIS IN A KOREAN POPULATION

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Background: Recently, genetic polymorphisms of interleukin (IL)-27 have been shown to play a role in inflammatory airway diseases. The purpose of this study was to examine the correlation between IL-27 polymorphisms in the promoter region of -964A/G and the exon region of 2095T/G, 4603G/A, and 4730T/C and the development of pulmonary TB according to radiographic characteristics.

Methods: Differences in the allele and genotype distributions of the -964A/G, 2095T/G, 4603G/A, and 4730T/C polymorphisms were analysed between 224 pulmonary TB patients and 233 healthy controls. Subgroup analysis was done between patients with single- and multi-lobar involvement, and between patients with and without cavitation. Serum IL-27 concentration was measured using an enzyme-linked immunosorbent assay.

Results: There were no significant differences in the allele or genotype distributions between patients with pulmonary TB and healthy controls. However, in patients with single-lobar involvement, the -964A/A genotype was more prevalent than the -964 A/G or -964 G/G genotype in patients with multi-lobar involvement (50.0% vs. 31.3%, P = 0.01, OR 2.19, 95% CI 1.17–4.12). There was no difference between patients with and without cavitation (P > 0.05). Serum median IL-27 concentration was significantly higher in patients with single-lobar involvement than those with multi-lobar involvement (P = 0.03) and with -964A/A genotypes than -964A/G or -964G/G genotypes (P = 0.02).

Conclusions: The genetic polymorphisms of IL-27 are not associated with the development of TB. However, the -964A/G genetic polymorphism of IL-27 and serum IL-27 concentrations are associated with the severity of pulmonary TB by radiographic characteristics.

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